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Welcome

On behalf of the Organizing Committee I am very pleased to welcome you to the second edition of the International Symposium on Synthesis and Catalysis (ISySyCat2017) at the historic University of Évora. The inaugural edition of this conference that took place in September 2015 (ISySyCat2015) was an enormous success and we wish to build on this success, and make this a regular biannual event, which we can be proud of.

The conference focuses on various aspects of organic, organometallic and inorganic synthesis, as well as all areas of catalysis, including metal based catalysis, organocatalysis and biocatalysis. Issues of current major interest will be discussed, which include the sustainable production of important bulk, high-added value and biologically active compounds, from both academic and industrial perspectives.

We are proud to have a delightful mixture of both academic and industrial chemists from all corners of the globe, making this yet again a very international event. This is also reflected in the fine line-up of speakers, which includes well-known chemists and up and coming “rising” stars. There is also a very nice line-up of short “flash” talk speakers, who in the main are junior researchers with some very exciting research to discuss. Besides, there will be a smorgasbord of poster presentations, covering all aspects of these pivotal areas. Prizes will be awarded (to be announced before the closing ceremony) for the best “flash” talks and poster presentations.

This conference should be the ideal venue to be updated on current developments and advances in these areas, for net-working, making new acquaintances, and at the same time allowing one to relax, soak up and enjoy the special surroundings, along with the unique food, drink and hospitality provided by this special region.

We are very grateful to the Portuguese Chemical Society (Sociedade Portuguesa de Química), the University of Évora, and all our generous sponsors and supporters, without their valuable support this special event would not be possible.

Last, but not least, we would like to thank all the participants at ISySyCat2017 for coming!

We hope that your participation will be rewarding, fulfilling and of course very enjoyable.

So, make the most of it and enjoy!

Anthony J. Burke

(Conference Chair)

Organization

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Artur Silva, University of Aveiro, Portugal

Lurdes Cristiano, University of the Algarve, Portugal

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Anthony J. Burke

Acknowledgments and Sponsors

The Organizing Committee is very grateful to the following companies and organizations for their kind sponsorship and support of ISySyCat 2017.

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Media Partner

molecules
an open access journal by MDPI

Molecules has kindly offered to sponsor a feature paper slot to publish free of charge for the best flash presentation.

Catalysts has kindly offered a prize of 500 CHF for the best poster presentation in the area of catalysis.

catalysts
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HETEROGENEOUS & HOMOGENEOUS & BIO-
CHEMCATCHEM
CATALYSIS

ChemCatChem will publish a special edition in 2018 that will cover both ISySyCat2015 and ISySyCat2017 and the work of various Portuguese groups active in the area of catalysis.

Thieme

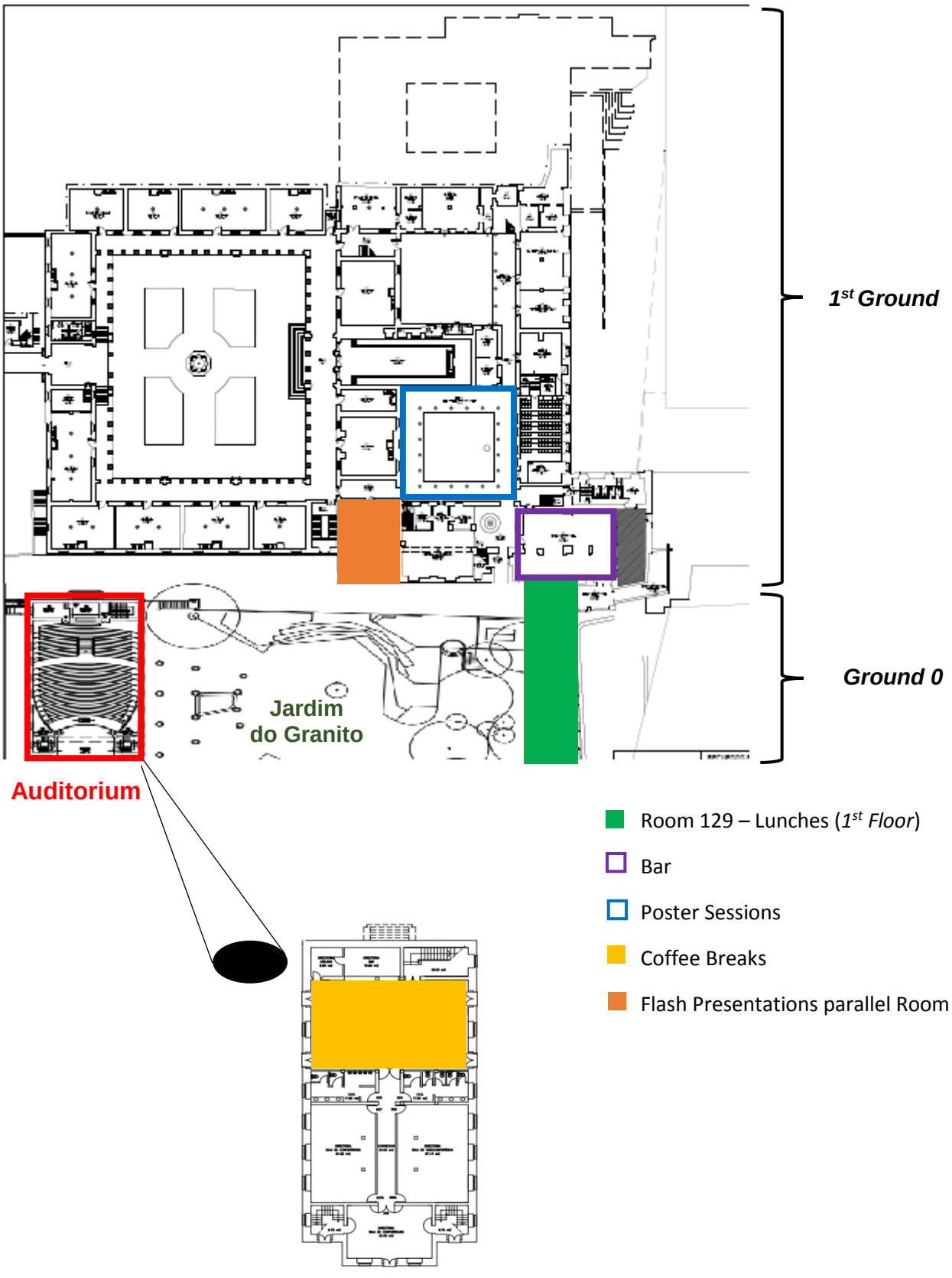
chimica oggi
CHEMISTRY TODAY

General Information

Meeting Venue

The meeting will take place at the auditory of Colégio Espírito Santo (CES) located in University of Évora, Largo dos Colegiais, number 2, 7004-516 Évora, Portugal.

Inside the CES building, the main conference room (the Auditorium), the speaker's preview room, poster session venue, exhibition and coffee break areas will be appropriately signposted, as illustrated in the map below.



Lunches

Lunches on Tuesday 5, Wednesday 6 and Thursday 7 of September will be served at the room 129 of CES, and are included in the registration fee. We kindly ask all the participants to present their lunch tickets to the staff.

Internet Access

A temporary login for the wireless Academic Network (eduroam) for the University of Évora has been created (valid from 3 to 10 of September). Please use the following credentials:

Guest User Name: ISySyCat2017

Password: ISySyCat2017

Scientific Information

Presentation Preview Room

Speakers are kindly asked to contact the organizing committee at the preview room 24 h before their presentation. Those speakers scheduled to speak in the morning of the 5th of September are kindly asked to provide the organizers with a copy of their talk during the registration in order to make sure that there are no problems with the presentation of their material. This is especially advised for those who have prepared their talk on an Apple® Macintosh computer.

Flash Sessions

On the 5th, 6th and 7th of September three parallel Flash session presentations will take place in the main Auditorium and in Room 124. The talks will have a maximum time of 8 minutes each.

Posters Sessions

Posters will be displayed in the selected halls of CES. Authors are requested to display their posters on the post panels during the first coffee break on 5th of September. Material to attach posters will be made available by the organizing committee at the front desks. Posters should be on display from Tuesday morning and left for the entire duration of the Conference. Authors are requested to stay near their posters during both sessions so they will be available to answer any questions from the participants and by the evaluation panel, who will select the posters for the Poster Prize awards.

Awards and Prizes

In ISySyCat 2017, a number of exciting Awards will be given, for both the best Poster presentations and the best Flash presentations.

Both Wiley-VCH Verlag GmbH & Co. KGaA – A company of John Wiley & Sons, Inc. and Molecules have very kindly agreed to award a textbook (Catalytic Asymmetric Methods: From the Academic Lab to Industrial Processes, Burke and Marques) and a feature paper slot as the prizes for the best flash presentations.

Catalysts will provide a prize of 500 CHF for the best poster presentation in the catalysis category.

Thieme (SynFacts) which is also sponsoring the plenary lecture of Professor Kilian Muñiz as the 2016 winner of the SYNTHESIS Best Paper Award, will provide a one-year personal subscription to SYNFACTS for the best poster in the category, Synthetic Methodology.

Organic & Biomolecular Chemistry (OBC) of the Royal Society of Chemistry, will kindly provide a one-year free e-subscription to the journal for the winner and runner-up for the best posters in the category: Total/Target based synthesis. They will also provide a one-year free e-subscription to the journal for the runner-up best poster in the Synthetic Methodology category.

Language

English is the official language of ISySyCat 2017.

Useful information

Time Zone: The time zone in Portugal is GMT.

Water: Tap water in Portugal is drinking water.

Electricity: In Portugal, the line voltage is 220 V and the connection is made by a two-pin plug. Travelers from the USA will require a voltage converter. Travelers from the UK will require a plug adapter and this is best bought in the UK as they are hard to find in Lisbon (can try at the Lisbon airport).

Currency, Banks and Post Offices: The national currency in Portugal is Euro. Banks are open from Monday to Friday between 8.30 am and 3 pm. Post offices are usually open between 8.30 am and 6 pm. Exchange houses operate everyday between 9 am and 1 pm and from 2 pm to 7 pm.

Going out in Évora: With your conference material, you will find a city map and a brochure of Évora with lots of necessary information.

Climate: In early September, the temperature in Évora is on average 30ºC (the nights are hot). Rain is very unlikely.

Social Programme

Reception Party *(included in the registration fee):*

The reception party will be in the garden in front of the Cloisters of CES on Tuesday the 5th of September at 19:45h. It will include appetizers, drinks and a live DJ.

Banquet Dinner *(included in the registration fee):*

PALÁCIO CADAVAL
ÉVORA
SINCE1390

On Thursday the 7th of September at 20h, the conference banquet will take place in the spectacular location of the Cinco Quinas restaurant, within the confines of the historic Palácio Cadaval, dating back over 600 years. This space has been opened to the public for several functions/events and claims of an excellent cuisine, with a fine selection of local regional dishes and wines.

"With more than six centuries of history, a unique venue to celebrate life, an unmistakable destination in the Alentejo, an invitation to embark on a journey and to dream."
Diana, Duchess of Cadaval

Excursions on the 8th of September:

On the afternoon of the 8th of September, conference participants are invited to part-take in a delightful social program. One includes a coach trip to the famous Carmim Winery followed by a visit to the historic unique mediaeval village of Monsaraz overlooking the beautiful artificial lake known as Alqueva, and the other which is kindly provided by the Évora Town Council, will be a walking guided tour to the most exciting historic sites around the city of Évora. Full details will be given during the conference.

CARMIM
REGUENGOS

- Carmin Reguengos Winery (not included in the registration fee):

This well-known winery was founded in 1970 and is located in the historical town of Reguengos, which is close to the mediaeval village of Monsaraz (which will also be visited) and overlooks the spectacular artificial lake and tourist attraction, Alqueva (which you will also see). Carmim is the largest winery in the Alentejo region, which boasts of being one of the largest in the country and in terms of wine production and bottling, one of the most technologically advanced wineries in the whole Iberian Peninsula. It is a well-respected brand in Portugal.

After a delightful lunch at the renowned Carmim Reguengos winery restaurant (see below for further information), it will be given a ninety-minute tour of the whole winery and a unique view of the whole wine production process.
This will be the ideal time to visit the winery, as it overlaps with the heart of the harvest season, and you will see for yourself the whole process in action, from the delivery of the grapes to the factory, right to the bottling and storage of the wine.

This tour will end with a wine-tasting opportunity, of two classy wines - a red variety (*tinto*) and a white variety (*branco*) - chosen specifically for your palate by experts from the Carmim winery. This session will be accompanied by one of the experienced wine tasters from this winery, to give you an appreciation of the hidden secrets of these remarkable wines.

Lunch
After a welcome drink served with Espumante Monsaraz, lunch will be served and consist of the following tasty dishes:

Starters (Pâté, olives and a selection of ham and cheese from the region) accompanied by Monsaraz Rosé wine;
First dish (Baked Codfish in the oven) accompanied by exclusive Régia Colheita white wine;
Second dish (Baked Pork Cheeks) accompanied by Monsaraz Reserva Tinto red wine;
Desert, accompanied by Vinho Licoroso Carmim, liquor.

Important Note: Persons with dietary restrictions should indicate this on the registration form (preferentially) or in the registration desk during the conference so that an alternative can be arranged.

MONSARAZ

After the visit to the Carmim winery, you will be taken by coach to visit the historically unique medieval village of Monsaraz, which is one of the oldest villages in Portugal. This amazing place, with a very strong sense of medieval days gone by, dates back more than a thousand years. Some of the highlights to be visited, include the parish church which stands accompanied by an unusual 18th century pillory topped by a sphere of the universe, and a church interior containing gilded altars and painted pillars), as well as the granite castle with impressive battlements for eagle-eye views of the houses within the village walls and for the breath-taking landscape of the surrounding countryside. Within its confines, it houses an unusual bullfight arena that is the host to various bull-fight events several times a year. In fact, it is expected that your visit to Monsaraz will coincide with its yearly summer festival, which is expected to be in full swing (so you never know what to expect…). You will also encounter many other small treats along the way.

- Walking Guide tour to Évora (included in the registration fee):

The participants who are interested in this tour should contact the staff on the first day of the conference to book their place. It will be in the 8th of September at 14h. The meeting point will be in the Tourist Office in Geraldo's square and the participants should present the corresponding badge of the conference.

Scientific Programme

Conference Time Schedule:

Time	5th Sept	6th Sept	7th Sept	8th Sept	Time 8th Sept
9.00-9.45	Registration and Opening Ceremony	(PL 5) David Milstein	(PL 9) Masakatsu Shibasaki	(PL 13) Lutz Ackermann	
9.45-10.05		(OC 7) Luisa Maia	(OC 16) Moshe Portnoy	(OC 25) Mariette Pereira	
10:05-10:25	(PL 1) Scott Denmark	(OC 8) José Pérez Sestelo	(OC 17) Alessandra Lattanzi	(PL 14) Ian Baxendale	
10.25-10.50		(OC 9) Sérgio Rossi	(OC 18) Lawrence Wolf		
	Coffee Break				
11.20-12.05	(PL 2) Chris Senanayake	(PL 6) Polly Arnold	(PL 10) Carlos Mateos	(PL 15) Ana Cruz	11.20-12.15
12.05-12:25	(OC 1) Kengo Hyodo	(OC 10) Hans-Jürgen Federsel	(OC 19) Ivan Shuklov	Awards and Closing Ceremony	12:15-12.40
12:25-12:45	(OC 2) Adrian Tlaheuxt-Aca	(OC 11) Mário Simões	(OC 20) Isidro Pastor		
Lunch				Social Program	
14.05-14:50	(PL 3) Janine Cossy	(PL 7) Armando Pombeiro	(PL 11) Stefan Mix		
14:50-15:10	(OC 3) Carlos Palo-Nieto	(OC 12) Pavel Mykhailiuk	(OC 21) Beatriz Royo		
15:10-15:30	(OC 4) Konstantin Luzyanin	(OC 13) Talia Pettigrew	(OC 22) Alex Szpilman		
15:30-15:50	(OC 5) Hans Nedden	(OC 14) Shaoguang Zhang	(OC 23) David Jenkins		
Coffee Break					
16:30-17:15	(PL 4) Manfred Reetz	(PL 8) Thomas Schaub	(PL 12) Kilian Muniz		
17:15-17:35	(OC 6) Maria M. Marques	(OC 15) Arkaitz Correa	(OC 24) Fernando López-Ortiz		
17:35-18:45	Flash Talks (parallel)	Flash Talks (parallel)	CAS SciFinder Work-Shop		
18:45-19:40	Poster session	Poster session	Flash Talks (parallel)		
19:45-23:00	Reception Party		Banquet (20h-23:30h)		

Detailed Scientific Programme:

Tuesday, the 5th of September of 2017

9:00	**Registration**	
9:45	**Opening Ceremony,** which includes the Rector of the University of Évora, Professor Ana Costa Freitas (or representative), the director of the Institute for Research and Advanced Studies of the University of Évora, Professor Collares Pereira, the director of the School of Science and Technology of the University of Évora, Professor Mourad Bezzeghoud, the director of the Chemistry Center of the University of Évora, Professor Peter Carrott, the general secretary of the Portuguese Chemical Society (SPQ), Professor Adelino Galvão and the conference Chairman, Professor Anthony Burke.	
Chairman: Anthony Burke		
10:05	**PL 1**	**Transmetalation in the Suzuki-Miyaura Cross-Coupling Reaction: Mechanistic Insights and Preparative Implications** Scott E. Denmark
10:50	**Coffee Break**	
Chairman: Martin Ernst		
11:20	**PL 2**	**Important Asymmetric and Catalytic Transformations for Drug Development** Chris Senanayake
12:05	**OC 1**	**Brønsted Acid Catalyzed Nitrile Synthesis from Aldehydes via Transoximation under Mild Conditions** Kengo Hyodo
12:25	**OC 2**	**Alkyne and Alkene Functionalization by Visible-Light-Mediated Photoredox Catalysis** Adrian Tlahuext-Aca
12:45	**Lunch**	
Chairman: Adelino Galvão		
14:05	**PL 3**	**Transition Metal Catalysts - Construction and Functionalization of Heterocycles** Janine Cossy

14:50	**OC 3**	**Catalysed Stereoselective Synthesis of Deoxyglycosides** Carlos Palo-Nieto
15:10	**OC 4**	**Orthogonal Substrate-Selective C-H Functionalisation of Organosulphur Compounds Originating from Crude Oil** Konstantin V. Luzyanin
15:30	**OC 5**	**Catalytic Processes that are Suitable for the Large Scale Reduction of Aldehydes and Ketones** Hans Günter Nedden
15:50	**Coffee Break**	

Chairman: Isabella Rimoldi

16:30	**PL 4**	**Directed Evolution of Stereoselective Enzymes: A Prolific Source of Catalysts for Asymmetric Reactions** Manfred T. Reetz
17:15	**OC 6**	**A Metal-Catalyzed Journey to New Azaindole Synthesis** Maria Manuel B. Marques
17:35	**Flash Talks**	

	Catalysis *Main Auditorium* *Chairman: Maurizio Benaglia and Narciso Garrido*	*Synthetic Methodology* *Room 124* *Chairman: Anthony Burke and Martin Ernst*
17:35	**F 1** Caroline M. Zinser	**F 7** Zsófia E. Blastik
17:45	**F 2** Anastassia Matviitsuk	**F 8** Soyeong Kang
17:55	**F 3** Ana Cristina Fernandes	**F 9** Aleksandra J. Wierzba
18:05	**F 4** Tamal Roy	**F 10** Maria H. T. Kwan
18:15	**F 5** Selwyn F. Mapolie	**F 11** Michal Urban
18:25	**F 6** Marilé Landman	**F 12** Vasco F. Batista

18:45	**Poster Session**	
19:45	**Reception Party**	

Wednesday, the 6th of September of 2017

Chairman: David Diéz		
9:00	**PL 5**	**Design and Applications of Sustainable Metal-Catalyzed Reactions** David Milstein
9:45	**OC 7**	**Reduction of Carbon Dioxide by Formate Dehydrogenase: Aiming to Develop a Catalyst for Carbon Dioxide Utilization** Luisa Maia
10:05	**OC 8**	**Indium(III)-Catalyzed Intramolecular Cycloisomerization Reactions of Alkynes: Synthesis of 2*H*-Chromenes, Benzo[*b*]furans and Derivatives** José Pérez Sestelo
10:25	**OC 9**	**Continuous-flow Stereoselective Catalytic Synthesis of Active Pharmaceutical Ingredients in Micro- and (3D-printed) Meso-Reactors** Sergio Rossi
10:50	**Coffee Break**	
Chairman: Alex Szpilman		
11:20	**PL 6**	**F-Block Organometallics for the Activation and Transformation of the Carbon Oxygenates CO, CO_2, and Esters** Polly L. Arnold
12:05	**OC 10**	**Enzyme Immobilization as an Enabler for Biocatalysis in Flow** Hans-Jürgen Federsel
12:25	**OC 11**	**The Influence of the Porphyrins' Macrocycle and its Metal on the Type, Efficiency and Selectivity of Catalysis** Mário M. Q. Simões
12:45	**Lunch**	
Chairman: Mariette Pereira		
14:05	**PL 7**	**Functionalization of Alkanes: a Challenge in Catalysis towards Organic Synthesis** Armando J. L. Pombeiro

14:50	**OC 12**	**Rapid Access to Novel Multifunctional Spirocyclic Cores for Drug Discovery** Pavel K. Mykhailiuk
15:10	**OC 13**	**Designed Aplyronine Warheads for Next-Generation Antibody-Drug Conjugates** Talia Pettigrew
15:30	**OC 14**	**Synthesis and Structures of Bimetallic Complexes Supported by Flexible Di(imino)pyridine-based Macrocycles** Shaoguang Zhang
15:50	**Coffee Break**	

Chairman: Sabine Fenner

16:30	**PL 8**	**CaRLa – Basic Research for Industrial Applications** Thomas Schaub
17:15	**OC 15**	**Pd-Catalyzed C-H Functionalization Events Directed by 1,2,3-Triazoles** Arkaitz Correa
17:35	**Flash Talks**	

	Catalysis *Main Auditorium* *Chairman: Maurizio Benaglia and Narciso Garrido*	*Synthetic Methodology* *Room 124* *Chairman: Anthony Burke and Martin Ernst*
17:35	**F 13** Dmytro S. Nesterov	**F 19** Alejandro Manchado
17:45	**F 14** Silvia Cabrera	**F 20** Bohdan Biletskyl
17:55	**F 15** Cynthia Cuevas-Chávez	**F 21** Andrea Guerrero
18:05	**F 16** Sándor Nagy	**F 22** James N. Sanderson
18:15	**F 17** Mohamad R. Khodadadi	**F 23** Bedřich Formánek
18:25	**F 18** Sara Realista	**F 24** Santiago Cañellas

18:45 **Poster Session**

Thursday, the 7th of September of 2017

Chairman: Maurizio Benaglia		
9:00	**PL 9**	**Recent Progress in Cooperative Asymmetric Catalysis** Masakatsu Shibasaki
9:45	**OC 16**	**Used of Branched and Dendritic Scaffolds for Controlling Selectivity in Organocatalysis** Moshe Portnoy
10:05	**OC 17**	**Organocatalysed Asymmetric Synthesis of Sulfur-Containing Heterocycles: from Tetrahydrothiophenes to 1,5-Benzothiazepines** Alessandra Lattanzi
10:25	**OC 18**	**Origin of Lewis Acid Induced *endolexo* Selectivity *Enhancement* in the Diels-Alder Reaction: Reduced Steric Penalty for *endo*** Lawrence M. Wolf
10:50	**Coffee Break**	
Chairman: Petrus van Rooyen		
11:20	**PL 10**	**Continuous Flow Chemistry: A Powerful Tool to Enable Chemistries and Scale-up Processes** Carlos Mateos
12:05	**OC 19**	**Bio- and Chemo-Catalysis in the Chemistry of Lactic Acid and PLLA** Ivan A. Shuklov
12:25	**OC 20**	**Sustainable Catalytic Systems based on Acyl-Functionalized Imidazoles** Isidro M. Pastor
12:45	**Lunch**	
Chairman: Silvia Cabrera		
14:05	**PL 11**	**Shortening the Path – Biocatalysis Applications in the Pharmaceutical Industry** Stefan Mix
14:50	**OC 21**	**Catalytic Reductions with Manganese N-Heterocyclic Carbenes** Beatriz Royo

15:10	**OC 22**	**Powerful New Umpolung C-C and C-N Bond Forming Reactions via Enolonium Species** Alex M. Szpilman
15:30	**OC 23**	**Synthesis of Next Generation Catalysts for C_2 + N_1 Aziridinations from Organic Azides and Alkenes** David M. Jenkins
15:50	**Coffee Break**	

Chairman: Ana Maria Philips

16:30	**PL 12**	**C-H Amination within the Halide Redox Manifold** Kilian Muñiz
17:15	**OC 24**	***In situ* Generation of Gold(I) Nanoparticles as Catalyst of Solventless A^3 Coupling Synthesis of Propargylamines** Fernando López-Ortiz
17:35	**CAS SciFinder Work-Shop**	
17:55	**Flash Talks**	

	Main Auditorium *Chairman: Maurizio Benaglia and Narciso Garrido*	*Room 124* *Chairman: Anthony Burke and Martin Ernst*
17:55	**F 25** Louis Monsigny	**F 34** Vasco Corti
18:05	**F 26** Rui M. B. Carrilho	**F 35** Eva Bednářová
18:15	**F 27** Indrek Kalvet	**F 36** Jan Lorkowski
18:25	**F 28** Sébastien Coufourier	**F 37** Yulia Dudkina
18:35	**F 29** Bruno G. M. Rocha	**F 38** Stefano Gazzotti
18:45	**F 30** Kashif Tanveer	**F 39** Romain Membrat
18:55	**F 31** André D. S. Barbosa	**F 40** Jamie H. Docherty
19:05	**F 32** Elif Okutan	**F 41** Alexis Lator
19:15	**F 33** Sofia Strekalova	**F 42** Imane Idris
19:25		**F 43** Pawel Wityk

20:00	**Banquet Dinner**	

Friday, the 8th of September of 2017

Chairman: Narcisso Garrido		
9:00	**PL 13**	**Selectivity Control in C-H Activation** Lutz Ackermann
9:45	**OC 25**	**Bio-inspired Catalysts for Activation of Small Molecules** Mariette M. Pereira
10:05	**PL 14**	**Flow Processes for the Synthesis of 'Challenging' Molecules** Ian R. Baxendale
10:50	**Coffee Break**	
Chairman: Anthony Burke		
11:20	**PL 15**	**Palladium Coupling Reactions Optimization as Part of the Development of an API Synthesis** Ana Cruz
12:15	**Awards** **Closing Ceremony**, which includes the representative from the Rectory of the University of Évora and the Conference Chairman, Professor Anthony Burke. **Social Program**	

Plenary Lectures

PL 1 **Transmetalation in the Suzuki-Miyaura Cross-Coupling Reaction: Mechanistic Insights and Preparative Implications**
Scott E. Denmark

PL 2 **Important Asymmetric and Catalytic Transformations for Drug Development**
Chris Senanayake

PL 3 **Transition Metal Catalysts - Construction and Functionalization of Heterocycles**
Janine Cossy

PL 4 **Directed Evolution of Stereoselective Enzymes: A Prolific Source of Catalysts for Asymmetric Reactions**
Manfred T. Reetz

PL 5 **Design and Applications of Sustainable Metal-Catalyzed Reactions**
David Milstein

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PL 9 **Recent Progress in Cooperative Asymmetric Catalysis**
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Ana Cruz

Oral Communications

OC 1 **Brønsted Acid Catalyzed Nitrile Synthesis from Aldehydes via Transoximation under Mild Conditions**
Kengo Hyodo

OC 2 **Alkyne and Alkene Functionalization by Visible-Light-Mediated Photoredox Catalysis**
Adrian Tlahuext-Aca

OC 3 **Catalysed Stereoselective Synthesis of Deoxyglycosides**
Carlos Palo-Nieto

OC 4 **Orthogonal Substrate-Selective C-H Functionalisation of Organosulphur Compounds Originating from Crude Oil**
Konstantin V. Luzyanin

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OC 12 **Rapid Access to Novel Multifunctional Spirocyclic Cores for Drug Discovery**
Pavel K. Mykhailiuk

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F 3 **Oxo-molybdenum and Oxo-rhenium Complexes as Efficient Catalysts for the Deoxygenation of Carbonyl Compounds**
Ana Cristina Fernandes

F 4 **Selective Synthesis of Spirooxindoles by an Intramolecular Heck-Mizoroki Reaction**
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F 5 **Hydroformylation of Olefins Employing Low Generation Metallodendrimers of Rh and Ru as Catalyst Precursors**
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Marilé Landman

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P 156 **One-Pot Four-Component Synthesis of 1,2,3-Triazole-Dihydropyrimidinone Hybrids by a Click-Biginelli Reaction**
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P 157 **Synthesis and Characterization of Silver Sulfide Nanoparticles for Catalytic Activity**
Saptasree Bose

P 158 **Kinetics of Product Formation between Nitrobenzenethiol and Benzoquinone Derivatives**
Victoria T. Adeleke

P 159 **One-Pot and One-Step Microwave-Assisted Synthesis of Tryptanthrin – a Relevant Natural Product in Medicinal Chemistry**
Pedro Brandão

P 160 **Oxindole Hybrids: the Quest for New Molecules with Drug-Like Properties (preliminary studies)**
Pedro Brandão

P 161 **Asymmetric Grignard Synthesis of Tertiary Alcohols**
Eoin Bourke

P 162 **Synthesis of Dimeric Porphyrin as a Model for Oxygen Carrier Inartificial Blood**
Arona F. Pires

P 163 **Oxidative Debenzylation of *O*-Benzyl Ethers Catalyzed by $VO(acac)_2$ and a Triazole based Ligand**
Raul SanMartin

P 164 **Synthesis of a Novel Potent Radiosensitizer**
Pawel Wityk

P 165 **Synthesis of 3,3-Dimethylchroman-4-ones and 3,3-Dimethylchroman-4-ols: Palladium-Catalyzed Intramolecular Addition of Aryl bromides to Aldehydes**
Luís Galvão

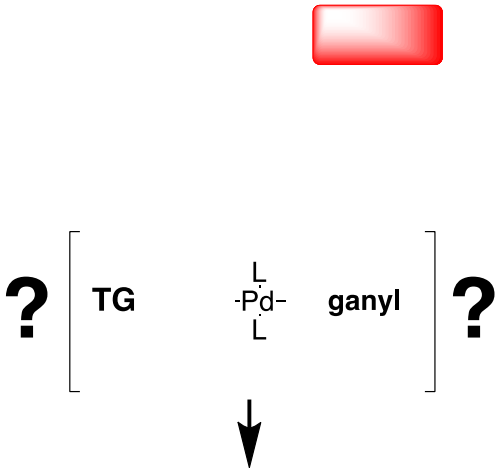
Plenary Lectures

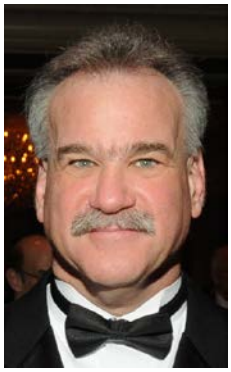
Transmetalation in the Suzuki-Miyaura Cross-Coupling Reaction: Mechanistic Insights and Preparative Implications

Prof. Scott E. Denmark, University of Illinois

Email: sdenmark@illinois.edu

The Suzuki-Miyaura reaction is by far the most commonly practiced and most powerful of the palladium catalyzed cross-coupling reactions. This reaction owes its widespread utility to the vast number of commercially available boronic acids and boronate derivatives as well as the mildness of the reaction conditions and the vast array of ligands that have allowed the coupling of unreactive and challenging substrates. Nevertheless, the molecular details of the critical transmetalation step have remained obscure because of the extreme reactivity of the hypothetical pre-transmetalation intermediate containing the key B–O–Pd linkage. Through the combination of spectroscopic analysis, independent synthesis, and kinetic measurements, we have unambiguously identified and characterized the elusive, pre-transmetalation species that undergo the Suzuki-Miyaura cross-coupling reaction from various boron derivatives.





Prof. Scott E. Denmark was born in New York on 17 June 1953. He obtained an S. B. degree from M.I.T. in 1975 and his graduate studies were carried out at the ETH Zürich under the direction of Professor Albert Eschenmoser, culminating in a D.Sc. Tech degree in 1980. That same year he began his career as assistant professor at the University of Illinois. He was promoted to associate professor in 1986, full professor in 1987 and then in 1991 named the Reynold C. Fuson Professor of Chemistry. Professor Denmark is primarily interested in the invention of new synthetic reactions and elucidating the origins of stereocontrol in novel, asymmetric reactions. The current emphasis in his laboratories focuses on the relationship between structure, reactivity and stereoselectivity in a variety of organoelement processes. He has pioneered the concept of chiral Lewis base activation of Lewis acids for catalysis in main group synthetic organic chemistry. His group has also developed palladium-catalyzed cross-couplings with organofunctional silicon compounds. In addition, his research program encompasses the development and application of tandem heterodiene cycloadditions for the synthesis of complex natural (alkaloids) and unnatural (fenestranes, phase transfer catalysts) nitrogen containing compounds. In recent years, his group has investigated the use of chemoinformatics to identify and optimize catalysts for a variety of organic and organometallic reactions. Professor Denmark has won a number of honours for both research and teaching. These include: A. P. Sloan Foundation Fellowship, NSF Presidential Young Investigator Award, Stuart Pharmaceuticals Award, A. C. Cope Scholar Award (ACS), Alexander Von Humboldt Senior Scientist Award, Pedler Lecture and Medal (RSC), the ACS Award for Creative Work in Synthetic Organic Chemistry, the Yamada-Koga Prize, the Prelog Medal (ETH Zürich), the H. C. Brown Award for Creative Research in Synthetic Methods (ACS), Robert Robinson Lecture and Medal (RSC), the ISHC Senior Award in Heterocyclic Chemistry, Paul Karrer Lectureship (Uni Zürich), the Frederic Stanley Kipping Award for Research in Silicon Chemistry (ACS) and the Harry and Carol Mosher Award (Santa Clara Section, ACS). He is a Fellow of the Royal Society of Chemistry and the American Chemical Society. He has received numerous honorary lectureships and visiting professorships and has served on many editorial advisory boards. He edited Volume 85 of *Organic Syntheses*, was Editor of Volumes 22-25 of *Topics in Stereochemistry* and was a founding Associate Editor of *Organic Letters* (1999-2004). After serving on the editorial board from 1994-2003, he became Editor-in-Chief and President of *Organic Reactions, Inc.* in 2008.

REPRESENTATIVE PUBLICATIONS (out of over 360)

1. Lewis Base Catalysis in Organic Synthesis (with G. Beutner), *Angew. Chem., Int. Ed.* **2008**, *47*, 1560-1638.
2. On the Mechanism of Lewis Base Catalyzed Aldol Addition Reactions: Kinetic and Spectroscopic Investigations Using Rapid-Injection NMR (with B. M. Eklov, P. J. Yao, and M. D. Eastgate) *J. Am. Chem. Soc.* **2009**, *131*, 11770-11787.
3. Silicon-Based Cross-Coupling Reactions in the Total Synthesis of Natural Products (with J. H.-C. Liu) *Angew. Chem. Int. Ed.* **2010**, *49*, 2978-2986.
4. A Systematic Investigation of Quaternary Ammonium Ions as Asymmetric Phase-Transfer Catalysts. Synthesis of Catalyst Libraries and Evaluation of Catalyst Activity (with N. D. Gould and L. M. Wolf) *J. Org. Chem.* **2011**, *76*, 4260-4336.
5. Lewis Base Catalyzed, Enantioselective, Intramolecular Sulfenoamination of Olefins (with H. M. Chi) *J. Am. Chem. Soc.* **2014**, *136*, 8915-8918.
6. Catalytic, Stereospecific Syn-Dichlorination of Alkenes (with A. J. Cresswell and S. T.-C. Eey) *Nature Chemistry* **2015**, *7*, 146-152.
7. Mechanistic Significance of the Si-O-Pd Bond in the Palladium-Catalyzed Cross-Coupling Reactions of Arylsilanolates (with S. A. Tymonko, R. C. Smith, A. Ambrosi, M. H. Ober, and H. Wang) *J. Am. Chem.Soc.* **2015**, *137*, 6200-6218.
8. Catalytic, Stereoselective Dihalogenation of Alkenes: Challenges and Opportunities (with A. J. Cresswell and S. T.-C. Eey) *Angew. Chem. Int. Ed.* **2015**, *54*, 15642-15682.
9. Pre-Transmetalation Intermediates in the Suzuki-Miyaura Reaction Revealed: The Missing Link (with A. A. Thomas) *Science* **2016**, *352*, 329-332.
10. Harnessing the Power of the Water-Gas Shift Reaction for Organic Synthesis (with A. Ambrosi) *Angew. Chem. Int. Ed.* **2016**, *55*, 12164-12189.

Important Asymmetric and Catalytic Transformations for Drug Development

Chris Senanayake, Ph.D.

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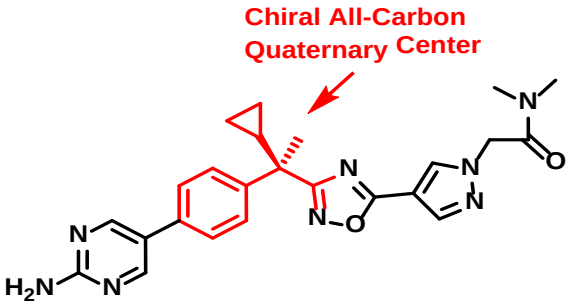
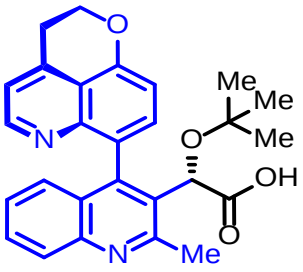
During the past two and half decades, my process research group is involved in the development of a truly efficient, reliable, greener and economically viable innovative process transformations for many drugs and drug candidates. Due to finding of effective innovative process solutions in a timely manner for important drug candidates, have provided many advantages to produce complex APIs in a rapidly for clinical development. This lecture will be centered on several highlights of these solutions for ideal and greener synthesis of important drug candidates.





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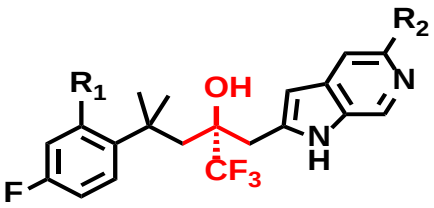
- ❑ Asymmetric construction of all carbon quart center

FLAP Inhibitor

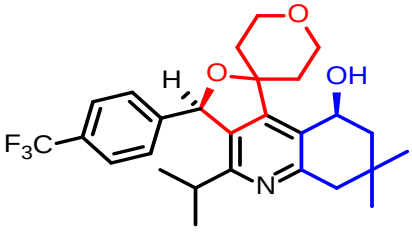


- ❑ Asymmetric Propagylation of challenging ketone

Glucocorticoid Agonists

- ❑ Asymmetric Suzuki for axial chiral center

HIV Integrase Inhibitor



- ❑ Rapid construction of fully substituted pyridine
- ❑ Asymmetric reduction of challenging ketone substrate

CEPT Inhibitor

References

1. Han, Z.; Senanayake, C. et.al. *J. Am. Chem. Soc.* 2013, 135, 2474;
2. Han, Z.; Senanayake, C.H. et.al. *Angew. Chem. Int. Ed.* 2013, 52(26), 6713;
3. Fandrick, K; Senanayake, C. et.al., *J. Org. Chem.* **2015**, *80*, 1651;
4. Fandrick, K; Senanayake, C. et.al., *Angew. Chem., Int. Ed*., **2015**, *54*, 7144;
5. Han, Z.; Senanayake, C. et.al., *Org. Lett*. **2014**, *16*, 4142;

Dr. Chris H. Senanayake was born in Sri Lanka and received a BS degree (First Class) in Sri Lanka. After coming to the United States, he completed his MS at Bowling Green State University with Professor Thomas Kinstle in synthetic chemistry. He obtained his Ph.D. under the guidance of Professor James H. Rigby at Wayne State University in 1987 where he worked on the total synthesis of complex natural products such as, ophiobolanes, and completed the first total synthesis of Grosshemin from the guaianolide family. He then undertook a postdoctoral fellowship with Professor Carl R. Johnson and worked on the total synthesis of polyol systems such as Amphotericin B and Compactin analogous, and the synthesis of C-nucleoside precursors. In 1989, he joined the Department of Process Development at Dow Chemical Co. In 1990, he joined the Merck Process Research Group. After 6 years at Merck, he accepted a position at Sepracor, Inc. and in 1996 he was promoted to Executive Director of Chemical Process Research. In 2002, he joined Boehringer Ingelheim Pharmaceuticals. Currently, he is the Vice President of Chemical Development and leading a group of highly talented scientists, engineers, and administrative staff located in Ridgefield, CT.

Dr. Senanayake's research interests focus on the development of new asymmetric methods for the synthesis of bioactive molecules and heterocycles and on catalytic, enzymatic, and mechanistic studies. He has published and lectured in the area of practical asymmetric synthesis and many disciplines of organic chemistry, particularly on how to develop drugs on an economical, greener and practical manner at large-scale for the rapid development of drugs. He is the co-author more than 375 papers, patents, book chapters and review articles in many areas of synthetic organic chemistry, drug development and design of improved chemical entities. He is an Editorial Advisory Board member of the Organic Process Research & Development Journal. In 2008, he was the chairperson of the Stereochemistry Gordon Conference. In 2010, he received the prestigious Siegfried gold medal award for development of practical processes for APIs and Process Chemistry. In 2011, he was appointed to the editorial board of the Advanced Synthesis & Catalysis Journal. In 2012 he was appointed to the advisory board of the Asian Journal of Organic Chemistry. In 2013 he was appointed to the board of editors of Organic Syntheses.

Transition Metal Catalysts

Construction and Functionalization of Heterocycles

Janine Cossy

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In general, the synthesis of complex biologically active molecules possessing heterocycles is problematic but the problems, encountered during the syntheses, can be a good source of inspiration to develop methods. One major challenge is the design of concise strategies as well as chemoselective and efficient methods that rapidly lead to the skeleton framework of natural and/or biologically active heterocyclic compounds.

In this context, we have explored the construction of heterocycles using catalytic reactions involving transition metal catalysts and heat. Metal catalysts and heat can induce rearrangements, cyclizations, functionalizations which can be highly diastereoselective and enantioselective if a chiral ligand is added in the reaction media. These reactions and their applications to the synthesis of heterocyclic natural and non-natural products will be presented.

Prof. Janine Cossy's early career was spent in Reims, where she did her undergraduate and graduate studies at the University of Champagne-Ardenne, working on photochemistry under the supervision of Prof. Jean Pierre Pète. After a postdoctoral stay with Prof. Barry M. Trost, for two years at the University of Wisconsin (USA), she returned to Reims where she became, in 1990, Director of Research at the CNRS. In the same year, she moved to Paris and, since 1990, she is Professor of Organic Chemistry at the ESPCI Paris. Janine Cossy's research interests focus on the synthesis of natural products and biologically active molecules and on the development of synthetic methods (organometallic reactions, catalysis, ring expansions, opening of strained rings, methods for the synthesis of heterocyclic compounds, stereoselective reactions). She has many collaborations with pharma and agro companies. Her research efforts have resulted in more than 470 publications and 15 patents. Among the awards, she received the CNRS Bronze Medal (1987), the CNRS Silver Medal (1996), UK Royal Society Rosalyn Franklin International Lecturership awarded to internationally recognized women scientists (2005), Le Bel Award from the French Chemical Society (France) (2009). In 2013, she was nominated Chevalier de la Légion d'Honneur and in 2015, she obtained the E.C. Taylor Senior Award and the UR Ghatak endowment award (IACS, India). Since 2005, she has been one of the Organic Letters associate editors.

Directed Evolution of Stereoselective Enzymes: A Prolific Source of Catalysts for Asymmetric Reactions

Manfred T. Reetz

Department of Chemistry, Philipps-University, Hans-Meerwein-Str. 4, 35032 Marburg, Germany, and Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470 Mülheim, Germany

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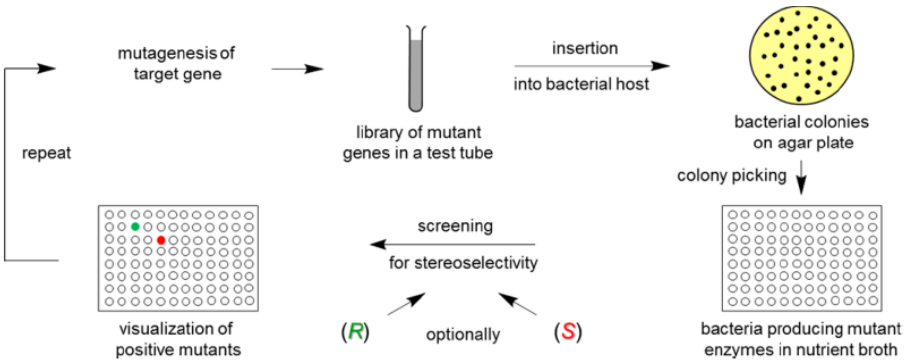
Since its conception some time ago[1], the idea of directed evolution of stereoselective enzymes as a novel approach to asymmetric catalysis has been generalized by us and other research groups to include essentially all of the known enzyme types, including hydrolases, reductases, oxygenases, transferases, and C-C bond forming enzymes such as aldolases, oxynitrilases and pyruvate decarboxylases. It involves repeating cycles of gene mutagenesis and screening, which builds up "evolutionary pressure" in each cycle, quite different from developing selective transition metal catalysts or organocatalysts. Since the screening step is the bottleneck of this Darwinian laboratory evolution, the real challenge is to obtain mutant libraries of highest quality requiring a minimum of screening effort. Iterative saturation mutagenesis (ISM) around the binding pockets of enzymes has proven to be an exceptionally valuable tool.[2] Recent examples concern the control of regio- and stereoselectivity of P450-catalyzed late-stage oxidative hydroxylation of steroids and of synthetic non-natural compounds, desymmetrization of epoxides by epoxide hydrolases, and ADH-catalyzed asymmetric reduction of "difficult-to-reduce" ketones. The construction of designer cells for cascade processes is another type of application. The lecture emphasizes that such selective transformations are not possible using modern transition metal catalysts or organocatalysts, demonstrating the complementarity of the different approaches.



References:

1. Reetz, M. T.; Zonta, A.; Schimossek, K.; Liebeton, K.; Jaeger, K.-E., *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 2830.
2. Recent reviews and key papers: a) Reetz, M.T., *J. Am. Chem. Soc.* **2013**, 135, 12480; b) Reetz, M. T., *Chem. Record* **2016**, 16, 2449; c) Reetz, M. T., *Directed Evolution of Selective Enzymes: Catalysts for Organic Chemistry and Biotechnology*, Wiley-VCH, Weinheim, **2016**; d) Reetz, M. T., *et al*, *Nature Comm.* **2017**, 8: 14876.

Prof. Manfred T. Reetz (born 1943 in Germany) is currently emeritus group leader of the Max-Planck-Institut für Kohlenforschung (MPI) in Mülheim and simultaneously Hans-Meerwein-Research-Professor at the University of Marburg/Germany, where he runs his current group. Previously he was director at the MPI for two decades, and before that he held a chair for organic chemistry in Marburg. Prof. Reetz earned Bachelor and Master degrees in the USA (1965-67) and a doctoral degree in organic chemistry at Göttingen University (1969). For many years the Reetz group developed novel organometallic reagents, chiral catalysts and methods for application in organic chemistry. In 1995 the group turned to biocatalysis and pioneered the concept of directed evolution of stereo- and regioselective enzymes as efficient catalysts in organic chemistry and biotechnology. Together with other groups, the long-standing limitations of enzymes were eliminated. Today it constitutes a prolific source of catalysts for a wide variety of different asymmetric transformations, including enantioselective hydrolysis, oxidation, reduction, and C-C bond forming reactions. Ongoing methodology development in the Reetz group continues to enhance the efficacy of this protein engineering method.

Design and Applications of Sustainable Metal-Catalyzed Reactions

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The design of ”green” synthetic methodology and new approaches to sustainable energy are major goals of modern catalysis. Traditionally, catalysis by metal complexes has been based on the reactivity of the metal center, while the ligands bound to it influence its reactivity, but do not interact directly with the substrate. In a major advance in homogeneous catalysis, complexes based on “cooperating” ligands were developed, in which both the metal and a ligand undergo bond making and breaking in key steps of the catalytic cycle, thus providing exciting opportunities for catalytic design.

We have developed a new mode of metal-ligand cooperation, involving ligand aromatization – dearomatization, which provides a new approach to the activation of chemical bonds. Pincer-type complexes of several transition metals exhibit such cooperation, including complexes of Ru, Fe, Co, Rh, Ir, Ni, Pd, Pt, Mn and Re. This has led to fundamentally new, environmentally benign catalytic reactions, including several reactions which either produce dihydrogen or consume it. Applications of these reactions in organic synthesis and in energy related transformations will be described.

David Milstein is the Israel Matz Professor of Chemistry and the director of the Kimmel Center of Molecular Design at the Weizmann Institute of Science in Israel. He received a Ph.D. degree at the Hebrew University in Israel in 1976 with Prof. Blum, and performed postdoctoral research at Colorado State University, where together with his advisor, Prof. John Stille, he discovered the Stille Reaction. In 1979 he joined DuPont Company's CR&D in Wilmington, USA as a Group Leader, and in 1986 he moved to the Weizmann Institute of Science in Israel, where he headed the Department of Organic Chemistry in 1996-2005. His research interests include fundamental organometallic chemistry, and the design and application of metal-catalyzed reactions for sustainable chemistry. He has received several awards, including the 2012 Israel Prize (Israel's highest honor) and The ENI Award for protection of the environment (2016). He is a member of the Israel Academy of Sciences and Humanities, and the German National Academy of Sciences-Leopoldina.

F-Block Organometallics for the Activation and Transformation of the Carbon Oxygenates CO, CO_2, and Esters

Polly L Arnold, Andrew Smith, Kai Wang, Jordann Wells, Megan Seymour, Connor Halliday, Ryan Kerr, Cath Weetman, Johann Hlina

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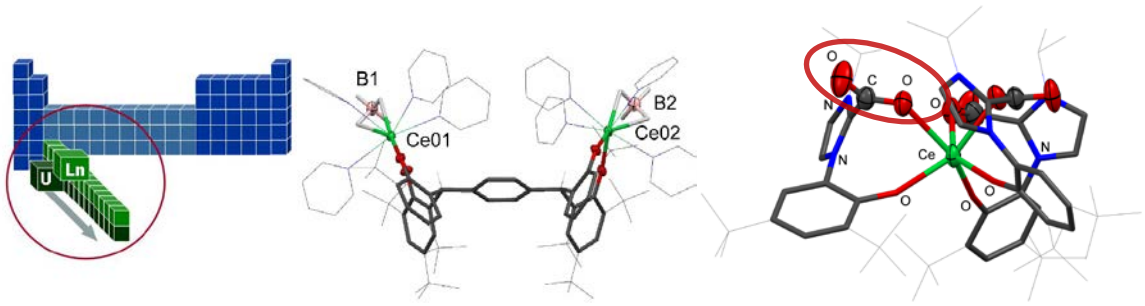
The subtleties of structure and bonding in compounds of the rare earths (Group 3 and the lanthanides) and uranium, the heaviest naturally occurring element, are still poorly-understood. However, their complexes can exhibit strong and tuneable Lewis acidity, high and tuneable reduction capacity, and the capacity for rapid ligand exchange reactions. Organometallic compounds of the lanthanides and actinides have shown many interesting small molecule activation reactions, including hydrocarbon C-H bond cleavage, over the last 25 years, and interest is increasing in their activity as catalysts, since the recognition that many rare earths are at least as abundant as iodine, and many are cheap and less toxic than iron.

We will show new f-block organometallics that are capable of the reductive activation and functionalisation of CO, CO_2, N_2, and arenes, even using simple bulky ligands that have been previously overlooked. The dominance of single-electron redox reactivity is a potential drawback they share with the 3d metal catalysts. We will present some dinuclear f-block complexes supported by new platform ligands, and their multiple-electron redox chemistry and catalysis, with a particular focus on cerium.



Time allowing, we will also show how the NHC can be incorporated as a labile, small molecule directing group into simple f-block aryloxide complexes, for the reductive activation and catalytic co-polymerisation of CO_2 with epoxides.

Reviews:

1. Reviews: P. L. Arnold, Z. R. Turner, Nature Chem. Rev. 2017, 1, 17. P.L. Arnold, M.W. McMullon, F.E. Kühn, J. Rieb, *Angew. Chem., Int. Ed.* **2015**, 54, 82.
2. J. A. L. Wells, M. L. Seymour, M. Suvova, P. L. Arnold, *Dalton Trans.* **2016**, 45, 16026.
3. P. L. Arnold, Z. R. Turner, R. Bellabarba, R. B. Tooze, *Chem. Sci.*, **2011**, 2, 77.
4. S. M. Mansell, N. Kaltsoyannis, P. L. Arnold, *J. Am. Chem. Soc.*, **2011**, 133, 9036.
5. P. L. Arnold, S. M. Mansell, D. McKay, L. Maron, *Nature Chem.*, **2012**, 4, 668.

Polly Arnold holds the Crum Brown Chair of Chemistry at the University of Edinburgh. She obtained degrees from Oxford and Sussex, and was a Fulbright postdoctoral fellow at MIT before returning to the UK to a lectureship in 1999. Her research is focused on the design and synthesis of highly reactive f-block complexes that can activate inert small molecules such as carbon oxides and hydrocarbons, and that can provide fundamental information on structure and bonding at the bottom of the periodic table. For more information see: www.homepages.ed.ac.uk/parnold. www.chemicalimbalance.co.uk.

Functionalization of Alkanes: a Challenge in Catalysis towards Organic Synthesis

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The search for new feedstocks for organic synthesis is a matter of current interest which relates to the over consumption of non-renewable fossil fuels. In particular, the extensive use as fuels of alkanes, which are abundant and carbon-rich species, is a matter of serious concern not only associated to their irreversible loss, but also to the transfer of carbon to the atmosphere leading to the accumulation of carbon dioxide therein with environmental consequences. This talk addresses the following relevant questions: can the current general application of alkanes be replaced by their use as alternative raw materials for synthesis, and can that be achieved under sustainable conditions? Approaches followed by the author´s research Group towards the development of selective catalytic processes for alkane functionalization under mild conditions to afford organic compounds with an added value will be discussed, namely concerning the following types of reactions:

- Oxidation of alkanes to alcohols and ketones;

- Oxidation of cyclohexane to adipic acid;

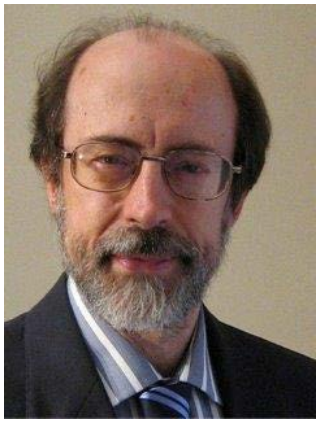
- Carboxylations (including hydrocarboxylation) of alkanes to carboxylic acids.

The use of different types of media (namely water, ionic liquid or organic solvent) and of catalysts (based on either transition metals or non-transition ones, with various types of ligands; homogeneous or supported ones) will be discussed. Some systems exhibit the highest reported catalytic activities in this field. Mechanistic proposals will be presented and prospects discussed.

Acknowledgements: This work has been partially supported by the Fundação para a Ciência e Tecnologia, namely through the projects PTDC/QEQ-QIN/3967/2014 and UID/QUI/00100/2013. The co-authors cited in the references are gratefully acknowledged.

References:

1. A.J.L. Pombeiro, "*Toward Functionalization of Alkanes under Environmentally Benign Conditions", in "Advances in Organometallic Chemistry and Catalysis*", A.J.L. Pombeiro (ed.), J. Wiley & Sons, **2014**, Chapter 2, pp. 15-25.
2. L.M.D.R.S. Martins, A.J.L. Pombeiro, *Coord. Chem. Rev.,* **2014**, 265, 74-88.
3. A.P.C. Ribeiro, L.M.D.R.S. Martins, M.L. Kuznetsov, A.J.L. Pombeiro, *Organometallics*, **2017**,36, 192-198.
4. A. P. C. Ribeiro, L. M. D. R. S. Martins, A. J. L. Pombeiro, *Green Chem.*, **2017**,19, 1499-1501.
5. M.L. Kuznetsov, B.G.M. Rocha, A.J.L. Pombeiro, G.B. Shul'pin, *ACS Catal*., **2015**, 5, 3823–3835.
6. M.L. Kuznetsov, F.A. Teixeira, N.A. Bokach, A.J.L. Pombeiro, G.B. Shul´pin, *J. Cat*., **2014**, 313, 135-148.
7. A.S. Novikov, M.L. Kuznetsov, A.J.L. Pombeiro, N.A. Bokach, G.B. Shul'pin, *ACS Catal*., **2013**, 3, 1195-1208.
8. L.M.D.R.S. Martins, M. Peixoto de Almeida, S.A.C. Carabineiro, J.L. Figueiredo, A.J.L. Pombeiro, *ChemCatChem*, **2013**, 5, 3847–3856.
9. D.S. Nesterov,E. N. Chygorin,V. N. Kokozay,V. V. Bon, R. Boča, Y. N. Kozlov,L. S. Shul'pina, J. Jezierska, A. Ozarowski, A. J. L. Pombeiro, G. B. Shul'pin, *Inorg.Chem*., **2012**, 51, 9110-9122.
10. M.V. Kirillova, M.L. Kuznetsov, Y.N. Kozlov, L.S. Shul'pina, A. Kitaygorodskiy, A.J.L. Pombeiro, G.B. Shul'pin, *ACS Catalysis,* **2011**, 1, 1511-1520.
11. D.S. Nesterov, V. N. Kokozay, J. Jezierska, O. V. Pavlyuk, R. Boca, A. J. L. Pombeiro, *Inorg. Chem*., **2011**, 50, 4401–4411.
12. M. Kuznetsov, A.J.L. Pombeiro, *Inorg. Chem*., **2009**, 48, 307-318.
13. M.V. Kirillova, M.L. Kuznetsov, P.M. Reis, J.A.L. Silva, J.J.R. Fraústo da Silva, A.J.L. Pombeiro, *J. Am. Chem. Soc*., **2007**, 129, 10531-10545.
14. A.M. Kirillov, M.N. Kopylovich, M.V. Kirillova, M. Haukka, M.F.C. Guedes da Silva, A.J.L. Pombeiro, *Angew. Chem., Int. Ed.,* **2005**, 44, 4345-4349.



Armando J. L. Pombeiro is a Full Professor at the Instituto Superior Técnico (IST), Universidade de Lisboa, President of the Centro de Química Estrutural and Coordinator of its Synthesis and Catalysis thematic line, Director of the Catalysis and Sustainability (CATSUS) PhD program, Full Member of the Academy of Sciences of Lisbon and former President of the Portuguese Electrochemical Society. His research Group investigates the activation of small molecules with industrial, environmental or biological significance, including (i) metal-mediated synthesis and (bioinspired) catalysis under mild/sustainable conditions (e.g., functionalization of alkanes, water oxidation, water in catalysis, alcohol/ketone oxidations, C-C couplings, CO_2 utilization, catalysis in ionic liquids, in supercritical medium, under microwaves and/or metal-free, (ii) crystal engineering of coordination compounds, design and self-assembly of polynuclear and supramolecular structures (e.g., coordination polymers and MOFs), (iii) non-covalent interactions in synthesis, (iv) coordination compounds with anti-tumor and anti-bacterial activity), (v) molecular electrochemistry and (vi) theoretical studies. He was Chairman of the 25th International Conference on Organometallic Chemistry (ICOMC) in 2012, will chair the 7th EuCheMS Conference on N-Ligands in 2018 and the 22nd International Symposium on Homogeneous Catalysis in 2020. He teaches courses on homogeneous catalysis. He authored one book (plus four as editor), (co-)authored over 700 research publications, 38 patents, and presented 100 invited lectures at international conferences. His work has received over 15,000 citations and has an h-index of 56 (Web of Science). He was awarded the Madinabeitia-Lourenço Prize (Spanish Royal Chemical Society) including prizes from the Portuguese Chemical and Electrochemical Societies.

CaRLa – Basic Research for Industrial Applications

Thomas Schaub[1,2]

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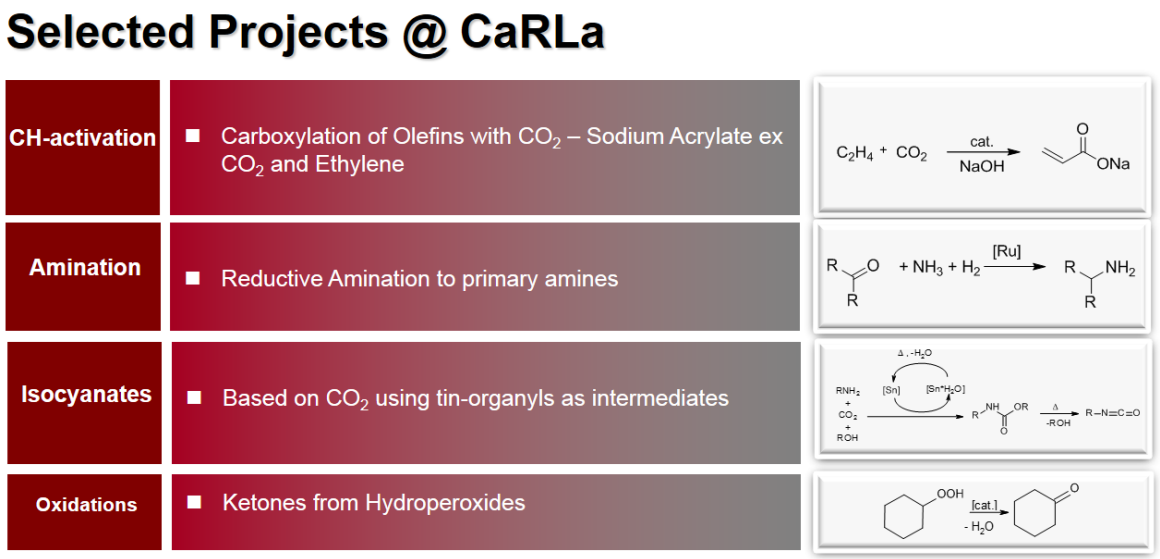
[2] *BASF SE, Synthesis and Homogeneous Catalysis, Ludwigshafen, Germany*

Email: thomas.schaub@basf.com

CaRLa is a collaborative laboratory jointly financed by BASF and the University of Heidelberg. We are working on leapfrog innovations for industrial relevant reactions through intensive exchange between basic academic and applied industrial research. This will be exemplified on four projects presented in this lecture: a) sodium acrylate from CO_2,[1] b) reductive amination of ketones with NH_3/H_2,[2] c) phosgene free synthesis of isocyanates using CO_2[3] and d) selective dehydroperoxidation.[4]



[1] a) S. Manzini, N. Huguet, O. Trapp, T. Schaub, Eur. *J. Org. Chem.* **2015**, 32, 7122-7130; b) S. Manzini, N. Huguet, O. Trapp, R. Paciello, T. Schaub, *Catal. Today* **2017**, 281, 379-386; c) S. Manzini, A. Cadu, A.C. Schmidt, N. Huguet, O. Trapp, R. Paciello, T. Schaub, *ChemCatChem*, **2017**, DOI: 10.1002/ccts.201601150.
[2] J. Gallardo-Donaire, M. Ernst, O. Trapp, T. Schaub, *Adv. Synth. Catal.* **2016**, 358, 358-363.
[3] a) N. Germain, I. Müller, M. Hanauer, R. Paciello, R. Baumann, O. Trapp, T. Schaub, *ChemSusChem*, **2016**, 9, 1586-1590; b) N. Germain, M. Hermsen, T. Schaub, O. Trapp, *Appl. Organomet. Chem.* **2017**, DOI: 10.1002/aoc.3733.
[4] A.C. Schmidt, M. Hermsen, F. Rominger, R. Dehn, J.H. Teles, A. Schäfer, O. Trapp, T. Schaub, *Inorg. Chem.* **2017**, DOI: 10.1021/acs.inorgchem.6b02322.

Dr. Thomas Schaub was born in 1980. He conducted undergraduate studies in Chemistry at the University of Karlsruhe (TH) (1999-2002) and graduate studies (diploma in Chemistry and Diploma-Thesis with Dr. U. Radius at the Institute of Inorganic Chemistry) (2002-4) followed by a PhD at the same laboratory (2004-6). He then conducted post-doctoral research in the group of Prof. David Milstein at the Weizmann Institute of Science in Israel (2007-8), followed by a position of research scientist in the homogeneous catalysis development unit within the Process Research and Chemical Engineering Unit ("Ammonlabor") at BASF SE in Ludwigshafen, Germany (2008-14). In 2014, he became the lab head of the Catalysis Research Laboratory (CaRLa) in Heidelberg. He is the co-author of 30 scientific publications and the co-inventor on 56 patents. He has given talks as an invited speaker at different Conferences and gives lectures at several universities (including the University of Marburg and Imperial College London). He has received some prestigious fellowship awards that include, fellow of the Fritz-ter-Mer foundation (Leverkusen) (2002-4) and the Feodor Lynen Research Fellowship of the Minerva foundation (Munich) (2007-8). His main research interests include, process development using homogeneous catalysis (e.g. hydrogenations, aminations, carbonylations, etc), mechanistic investigations on homogeneous catalyzed reactions (e.g. use of CO_2 as a building block, organometallic synthesis and high pressure chemistry.

Recent Progress in Cooperative Asymmetric Catalysis

Dr. Masakatsu Shibasaki

Chairman of Board of Directors
Institute of Microbial Chemistry
Japan

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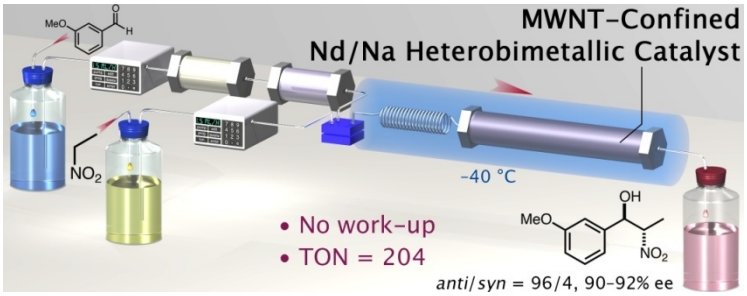
Our research focuses on the development of catalytic asymmetric C-C bond-forming reactions with particular emphasis on high atom economy and their application to the synthesis of biologically significant compounds. Thus, the concept of cooperative asymmetric catalysis such as Lewis acid-Brønsted base catalysis [1,2] and Lewis acid-Lewis base catalysis [3] plays the key role in our research paradigm. In this lecture, we report our recent progress in asymmetric Lewis acid-Brønsted base cooperative catalysis. In 1995, we developed the first example of a syn-selective catalytic asymmetric nitroaldol reaction using LLB (La-Li-BINOL) as a catalyst. At this time the anti-selective reaction remained a longstanding problem. Finally, by changing the catalyst design to a Nd/Na heterobimetallic catalyst possessing a chiral amide ligand, we succeeded in developing an efficient and practical anti-selective catalytic asymmetric nitroaldol reaction. Moreover, we documented an anti-selective asymmetric nitroaldol reaction in a continuous-flow system as shown below. The development of a direct catalytic asymmetric aldol-type reaction of thioamides with aldehydes such as RCH_2CHO was considered to be impossible due to the low acidity of the α-hydrogen. Recently we could overcome this inherent problem by identifying an asymmetric soft Lewis acid- hard Brønsted base cooperative catalyst. How this problem was overcome, as well as application to an efficient and practical catalytic asymmetric synthesis of atorvastatin, and membrenone B, will be discussed. Moreover, several catalytic asymmetric carbon-carbon bond-forming reactions mediated by the use of 7-azaindoline amide derivatives including direct catalytic asymmetric aldol reactions of α-alkylamides will be also presented.



References
[1] M. Shibasaki, M. Kanai, S. Matsunaga, and N. Kumagai, "Recent Progress in Asymmetric Bifunctional Catalysis Using Multimetallic Systems", *Acc. Chem. Res.*, 42, 1117-1127 (**2009**).
[2] N. Kumagai, and M. Shibasaki, "Recent Advances in Direct Catalytic Asymmetric Transformations Under Proton Transfer Conditions", *Angew. Chem. Int. Ed.*, 50, 4760-4772 (**2011**).
[3] M. Kanai, N. Kato, E. Ichikawa, and M. Shibasaki, "Power of Cooperativity: Lewis Acid-Lewis Base Bifunctional Asymmetric Catalysis", *Synlett*, 10, 1491-1508 (**2005**).

Prof. Masakatsu Shiasaki earned his Bachelor Degree in 1969 and his Ph.D in 1974 at the University of Tokyo under the direction of Professor Shun-ichi Yamada. From 1974–1977, he did postdoctoral studies with Professor E. J. Corey at Harvard University and in 1986, he took a professorship at Hokkaido University, before returning to the University of Tokyo as a professor in 1991. In 2006 he was appointed as the Dean of the Graduate School of Pharmaceutical Sciences, at the University of Tokyo (2006-08). In 2010 after retiring from the University of Tokyo he was appointed director of the Institute of Microbial Chemistry, Tokyo.

His awards and honors include: The Pharmaceutical Society of Japan Award for Young Scientists, 1981 (Japan); Inoue Prize for Science, 1994 (Japan); Fluka Prize (Reagent of the Year 1996), 1996 (Switzerland); The Elsevier Award for Inventiveness in Organic Chemistry (Tetrahedron Chair), 1998 (Belgium); The Pharmaceutical Society of Japan Award, 1999 (Japan); Molecular Chirality Award, 1999 (Japan); The Naito Foundation Research Prize for 2002 (Japan); ACS Award: Arthur C. Cope Senior Scholar Award, 2002 (USA); Medal with Purple Ribbon, 2003 (Japan); The Toray Science Award, 2004 (Japan); The Japan Academy Prize, 2005 (Japan); Takamine Memorial Sankyo Award, 2006 (Japan); The Rare Earth Society of Japan Award, 2007 (Japan); ACS Award: Creative Work in Synthetic Organic Chemistry, 2008 (USA); Centenary Medal and Lectureship (Royal Society of Chemistry), 2008 (UK); Prelog Medal, 2008 (ETH, Switzerland); Special Award of Synthetic Organic Chemistry of Japan, 2010 and Ryoji Noyori Prize 2012 (Japan).

Continuous Flow Chemistry: A Powerful Tool to Enable Chemistries and Scale-up Processes

Carlos Mateos

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Continuous Flow Processing is currently being used quite extensively in the chemical industry and it is considered as a key technology for manufacturing processes in the face of global competition and cost efficiency. However, while the advantages of this technology are increasingly appreciated by the pharmaceutical industry, its overall implementation in this sector has been slow and is still in transition, so it is not yet a preferred strategy for the development and preparation of drug products. Even the Food and Drug Administration (FDA) has recently suggested that pharma manufacturers should switch more aggressively into Continuous Flow Processing. Flow Chemistry and Continuous Processing has been a very active field of research in Eli Lilly and Company during the last 12 years, and significant investment has been made in this technology with the objective of becoming an essential part of its Discovery and Development research organizations. To foster new flow chemistry developments, we have established some very fruitful collaborations with expert academic groups. The presentation will demonstrate, through a selection of case studies, the advantages that can be leveraged through the use of continuous flow reactor technology including the use of light as reaction promoter, control of hazardous processes, intensified process conditions (high T/P), scale-up reliable processes, etc..

In particular, examples showing the following topics will be showcased:

- Visible-light photochemistry
- Electrochemistry
- Solid supported reagents.
- Hydrogen transfer oxidations and reductions
- Internal Lilly examples of successful continuous flow processes implementation

Dr. Carlos Mateos obtained his first degree in Organic Chemistry, in 1998, at the University of Oviedo (Spain). Then, he moved to Leverkusen, (Germany) to enjoy an industrial internship in Bayer AG working on the industrial development of azo-dyes. In 1999 he moved back to Spain and decided to pursue a PhD on natural product synthesis, at the University of Oviedo under the supervision of the late Professor José Barluenga. After receiving his PhD in 2004, Carlos joined the company Galchimia (a leading Spanish Contract Research Organization in Santiago de Compostela, Spain) as a project manager. In 2006, he moved to Alcobendas, Madrid to join Eli Lilly and Co. where he has been working in early discovery medicinal chemistry projects. He has recently become interested in developing new methodologies in Continuous Flow Chemistry and expanding the knowledge and capabilities of his group in that field. To that end, he has established several fruitful and enjoyable collaborations with academia.

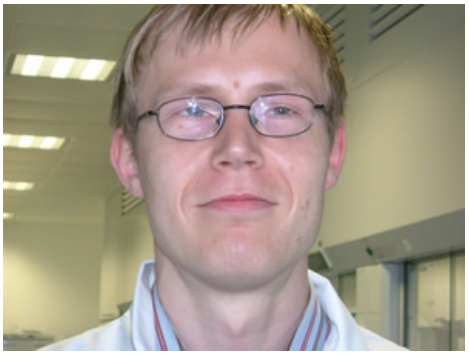
Shortening the Path – Biocatalysis Applications in the Pharmaceutical Industry

Dr Stefan Mix / Almac Group

Almac, Department of Biocatalysis & Isotope Chemistry, Seagoe Industrial Estate Craigavon, N. Ireland BT63 5QD UK

Email: stefan.mix@almacgroup.com

Biocatalytic synthetic methods have received much attention and gained importance for the generation of pharmaceutical materials, ranging from medicinal chemistry to commercial API scale. This trend has been facilitated by advances in molecular biology and bioinformatics, enabling ever more rapid and competitive access to an increasing variety of biocatalysts and enzyme classes, e.g. hydrolases, aminotransferases, alcohol and amino acid dehydrogenases, amine oxidases and imine reductases. Recent examples of application of these enzymes at Almac are presented and discussed in the context of comparing the chosen methods with competing alternative technologies.



Dr. Stefan Mix was born in Berlin / East Germany, where he also completed his secondary education. After graduation with a Diploma in chemistry, he received his doctorate in 2004 from the Technical University of Berlin after working in the group of Prof. Siegfried Blechert on stereoselective synthetic methodology and olefin metathesis. He is the author of several publications, and has been working with Almac Group since 2005. He has gained broad industrial experience including expertise in the fields of biocatalysis, crystallisation development, process development for chiral building blocks and APIs, and technology transfer to manufacturing network partners. His hobbies include sailplane gliding, kayaking and gardening.

C-H Amination within the Halide Redox Manifold

Muñiz K.[a,b]

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The development of light-initiated catalytic Hofmann-Löffler reactions has been accomplished using novel iodine catalysts that are directly generated from molecular iodine.[1] These processes can be tuned to involve either an iodine(-I/I) or (I/III) redox manifold. The iodine redox manifold depends on the chosen terminal oxidant, which can be an iodine(III) reagent or molecular dioxygen within photocatalysis. The reactions proceed within a unique scenario of two intertwined catalytic cycles (Figure 1).[1] Mechanistic details including the isolation of catalyst derivatives[2] and the unprecedented scope including primary, secondary and tertiary C-H bonds will be discussed. In the final section of the talk, a first approach to piperidine synthesis through iodine-catalysed C-H amination will be presented.[3]

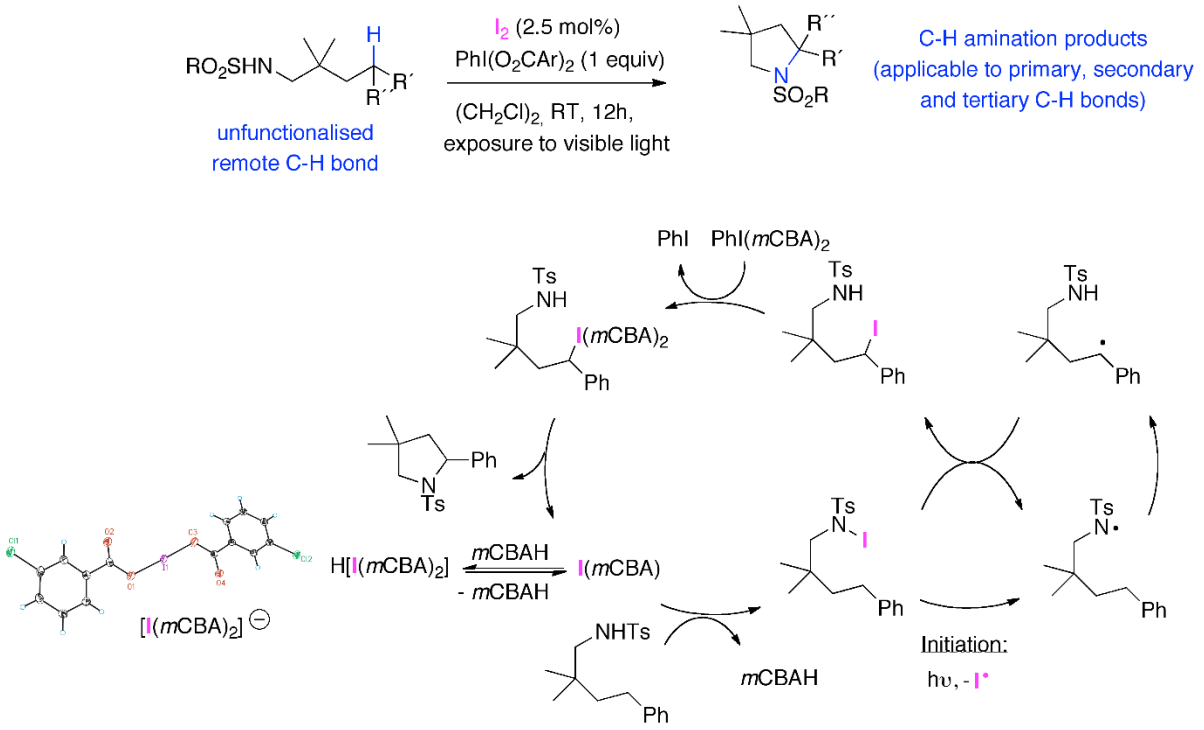

Figure 1: Iodine(I/III)-catalysed Hofmann-Löffler reaction.

References:

1. a) Martínez, C.; Muñiz, K. *Angew. Chem.* **2015**, 127, 8287; *Angew. Chem. Int. Ed.* **2015**, 54, 8405. b) Becker, P.; Duhamel, T.; Stein, J. C.; Reiher, M.; Muñiz, K. *Angew. Chem.* **2017**, DOI: 10.1002/ange.201703611; *Angew. Chem. Int. Ed.* **2017**, DOI: 10.1002/anie.201703611.
2. Muñiz, K. García, B.; Martínez, C.; Picinelli, A. *Chem. Eur. J.* **2017**, 23, 1539.
3. Zhang, H.; Muñiz, K. *ACS Catal.* **2017**, DOI: 10.1021/acscatal.7b00928.

Prof. Kilian Muñiz was born in 1970 in Hildesheim, Germany. He received a doctorate in Chemistry from the RWTH Aachen in 1998 for work with Professor Carsten Bolm and was an Alexander von Humboldt/JSPS postdoctoral associate with Professor Ryoji Noyori at Nagoya University, Japan (1999-2000). From 2001-2005 he was a Liebig fellow at Bonn University, before accepting a full professorship at Strasbourg University (France). He was elected as a junior member to the Institute Universitaire de France in 2008. Kilian Muñiz moved to his present position at ICIQ in Tarragona (Spain) in 2009. Since 2010 he has also been an ICREA research professor. He received a 2015 Award for Excellence in Research from the Royal Spanish Chemical Society (RSEQ) and a 2016 Yoshida Lectureship from the IOCF. His research throughout the past decade has mainly dealt with the development of new synthetic methodology in the area of amination chemistry, particularly the oxidative diamination of alkenes.

Selectivity Control in C–H Activation

Lutz Ackermann

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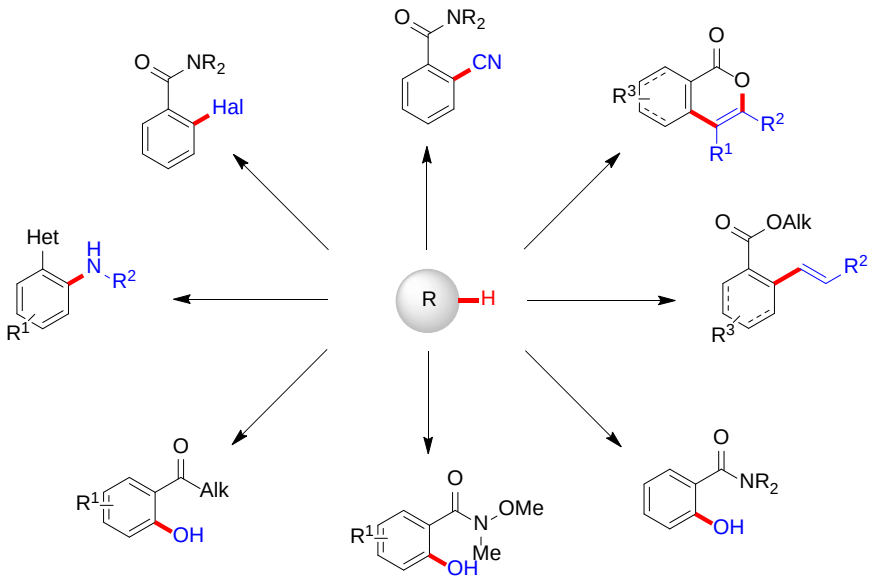
C–H activation has surfaced as a powerful platform in molecular synthesis, with transformative applications to material sciences and drug discovery, among others.[1] Thus, we have introduced secondary phosphine oxides and carboxylates as additives for positional selective C–H arylations and alkylations with versatile ruthenium(II) complexes,[2] displaying complementary chemo- and site-selectivities as compared to palladium,[3a] nickel,[3b] cobalt,[3c] iron,[3d] copper[3e] or manganese[3f] catalysis. Detailed mechanistic insights into the working mode of the key C–H ruthenation step set the stage for ruthenium(II)-catalyzed twofold C–H bond functionalizations as well as step-economical oxidative alkyne annulations.[4,5] The oxidative C–H bond functionalization strategy proved broadly applicable and enabled, among others, ruthenium(II)-catalyzed oxygenations, nitrogenations, cyanations and halogenations, as well as meta-and para-selective arene diversification.[6]



References:

1. Selected reviews: (a) Zhu, R.-Y.; Farmer, M. E.; Chen, Y.-Q.; Yu, J.-Q., *Angew. Chem. Int. Ed.* **2016**, 55, 10578–10599. (b) Daugulis, O.; Roane, J.; Tran, L. D., *Acc. Chem. Res.* **2015**, 48, 1053–1064. (c) Ackermann, L.; Vicente, R.; Kapdi, A. *Angew. Chem. Int. Ed.* **2009**, 48, 9792–9826. (d) Ackermann, L. *Modern Arylation Methods*, Wiley-VCH, Weinheim, **2009**.
2. Ackermann, L. *Chem. Rev.* **2011**, 111, 1315–1345.
3. Representative examples: (a) Ackermann, L.; Althammer, A.; Fenner, S. *Angew. Chem. Int. Ed.* **2009**, 48, 201–204. (b) Song, W.; Lackner, S.; Ackermann, L. *Angew. Chem. Int. Ed.* **2014**, 53, 2477–2480. (c) Li, J.; Ackermann, L. *Angew. Chem. Int. Ed.* **2015**, 54, 8551–8554. (d) Gu, Q.; Al Mamari, H. H.; Graczyk, K.; Diers, E.; Ackermann, L. *Angew. Chem. Int. Ed.* **2014**, 53, 3868–3871. (e) Yang, F.; Koeller, J.; Ackermann, L., *Angew. Chem. Int. Ed.* **2016**, 55, 4759–4762. (f) Ruan, Z.; Sauermann, N.; Manoni, E.; Ackermann, L., *Angew. Chem. Int. Ed.* **2017**, 56, 3172–3176.
4. (a) Warratz, S.; Kornhaaß, C.; Cajaraville, A.; Niepötter, B.; Stalke, D.; Ackermann, L., *Angew. Chem. Int. Ed.* **2015**, 54, 5513–5517. (b) Ackermann, L. *Acc. Chem. Res.* **2014**, 47, 281–295.
5. Bechtoldt, A.; Tirler, C.; Raghuvanshi, K.; Warratz, S.; Kornhaaß, C.; Ackermann, L., *Angew. Chem. Int. Ed.* **2016**, 55, 264–267.
6. (a) Ruan, Z.; Zhang, S.-K.; Zhu, C.; Ruth, P. N.; Stalke, D.; Ackermann, L., *Angew. Chem. Int. Ed.* **2017**, 56, 2045–2049. (b) Li, J.; Warratz, S.; Zell, D.; De Sarkar, S.; Ishikawa, E. E.; Ackermann, L. *J. Am. Chem. Soc.* **2015**, 137, 13894–13901. (c) Hofmann, N.; Ackermann, L. *J. Am. Chem. Soc.* **2013**, 135, 5877–5884.

Lutz Ackermann FRSC is a full professor of chemistry at Georg-August-University Göttingen, he obtained a Diploma in Chemistry at the Christian-Albrechts-Universität zu Kiel (1993–98), then he conducted Ph.D. research under the guidance of Prof. Alois Fürstner at MPI Kohlenforschung in Mülheim (1998 – 2001), this was followed by a post-doctoral fellowship with Prof. Robert G. Bergman at UC Berkeley (2001-3) and then an Emmy Noether-Fellow (DFG) (Independent researcher) at the LMU München (2003 –7). In 2007 he was appointed to a position of Full Professor (W3) at the Georg-August-University Göttingen. From 2011-13 he was the Dean of the Faculty of Chemistry at Georg-August-University Göttingen, and from 2013 –15 the Dean of Research at the same department. In 2015 he was appointed as the Director of the Institute of Organic and Biomolecular Chemistry at this University. He is an adjunct professor at the Università di Pavia, Italy and a visiting professor at the Università degli Studi di Perugia, Italy. In 2009 he held a JSPS Visiting Professor Fellowship at Osaka University, Japan, in 2008 he was a Goering Visiting Professor at the University of Wisconsin at Madison and in 2007 a Visiting Professor at Università Milano. He has an h-index of ≥ 72 (≥ 220 publications) and has given more than 200 invited lectures. His main interests are in; C–H activation, homogenous catalysis, peptide chemistry, reaction mechanisms and base metal catalysis. He has received numerous awards, recognitions or grants, that include: the Gottfried-Wilhelm-Leibniz Prize (2017), Thomson Reuters (Web of Science) ISI Highly Cited Researcher (2016), Invited Chair Professor Joliot at the Ecole superieure de physique et de chimie industrielles de la ville de Paris (ESPCI) (2016), Molecular Science Frontier Lecture Professorship, Institute of Chemistry, Chinese Academy of Sciences (ICCAS) (2016), is a member of the Academy of Sciences and Humanities, Göttingen (2016), the Ta-Shue Chou Lectureship Award, Academia Sinica, Taiwan (2015), an ERC Independent Researcher Consolidator Grant (2012), the AstraZeneca Excellence in Chemistry Award (2011), Dozentenstipendium (FCI), ADUC prize (GDCh) (2007) and the ORCHEM-Preis für Naturwissenschaftler (GDCh) (2006).

Flow Processes for the Synthesis of ‘Challenging’ Molecules

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Flow chemistry has now been accepted as a main stream tool for the processing of reactive chemical streams especially in telescoped multi-step transformations. The efficiency and complexity of the molecules that can now be prepared means it has for many academic and industrial laboratories become the first go-to approach over batch. However, there are still many aspects in which additional gains could be made through judicious engineering solutions and improvements in the technologies applied. Often at the core of the improvements is the design and implementation of new chemical routes specifically conceived for flow processing scenarios rather than translated from existing batch based syntheses. Our presentation will illustrate a number of purpose built multi-stage and multi-step preparation of target molecules using current flow based processing strategies but also highlighting some of the areas still in need of further development.

Prof. Ian Baxendale obtained his PhD under the supervision of Prof. Pavel Kocovsky at the University of Leicester. He then moved to a postdoctoral position with Prof. Steven V. Ley at the University of Cambridge. In 2003 he was awarded a Wolfson Royal Society Fellowship. In 2008 he was promoted to a Senior Research Associate in the Department of Chemistry and then in 2009 was awarded a Royal Society University Research Fellowship. In 2012 he moved to Durham to take up the Chair of Synthetic Chemistry. His current research interests are the design and implementation of new enabling technologies such as Flow Chemical Synthesis (FCS), Synthesis Automation Methodologies (SAM), microwave reactors and immobilised reagents and scavengers to expedite complex chemical syntheses.

Palladium Coupling Reactions Optimization as Part of the Development of an API Synthesis

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Palladium coupling reactions represent an important tool for modern organic synthesis and have been extensively used in the pharmaceutical industry for over the past 30 years to produce APIs presenting complex structures. Two case studies are discussed where Hovione has studied palladium coupling reactions with the goal of having an efficient, economical and robust process able to produce APIs at an industrial and commercial scale.

Dr. Ana Cruz has been a chemist at Hovione's Process chemistry development group for the last 7 years. She graduated in Applied Chemistry (Organic Chemistry Branch) from the New University of Lisbon in 2003. She spent one year working on a research project developing the synthesis of APIs in ITQB before moving to Bath (UK) to carry out a Ph.D in organic chemistry with Prof. Michael Willis. Her Ph.D work was focused on the development of C-H activation reactions catalyzed by palladium. After completing her Ph.D she joined Ascent Scientific as a synthetic chemist and in 2009 she returned to Portugal to join Hovione's R&D group. At Hovione she has worked on the development of processes to produce contrast agents and has worked on the chemistry of steroids and tetracyclines. More recently she has been working on process development and scale-up to produce APIs under a quality by design approach. Her main interests are palladium catalyzed reactions, crystallization processes and process modelling.

Oral Communications

Brønsted Acid Catalyzed Nitrile Synthesis from Aldehydes via Transoximation under Mild Conditions

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We recently focused on the transoximaze isolated from the pupae of silkworm and developted a Brønsted acid catalyzed transoximation.[1] In the present research, we demonstrate that the stable oxime is equivalent to explosive hydroxylamine. On the contray, *O*-protecting hydroxylamines containing electron-withdrawing groups are known to exhibit high reactivity for the amination reaction, however their reagents also showed explosive and unstable properties (ex. MSH reagent and HOSA etc.). Herein, we expanded our concept and considered that more stable *O*-protecing oxime could be treated as an equivalent of explosive *O*-protecting hydroxylamines in order to solve the problem (**Figure 1**). Based on the above concept, we atempted the reaction with aldehydes and *O*-sulfonyl oxime catalyzed by various Brønsted acid. As a result, the reacton were successfully proceeded under very mild conditions and the corresponding nitriles were generated *via* transoximation with good yield (**Figure 2**)[2]. We will discuss with the details in this synposium.

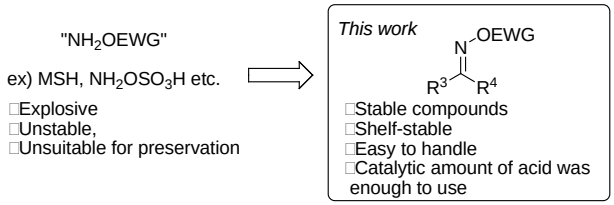

Figure 1. Advantages of using oxime instead of hydroxylamine derivatives

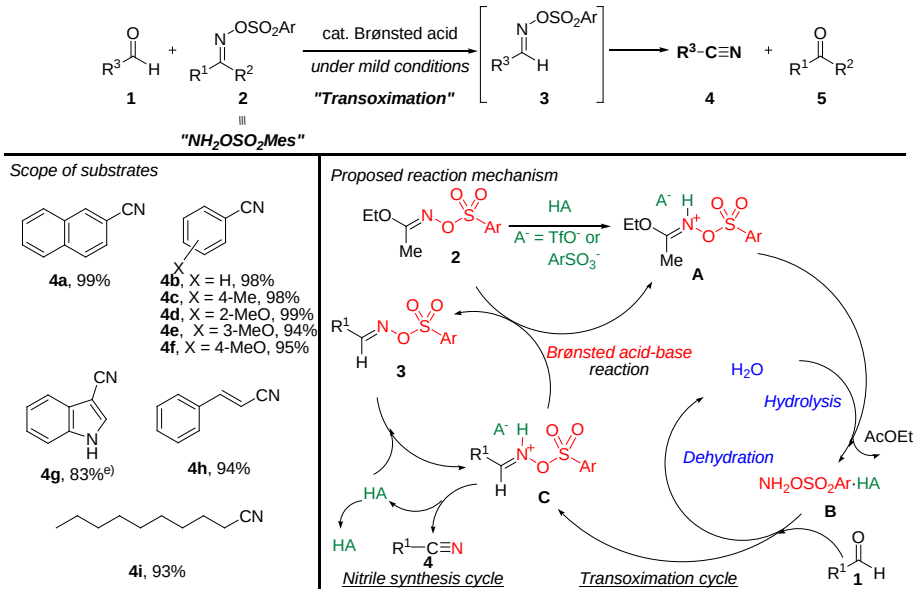

Figure 2. Brønsted acid catalyzed nitrile synthesis *via* transoximation.

Acknowledgements: We gratefully acknowledge the financial support from the Kaneka Award in Synthetic Organic Chemistry, Japan.

References:

1. Hyodo, K.; Togashi, K.; Oishi, N.; Hasegawa, G.; Uchida, K. *Green Chem.* **2016**, *18*, 5788.
2. Hyodo, K.; Togashi, K.; Oishi, N.; Hasegawa, G.; Uchida, K. *Org. Lett.* **2017**, *19*, 3005.

Scientific career:

2006- B.S. degree in Chemistry, Department of Applied Chemistry, Nagoya Institute of Technology, Japan, (Supervisor: Prof. Takeshi Toru)

2013- PhD degree in Chemistry, Department of Frontier Materials, Nagoya Institute of Technology, Japan, (Supervisor: Prof. Shuichi Nakamura)

2013- Postdoctoral fellow, Max-Planck-Institut für Kohlenforschung, Germany, (Supervisor: Prof. Benjamin List)

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Awards:

2011 The Prize of 5th Wakashachi Incentive Award, Aichi Prefectural Government

2012 The Poster Award of 2nd CSJ Chemistry Fest, Chemical Society of Japan

2012 Best Presentation Award, 92th Annual Meeting of CSJ, Chemical Society of Japan

2013 Postdoctoral fellowship, The Naito Fundation

2015 Kaneka Award,in Synthetic Organic Chemistry, The Society of Synthetic Organic Chemistry, Japan

Current research topics:

Catalytic reaction, Alternative reaction methodology, Greener synthesis

Alkyne and Alkene Functionalization by Visible-Light-Mediated Photoredox Catalysis

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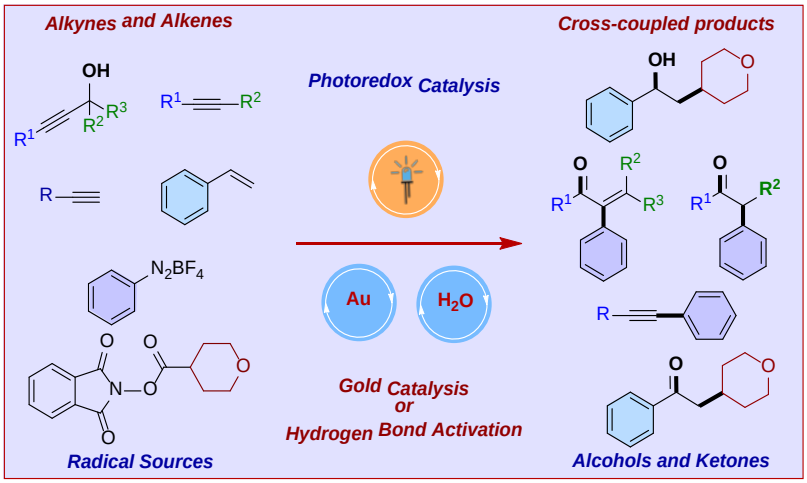
Photoredox catalysis has emerged in recent years as a powerful tool in organic synthesis to access reactive radical intermediates under mild conditions while using visible light as the main source of energy.[1] Based on this fascinating concept, we have developed novel catalytic strategies to achieve a variety of challenging C−C and C−O bond forming processes across alkynes and alkenes giving straightforward access to valuable cross-coupled and carbooxygenated products (scheme 1).[2,3] As highlighted here, the success of these strategies strongly relies on the combination of photoredox catalysis with other powerful chemistries such as homogeneous gold catalysis and hydrogen-bond activation to achieve higher degrees of chemical reactivity. For instance, we have demonstrated the ability of photogenerated aryl radicals to unlock oxidative addition processes to gold(I) catalysts enabling their use in cross-coupling chemistry with alkyne moieties.[2] Moreover, while using alkenes as substrates, either direct or hydrogen-bond mediated photoinduced electron transfer has allowed the access to C(sp^3)-centered radicals which can be manipulated to construct complex alcohols and ketones.[3]



Scheme1: alkyne and alkene derivatization based on photocatalytic approaches.

Acknowledgements: Financial support by the NRW Graduate School of Chemistry and the Deutsche Forschungsgemeinschaft (Leibniz Award) is gratefully acknowledged.

References:

1. a) Tucker J. W.; Stephenson C. R. J.; *J. Org. Chem.* **2012**, 77, 1617. b) Prier C. K.; Rankic D. A.; MacMillan D. W. C. *Chem. Rev.* **2013**, 113, 5322. c) Hopkinson M. N.; Sahoo B.; Li J.-L; Glorius F. *Chem. Eur. J.* **2014**, 20, 3874.
2. a) Tlahuext-Aca A.; Hopkinson M. N.; Sahoo B.; Glorius F. *Chem. Sci.* **2016**, 7, 89. b) Tlahuext-Aca, A.; Hopkinson M.N.; Garza-Sanchez R. A.; Glorius F. *Chem. Eur. J.* **2016**, 22, 5909. c) Tlahuext-Aca A.; Hopkinson M. N.; Glorius F. *Chem. Eur. J.* **2016**, 22, 11587. d) Hopkinson M. N.; Tlahuext-Aca A.; Glorius F. *Acc. Chem. Res.* **2016**, 49, 2261.
3. Tlahuext-Aca A.; Garza-Sanchez R. A.; Glorius F. *Angew. Chem. Int. Ed.* **2017**, 56, 3708.

Adrian Tlahuext-Aca was born in Mexico and received his B.Sc. and M.Sc. in Chemistry from the Universidad Autónoma del Estado de Morelos and the Universidad Nacional Autónoma de México, respectively. In 2014, he joined the NRW Graduate School of Chemistry and the group of Prof. Frank Glorius at the Westfälische Wilhelms-Universität Münster for his doctoral studies which have been focused on merging photoredox and transition-metal catalysis. In 2016, Adrian received the IPMI Metalor Technologies Graduate Student Award for his research on dual gold/photoredox catalysis.

Catalysed Stereoselective Synthesis of Deoxyglycosides

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Chiral acetals, of which carbohydrates are the most diverse and abundant biomolecules on earth are key components that are involve in a wide range of biological processes. The chemical synthesis of complex carbohydrates generally entails the coupling of a fully protected glycosyl donor bearing a leaving group at its anomeric centre, with a suitably protected glycosyl acceptor (R-OH). In many instances, these reactions lead to a mixture of two stereoisomers. [1] To this day, the stereoselective synthesis of glycosides remains one of the biggest challenges in carbohydrate chemistry. In particular, the synthesis of deoxyglycosides, which lack an OH functionality (often at C-2) in the ring scaffold represent a significant challenge. [2]

Herein we report the development of catalytic methods for the synthesis of deoxyglycosides. A practical approach has been developed for the glycosylation of D-glycals with a series of OH nucleophiles in excellent yields and α-stereocontrol using different novel catalytic systems (**Figure 1**). In addition to organocatalytic activation systems,[3a] we have recently been involved in the development of transition-metal catalyzed glycosylations. The mild and efficient methods are tolerant of a wide range of glycal donors, protecting groups and a variety of alcohols used as nucleophiles (primary and secondary). The methodology is exemplified in the synthesis of biologically interesting tri- and tetrasaccharide, in addition, preliminary mechanistic and kinetic studies were performed and will be discussed. [3b]

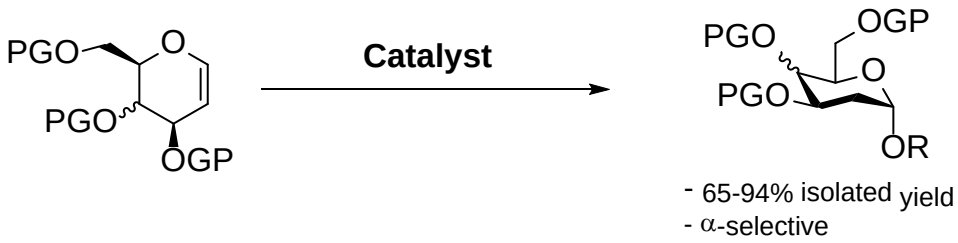

Figure 1: Stereoselective catalysis.

References:

[1] Galan, M. C.; Benito-Alifonso, D.; Watt. G. M. "Carbohydrate Chemistry in Drug Discovery". *Org. Biomol. Chem.* **2011**, *9* (10), 3598.
[2] a) Medina, S.; Galan M. C. "Recent Developments in the Stereoselective Synthesis of Deoxyglycosides". *Carbohydr. Chem.* **2016**, *41*, 59. b) Balmond, E. I.; Coe, D. M.; Galan, M. C.; McGarrigle, E. M. *Angew. Chem. Int. Ed*. **2012**, *51*, 9152.
[3] a) C. Palo-Nieto, A. Sau, R. Williams, M.C. Galan*. *Journal of Organic Chemistry,* **2017**, *82*, 407; b) A. Sau, R. Williams, C. Palo-Nieto, A. Franconetti, S. Medina, M. C. Galan *. *Angew.Chem. Int. Ed.* **2017**, *56*, 3640.

Dr. Carlos Palo-Nieto obtained his degree in Pharmacy (2008) and his PhD in the Department of Organic and Pharmaceutical Chemistry (2013) at the University of Sevilla (Spain). During his PhD, he worked on the stereoselective synthesis of new compounds with biological interest from carbohydrate starting materials and also performed the synthesis of small molecules in search of anticancer and antimicrobial activity. During his PhD, he spent six months in Stockholm University working on asymmetric catalysis. Afterwards, he spent a year at Mid Sweden University (Sundsvall) as a post-doctoral fellow working in heterogeneous catalysis. After a short time working in pharmaceutical industry, in 2015, he joined the group of M. Carmen Galan at the University of Bristol (England) as Newton International Postdoctoral Fellow where his research focuses on the application of catalysis to oligosaccharide synthesis.

Orthogonal Substrate-Selective C-H Functionalisation of Organosulphur Compounds Originating from Crude Oil

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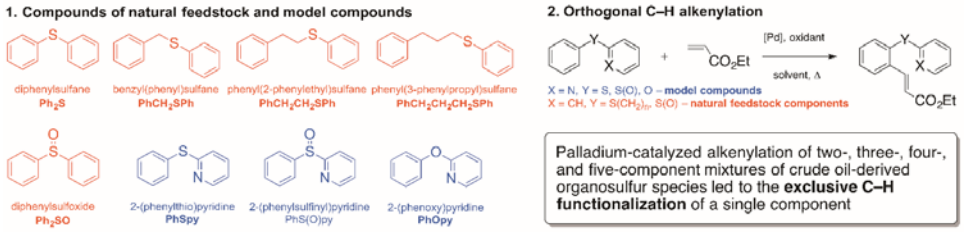
Direct utilization of natural feedstock in organic synthesis is an utmost challenge of modern chemistry. Crude oil represents the richest natural source of organosulphur compounds (present there as a complex mixture, **Scheme 1-1**), however, the direct functionalisation of those is an intrinsic industrial challenge. It is due to a fact that the selective preparation of one product from a mixture of starting materials requires an unprecedented substrate selectivity. Currently, production of organosulphur derivatives starts from the hydrodesulphurisation procedure that transforms all the sulphur compounds present in oil into elemental sulphur followed by the multistep organic synthesis to rebuild the required products. The overall process is totally unsustainable due to cost inefficiency, high energy consumption, and environmental contamination.

In pursuit of our studies on metal-catalysed C–H alkenylation,[1] we uncovered a more efficient single-step approach leading towards the orthogonal substrate-selective functionalisation of organosulphur components (**Scheme 1-2**).



Under optimized conditions (ethyl acrylate as an alkene, 1,2-dichloroethane as the solvent, 130 °C for 24 h), known palladium-catalysed C–H alkenylation of a mixture of organosulphur compounds[2–4] proceeds with unparalleled substrate selectivity. For all two-component mixtures of substrates, the reaction targets exclusively one component in the system, and naturally occurring thioethers were more reactive than the corresponding thiopyridines or sulfoxides. The same trend was detected for the three-, four-, and five-component systems where only one component was functionalised, and the order of reactivity of the substrates, observed for the two-component mixtures, is retained. These results demonstrate a promising potential of C–H functionalisation towards the processing of natural feedstock.

In the current report, we summarize data accumulated up to date regarding selective CH-alkenylation of sulphur-containing and related organic species. An emphasis is given to evaluation of the assistance provided by different sulphur-containing directing groups in comparison to other common directing moieties, nature of the observed substrate selectivity and first insight into the mechanism of this process.

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References:

1. Luzyanin K. V.; Marianov A. N.; Kislitsyn P. G.; Ananikov V. P. *ACS Omega* **2017**, *2*, 1419.
2. García-Rubia A.; Fernández-Ibánez M. A.; Gómez Arrayás R.; Carretero J. C. *Chem. Eur. J.* **2011**, *17*, 3567.
3. Yu M.; Xie Y.; Xie C.; Zhang Y. *Org. Lett.* **2012**, *14*, 2164.
4. Zhang X.-S.; Zhu Q.-L.; Zhang Y.-F.; Li Y.-B.; Shi Z.-J. *Chem. Eur. J.* **2013**, *19*, 11898.

Konstantin Luzyanin studied chemistry at Saint Petersburg State University (1997−2002). He received his Ph.D. in Chemistry from Technical University of Lisbon (in 2007), where he was also a postdoctoral researcher (2007−2008) and a senior research associate (2009−2012). For his Ph.D. studies, he was awarded Bruker's Antońio Xavier Prize for application of modern NMR techniques in organometallic chemistry. He was a co-founder of the Modern Methods of Structure Elucidation (MMSE) – Portuguse national training site, celebrating 10 years in 2018.

In 2013, Konstantin joined the newly created Center of Cluster Catalysis in Saint Petersburg as a Deputy Head and a Leading Scientist. In 2015, Konstantin moved to the University of Liverpool as the Head of the Analytical Services in Department of Chemistry and Researcher in Analytical Applications. He currently works on his habilitation project to be undertaken at Saint Petersburg State University.

Konstantin's current research interests include organometallic chemistry of late transition metals, activation of small molecules, mechanisms of metal-mediated and metal-catalyzed reactions, and application of modern techniques of NMR spectroscopy.

Dr. Luzyanin is an author of more than 70 original papers (h-index: 22), 5 patents, 2 reviews, as well as 4 book chapters. In the course of last years, he supervised several M.Sc. and Ph.D. students, delivered several university courses and received funding from various funding bodies.

Catalytic Processes that are Suitable for the Large Scale Reduction of Aldehydes and Ketones

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The standard technology for the large scale manufacture of benzylic alcohols from aromatic aldehydes is the reduction using complex hydrides of B and Al.[1] Heterogeneous metal catalysts have selectivity problems due to their ability to convert benzylic alcohols to methylaromatics, to reduce nitroaromatics and to de-halogenate aryl halides. There is scope to develop homogeneous catalysts for the reduction to benzylic alcohols and both Beller (hydrogenation and transfer hydrogenation with Fe catalysts)[2] and Dupau (mainly on aliphatic aldehyde hydrogenation)[3] have demonstrated reductions of aldehydes.

Johnson Matthey manufactures the Baratta's catalyst Ru-721 at 100's of kg scale for application in ketone reductions and has developed the synthesis of second generation catalysts **1**-**3 (Figure 1**).[4] Subsequently, processes for the effective reduction of commercial grade aldehydes using these catalysts, which prove to be more delicate substrates than ketones have been developed.[5] We will discuss these processes and compare with aldehyde and ketone reductions with alternative catalysts in this contribution.

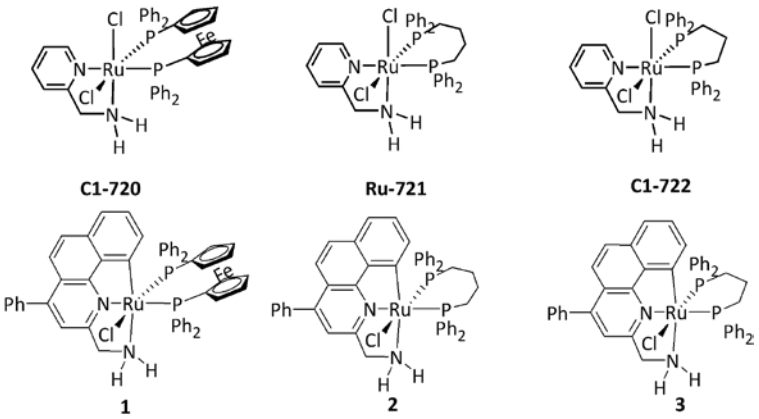

Figure 1: Baratta's catalyst structures

Acknowledgements: We thank Dr. S. Baldino, F. Christie and L. Browne for their contribution to this work.

References:

1. J. Magano, J. R. Dunetz, *Org. Process Res. Dev.* **2012**, *16*, 1156.
2. G. Wienhöfer, F. A. Westerhaus, K. Junge, M. Beller, *J. Organomet. Chem*, **2013**, *744*, 156.
3. Ph. Dupau, L. Bonomo, L. Kermorvan, *Angew. Chem. Int. Ed.* **2013**, *52*, 11347.
4. a) H. G. Nedden, A. Zanotti-Gerosa, E. Moya, S. Facchetti, W. Baratta et. al. *Organometallics*, **2016**, *35*, 277. b) G. Chelucci, S. Baldino, W. Baratta, *Coordination Chemistry Reviews*, **2015**, *300*, 29.
5. S. Baldino, S. Facchetti, H. G. Nedden, A. Zanotti-Gerosa, W. Baratta, *ChemCatChem* **2016**, *8*, 2279 and 3195.

Hans Günter Nedden completed his PhD (Dr. rer. nat.) in chemistry at the University in Tübingen (Germany) under the supervision of Prof. U. Nagel in 1997, working on the synthesis of chiral PN ligands and use in Ni-catalysed asymmetric cross couplings. After a postdoctoral stay with Prof. I. E. Marko in Belgium, working on iron (II)-bisimine pyridine catalysts for ethylene and propylene polymerisation, he joined ICI Synetix in 2001, later to become part of Johnson Matthey. His core interest is in catalytic research and in the synthetic development and scale-up of ligands and metal complexes with catalytic activity. He leads a team in Cambridge (UK) dedicated to bringing to market new homogenous catalysts for hydrogenation and transfer hydrogenation.

A Metal-Catalyzed Journey to New Azaindole Synthesis

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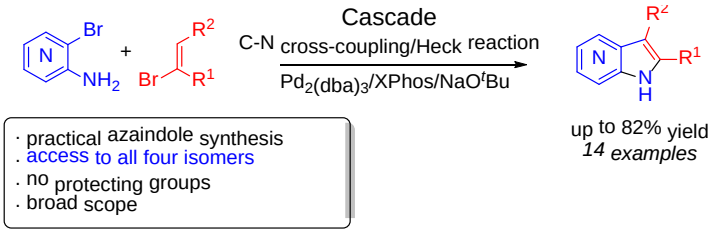
Azaindoles are bioisosteres of the indole nucleus, a privileged structure, which have enticed the interest of the scienti fic community for their physicochemical and pharmacological properties with potential applications in the field of medicinal chemistry.[1] Due to their important value, methods for the synthesis of azaindoles and derivatives have attracted considerable interest from the scientific community. Common synthetic strategies to prepare azaindoles rely on the use of aminopyridines, followed by building up the pyrrole ring. The strategy parallels the indole synthesis starting from anilines. However, the electron-deficient nature of the pyridine ring alters the electronic properties of the conjugated system in such a way that many classic indole synthetic methods are not as efficient or simply do not work.[2] Our group has been focused on metal-catalyzed cross-coupling reactions for the preparation of bioactive heterocy-cles, such as indole and benzimidazole,[3] and on the search for the straightforward synthesis of azaindoles from commer-cially available amino-*o*-halopyridines (**Scheme 1**).[4] The practical palladium-catalyzed cascade C–N cross-coupling/Heck reaction of alkenyl bromides with amino-*o*-bromopyridines previously described by our group allowed a straightforward synthesis of substituted 4-, 5-, 6-, and 7-azaindoles, but did not work when applied to N-aryl amino-o-bromopyridines towards 1,2-diaryl azaindoles. N-arylation of substituted azaindoles is generally difficult and low yielding.[5] The N-arylation of 2-aryl azaindoles, is even more challenging due to the steric hindrance, yet constituting an alternative route to 1,2-diaryl azaindoles, these protocols are scarce and products difficult to obtain.[5] Herein we will present our latest achievments o the first one-pot access to all four 1,2-diaryl azaindoles isomers from available amino-o-bromopyridines, avoiding the difficult N-arylation of 2-substituted-azaindoles



Scheme 1: Pratical Pd-catalyzed cascade C–N cross-coupling/Heck reaction of alkenyl bromides with amino-*o*-bromopyridines.

Acknowledgements: We thank to the FC&T for fellowship SFRH/BD/89518/2012. This work was supported by the Associated Laboratory for Sustainable Chemistry- Clean Processes and Technologies-LAQV which is financed by national funds from FCT/MEC (UID/QUI/50006/2013) and co financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007265). The NMR spectrometers are part of The National NMR Facility, supported by FC&T (RECI/BBB-BQB/0230/2012).

References:

1. a) Zhao S.-B., Wang S. *Chem. Soc. Rev.* **2010**, *39*, 3142. b) Mérour J.-Y.; Buron F.; Plé K.; Bonnet P., Routier S. *Molecules* **2014**, *19*, 19935.
2. Song J. J.; Reeves J. T.; Gallou F.; Tan Z.; Yee N. K.; Senanayake C. H. *Chem. Soc. Rev.* **2007**, *36*, 1120.
3. Carvalho L. C. R.; Ribeiro D.; Seixas R. S. G. R.; Silva A. M. S.; Nave M.; Martins A. C.; Erhardt S.; Fernandes E.; Cabrita E. J.; Marques M. M. B. *RSC Adv.* **2015**, *5*, 49098.
4. Pires M. J. D.; Poeira D. L.; Purificação S. I., Marques M. M. B. *Org. Lett.* **2016**, *18*, 3250.
5. a) Hong C. S.; Seo J. Y., Yum E. K. *Tetrahedron Lett.* **2007**, *48*, 4831. b) Klapars A.; Antilla J. C.; Huang X., Buchwald S. L. *J. Am. Chem. Soc.* **2001**, 1*23*, 7727. c) Qian G.; Hong X.; Liu B.; Mao H.; Xu B. *Org. Lett.* **2014**, *16*, 5294.

Maria Manuel Marques was born in Lisbon, Portugal in 1972. She studied chemistry at the new University of Lisbon, from where she also received her Ph.D. in organic chemistry in 2001 under the supervision of Prof. Dr. S. Prabhakar. From 2001 to 2003 she joined the group of Prof. Dr. J. Mulzer at the Institute of Organic Chemistry at the University of Vienna, as a postdoctoral research fellow. In 2003, she returned to the Faculty of Science and Technology, New University of Lisbon (Requimte) as a research fellow. Since 2004 she has been involved in organic chemistry teaching at the Chemistry Department, and in 2016 she obtained her Habilitation in Chemistry. Her research encompasses the development of new synthetic and sustainable methodologies involving metal-catalyzed reactions towards bioactive compounds, in particular heterocyclic molecules, and the development of new synthetic strategies to prepare glycopeptides in order to understand biological systems.

Reduction of Carbon Dioxide by Formate Dehydrogenase: Aiming to Develop a Catalyst for Carbon Dioxide Utilization

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Formate dehydrogenases (FDH) are enzymes that catalyze the reversible two-electron oxidation of formate to carbon dioxide (eq. 1).[1,2] FDHs can be divided into two major groups, based on their metal content and the consequent chemical strategy followed by the enzyme's active site to catalyze the reaction. The group of metal-dependent FDHs comprises only prokaryotic enzymes that hold different redox-active centers and whose active site harbors one molybdenum (or one tungsten) atom that mediates the formate oxidation/carbon dioxide reduction.

$$CO_2 + 2e^- + H^+ \rightleftharpoons HCOO^- \quad (1)$$

In this communication, the ability of the molybdenum-containing FDH from *Desulfovibrio desulfuricans* (Dd FDH) to reduce carbon dioxide will be discussed. The Dd FDH was found to be one of the most efficient carbon dioxide reducers so far described in the literature, with a k_{cat} of 47s^{-1} and a K_m^{CO2} of 16μM [3] and a novel FDH reaction mechanism was proposed:[3,4] formate oxidation and carbon dioxide reduction proceed through hydride transfer, through a mechanism where the sulfo group of the oxidized (Mo^{6+}=S) and reduced (Mo^{4+}-SH) molybdenum center are suggested to be the direct hydride acceptor and donor, respectively (Fig. 1).

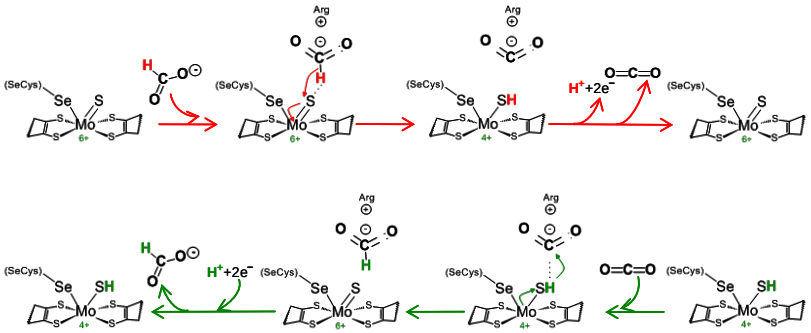

Figure 1: The hydride transfer mechanism proposed for the formate dehydrogenases reaction - FDH-catalysed formate oxidation (red arrows) and carbon dioxide reduction (green arrows). The two reactions were represented separately to be easer to follow the individual steps in each case, but the red and green arrows represent one unique reversible reaction, that can be driven in both directions, depending on the prevalent molybdenum oxidation state (Mo^{6+} or Mo^{4+}). For simplicity, for simplicity, only the dithiolene moiety of the pyranopterin cofactor is represented (its full structure can be found, *e.g.*, in [1]).

Acknowledgements: LBM thanks to Fundação para a Ciência e a Tecnologia, MCTES, for a fellowship grant (SFRH/BPD/111404/2015, which is financed by national funds and co-financed by FSE). This work was supported by the Unidade de Ciências Biomoleculares Aplicadas-UCIBIO, which is financed by national funds from FCT/MEC (UID/Multi/04378/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007728).

References:

1. Maia L.; Moura I.; Moura J.J.G. *Inorg. Chim. Acta* **2017**, *455*, 350 (doi: 10.1016/j.ica.2016.07.010).
2. Maia L.; Moura I.; Moura J.J.G. *J. Biol. Inorg. Chem.* **2015**, *20*, 287 (doi: 10.1007/s00775-014-1218-2).
3. Maia L.; Fonseca L.; Moura I.; Moura J.J.G. *J. Am. Chem. Soc.* **2016**, *138*, 8834 (doi: 10.1021/jacs.6b03941).
4. Niks D.; Duvvuru J.; Escalona M.; Hille R. *J. Biol. Chem.* **2016**, *291*, 1162 (doi: 10.1074/jbc.M115.688457).

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Indium(III)-Catalyzed Intramolecular Cycloisomerization Reactions of Alkynes: Synthesis of 2*H*-Chromenes, Benzo[*b*]furans and Derivatives

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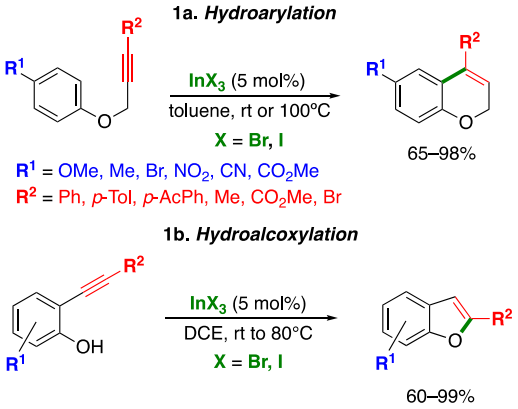
During the last years, indium(III) has been shown as an efficient Lewis acids for the activation of alkynes.[1] Indium(III) halides are softer than analogous species with boron or aluminum and present high affinity for alkynes. Additionally, indium catalysis is superior to Ag(I), Hg(I) or Au(I), in terms of cost or toxicity. Remarkable examples of this activity have been reported by Fürstner *et al.* in the synthesis of phenantrenes by hydroarylation reaction and by Corey *et al.* in polycyclization reactions of enynes.[1a,b] Our interest in metal-catalyzed reactions with organoindium reagents,[2] prompted us to undertake a project devoted to indium-catalyzed cycloisomerization reactions. In 2015, we reported the indium-catalyzed intramolecular hydroarylation (IMHA) reaction of aryl propargyl ethers and amines.[3a] The reaction proceeds regioselectively with terminal and internal alkynes bearing electron-rich and electron-deficient substituents affording only the *6-endo dig* cyclization product in good yields (**Scheme 1a**). This methodology was also extended to a one-pot sequential In(III)-catalyzed IMHA bromopropargyl aryl ethers and amines and Pd-catalyzed cross-coupling using triorganoindium reagents.[3b] Furthermore, we discovered that indium(III) catalyzes the hydroalcoxylation reaction of *o*-alkynyl phenols to afford 2-substituted benzo[*b*]furans (**Scheme 1b**).[4] In this communication we will discuss the synthetic scope of both reactions including mechanistic issues and further applications in polycyclization reactions using polyines systems.



Scheme 1. Indium-catalyzed Intramolecular Hydroarylation and Hydroalcoxylation reactions.

Acknowledgements: We gratefully acknowledge the Spanish Ministerio de Economía y Competividad (CTQ2015-68369-P), Xunta de Galicia (GRC2014/042) and European Development Research Fund (EDRF) for financial support.

References:

1. a) Mamane, V.; Hannen, P.; Fürstner, A. *Chem.–Eur. J.*, **2004**, *10*, 4556. b) Surendra, K.; Corey, E. J. *J. Am. Chem. Soc.* **2014**, *136*, 10918. c) Michelet, B.; Colard-Itté, J-R; Thiery, G.; Guillot, R.; Bour, C.; Gandon, V. *Chem. Commun*. **2015**, *51*, 7401.
2. Mato, M.; Pérez-Caaveiro, C.; Sarandeses, L. A. Pérez Sestelo, J. *Adv. Synth, Cat*. **2017**, *359*, 1388, and references therein.
3. a) Alonso-Marañón, L.; Martínez, M. M.; Sarandeses, L. A.; Pérez Sestelo, J. *Org. Biomol. Chem*. **2015**, *13*, 379. b) Alonso-Marañón, L.; Sarandeses, L. A.; Martínez, M. M.; Pérez Sestelo, J. *Org. Chem. Front.* **2017, *4***, 500.
4. Alonso-Marañón, L.; Sarandeses, L. A.; Martínez, M. M.; Pérez Sestelo, J. *XXXVI Reunión Bienal de la Real Sociedad Española de Química*, Sitges (Barcelona), June 25-29, 2017.

José Pérez Sestelo was born in Vigo (1966). He studied Chemistry at the University of Santiago de Compostela where he got his PhD degree in 1994. After postdoctoral studies at the University of Pennsylvania (1994-95) under the supervision of Prof. Amos B. Smith III, and Boston College (1996) with Prof. T. Ross Kelly, he joined the University of A Coruña in 1997 where he currently holds a position as Associate Professor of Organic Chemistry (habilitation as full professor in 2012). He has been visiting scholar at the University of Rostock (2011) and Michigan State University (2014). His research activity is focused on Organic Synthesis using organometallic compounds, highlighting his contributions in cross-coupling reactions using organoindium reagents. He has authored about 60 articles in high impact international journals.

Continuous-flow Stereoselective Catalytic Synthesis of Active Pharmaceutical Ingredients in Micro- and (3D-printed) Meso-Reactors

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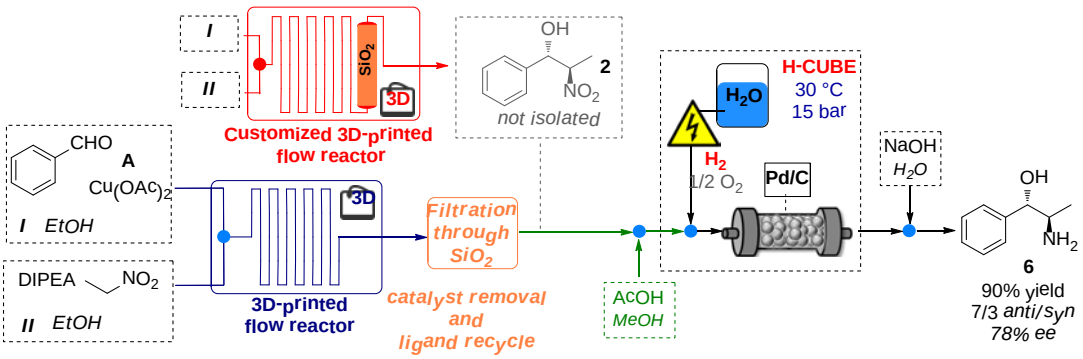
In the last few years, continuous-flow systems[1] have become very popular as a powerful tool for performing synthesis of organic molecules. In this context, we explored the use of different micro- and mesoreactors to develop stereoselective catalytic reactions under continuous flow conditions aimed to the synthesis of chiral Active Pharmaceutical Ingredients.[2]

In this field we reported the in-flow synthesis of chiral 1,2-amino alcohols displaying biological activities (norephedrine, metaraminol, and methoxamine) using 3D-printed reactors (**Scheme 1**).[3] These devices were designed, fabricated from different materials (PLA, HIPS, NYLON), and used in a catalytic stereoselective Henry reaction. The use of readily prepared and tuneable 3D-printed reactors allowed for a rapid screening of devices with different sizes, shapes and channel dimensions, aimed at the identification of the best performing reactor set up. The optimized process afforded products in high yields, moderate diasteroselectivity and up to 90% e.e. through two-steps, all-in-flow sequence that involves, after the nitroaldol reaction, a continuous flow hydrogenation.

To highlight the potential industrial application of this methodology, a multistep continuous synthesis of norephedrine has been realized: the product was isolated without any intermediates purification or solvent switching operation.



Scheme 1: Multistep in flow synthesis of pharmaceutically valuable chiral 1,2-amino alcohols.

References:

1. B. Gutmann, D. Cantillo, D.; C. O. Kappe, *Angew. Chem. Int. Ed.* **2015**, *54*, 6688.
2. For a review see: R. Porta, M. Benaglia, A. Puglisi, *Org. Proc. Res. Devel.*, **2016**, 20, 2-25; S. Rossi, M. Benaglia, A. Puglisi, C. C. De Filippo, M. Maggini, *J. Flow Chem*. **2014**, 5, 17-21 and R. Porta, M. Benaglia, F. Coccia, S. Rossi, A. Puglisi, *Symmetry* **2015**, 7, 1395-1409.
3. S. Rossi, R. Porta, D. Brenna, A. Puglisi, M. Benaglia, *Angew. Chem. Int. Ed*. **2017**, 56, 4290-4294.

Sergio Rossi was born in Bergamo in 1983. In 2007 he obtained his Laurea in Chemistry at the University of Milan (Italy) and in 2010 he completed his PhD on the activation of trichlorosilyl derivatives with chiral Lewis bases under the supervision of Prof. M. Benaglia, at the University of Milan.

In 2011, he joined the group of Prof. S.E. Denmark with a postdoctoral fellowship, at the University of Urbana-Champaign (USA), where he worked on Lewis base-catalyzed asymmetric sulfenylation reactions. In 2012 he moved back to Milan, as postdoctoral fellow, developing new enantiomerically pure tetrachlorosilane-based Lewis acids for catalysis. In 2013 he was awarded by a fellowship as brilliant young researchers granted by Cariplo Foundation and he was qualified and selected in a global competition among 600 young scientists worldwide to participate to the “63rd - Lindau Nobel Laureate meeting”. In 2017 he obtained an Assistant Professor position at the University of Milan, where he is currently working in the development of new stereoselective metal-free synthetic methodologies, in the stereoselective synthesis of chiral pharmaceutical products as well as in the development of catalytic stereoselective reactions under continuous-flow conditions in micro- and mesoreactors, taking advantage of new enabling technologies such as 3D-printing. He is currently member of the organizing committee of the International School of Process Chemistry (ISPROCHEM).

Enzyme Immobilization as an Enabler for Biocatalysis in Flow

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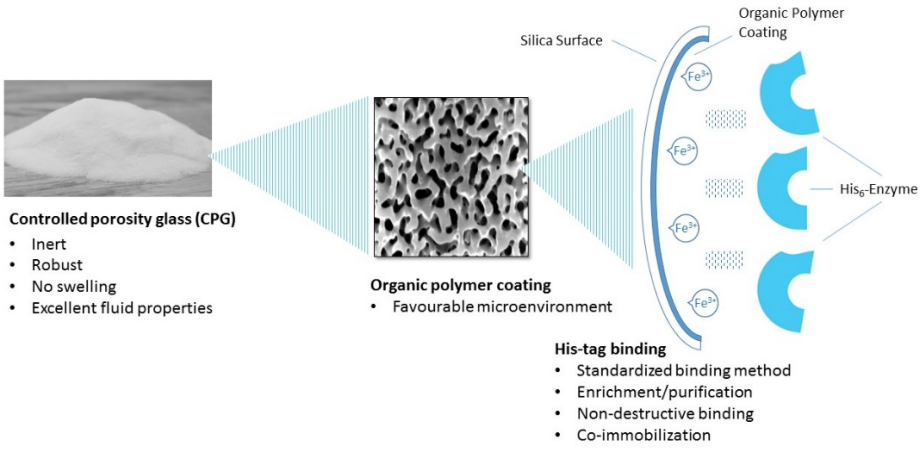
Enzymes are efficient catalysts with a broad scope, offering an attractive option for the chemical industry at large. In spite of this, there are significant barriers to the implementation of biocatalysis in general. Practical issues arise, since enzymes are homogenous catalysts and in a vast number of cases, the cost of the biocatalyst is the main obstacle for use on large scale. The cost-of-use can, however, be effectively lowered by enzyme immobilization, which, furthermore, enables the use under flow conditions. Laborious testing of the available immobilization alternatives is most often needed and offers a pronounced drawback for the user. Many methods are known, but the individual techniques are generally neither robust nor efficient enough for general purpose utilization.

To solve this problem, EnginZyme has developed a standard enzyme immobilization technology, EziG, which is useable for all enzyme types.[1] Any His-tagged enzyme can be bound to the EziG-carrier in a non-destructive, fast and selective way. Hereby, a pure immobilized preparation can be achieved in one step directly from cell lysate. The carrier has a core consisting of controlled-pore glass beads where the surface is tailored by the application of a thin layer of specific polymer coatings.

The properties of the bead material results in high binding capacity while the tailored surface stabilizes the enzyme catalyst. In total, this gives a non-swelling and robust porous support material suited for both aqueous and organic media. Due to the interconnecting pore structure and incompressible dense nature of glass, EziG is ideal for flow chemistry in column reactors minimizing back pressure problems. The immobilization procedure is simple and can even be performed in the reactor itself.

EziG has been successfully applied to a variety of enzymes: i.a. lipases, transaminases, ketone reductases.[2] Examples of biocatalysis with a few chosen enzymes will be presented, as well as the enzyme carrier material.



1. Engelmark Cassimjee K, Kadow M, Wikmark Y, Svedendahl Humble M, Rothstein M.L, Rothstein D.M, Bäckvall J-E. *Chem. Commun.* **2014**, *50*, 9134-9137.
2. Engelmark Cassimjee, K.; Federsel, H.-J. EziG: A Universal Platform for Enzyme Immobilization. *In Biocatalysis: An Industrial Perspective*; de Gonzalo, G.; Dominguez, P., Eds.; *RSC Catalysis Series*; *to be submitted*.

Hans-Jürgen Federsel, PhD in Organic Chemistry, Royal Institute of Technology (KTH), Stockholm (1980). Starting as process R&D chemist in Astra, Södertälje, Sweden (1974) he has occupied positions both as line and project manager. After the formation of AstraZeneca (1999) he became Director of Science, followed by appointment as Senior Principal Scientist. Academic qualifications lead to an Associate Professorship (KTH,1990) and a seat on the Board of the School of Chemical Science and Engineering. 2009 he was elected to the Royal Swedish Academy of Engineering Sciences. After closure of Södertälje R&D (2012), he relocated to Macclesfield, UK maintaining his previous role. In early 2017 (February) he decided to return to his home-country Sweden again, which meant leaving AstraZeneca after several decades of service and instead pick up a role as Chief Scientific Officer in EnginZyme – a newly founded biotech start-up focussing on developing a technology platform in biocatalysis, notably building on the immobilization of enzymes.

The Influence of the Porphyrins' Macrocycle and its Metal on the Type, Efficiency and Selectivity of Catalysis

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The synthetic versatility and the potential application of metalloporphyrins (MPs) in different fields have driven the researchers' interest to study these complexes, particularly to mimic biological systems such as cytochrome P-450.[1] The ability of the porphyrins' tetrapyrrolic core to accommodate different metal ions of various charges allow the tuning of their properties for different applications. In the field of catalysis, MPs proved to successfully oxidize several organic compounds under mild conditions. The development of selective, efficient, and easily recoverable and reusable catalysts for oxidation reactions has become one of the main challenges of modern chemistry. In recent years, we have focused our attention on the design of porphyrins and derivatives, the coordination with suitable metals and the investigation of their catalytic efficiency in homogeneous and heterogeneous systems.[1-7] Following our interest on this topic, we report here the synthesis and characterization of iron, manganese and copper porphyrins obtained by structural modification of 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin with the nucleophiles: ethylene glycol (**P2-P5**), 4-mercaptobenzoic acid (**P6-P7**), a galactodentritic derivative (**P8**), ethylenediamine (**P9**), and 4-mercaptopyridine (**P10**). The mono and tetra-substituted derivatives (**P2** and **P5**) were metallated with iron and manganese. The glycol derivatives were immobilized onto two supports: layered double hydroxide (LDH) or silica obtained by the sol-gel process.[1] These MPs provided good results in the oxidation of cyclooctene and cyclohexane in homogeneous and heterogeneous media. The selectivity and efficiency of a series of manganese porphyrins (**MnP2-MnP5**)[2] were compared with manganese chlorins in the oxidation of cyclooctene and cyclohexane using hydrogen peroxide as oxidant.[3] The results showed that MPs are catalytically active and more stable if compared with manganese chlorins. Iron, manganese and copper complexes of **P6** and **P7** bearing one or four 4-mercaptobenzoic moieties provided good to excellent yields for cyclooctene, cyclohexane, and heptane oxidation in homogeneous and heterogeneous media; the products' profile depends on the porphyrin structure and the metal. The tetra-substituted free-base porphyrins (**P8**, **P9** and **P10**), after metallation with Cu(II) ions, afforded a structured and very insoluble solid allowing its use as heterogeneous catalysts.[4-7] The structured solids based on copper porphyrins as coordination polymers can efficiently mimic the activity of catecholase. These works show that it is possible to modulate the selectivity and chemical efficiency of catalytic systems by choosing the appropriate substituent and metal using synthetic metalloporphyrins with both simple and more sophisticated structures. Additionally, some derivatives were characterized by using single-crystal X-ray diffraction studies.

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References:

1. Castro, K.A.D.F.; Simões, M.M.Q.; Neves, M.G.P.M.S.; Cavaleiro, J.A.S.; Wypych, F.; Nakagaki, S., *Catal. Sci. Technol.* **2014,** *4*, 129.
2. Castro, K.A.D.F.; de Lima, F.H.C.; Simões, M.M.Q.; Neves, M.G.P.M.S.; Paz, F.A.A.; Mendes, R.F.; Nakagaki, S.; Cavaleiro, J.A.S., *Inorg. Chim. Acta* **2017,** *455*, 575.
3. Castro, K.A.D.F.; Pires, S.M.G.; Ribeiro, M.A.; Simões, M.M.Q.; Neves, M.G.P.M.S.; Schreiner, W.H.; Wypych, F.; Cavaleiro, J.A.S.; Nakagaki, *J. Coll. Int. Sci* **2015,** *450*, 339.
4. Castro, K.A.D.F.; Simões, M.M.Q.; Neves, M.G.P.M.S.; Cavaleiro, J.A.S.; Ribeiro, R.R.; Wypych, F.; Nakagaki, S., *Appl. Catal. A* **2015,** *503*, 9.
5. Castro, K.A.D.F.; Silva, S.; Pereira, P.M.R.; Simões, M.M.Q.; Neves, M.G.P.M.S.; Cavaleiro, J.A.S.; Wypych, F.; Tomé, J.P.C.; Nakagaki, S., *Inorg Chem* **2015,** *54*, 4382.
6. Castro, K.A.D.F.; Rodrigues, J.M.M.; Mendes, R.F.; Neves, M.G.P.M.S.; Simões, M.M.Q.; Cavaleiro, J.A.S.; Paz, F.A.A.; Tomé, J.P.C.; Nakagaki, S., *J. Catal.* **2016,** *344*, 303.
7. Castro, K.; Figueira, F.; Mendes, R.; Cavaleiro, J.; Neves, M.; Simões, M., Paz, F.A.; Nakagaki, S.; Tomé, J.P.C., ChemCatChem **2017**, doi:10.1002/cctc.20170048.

Mário M. Q. Simões was born at Coimbra in 1965 and obtained his PhD degree in 2001 at the University of Aveiro under the guidance of Professor José A. S. Cavaleiro and Professor Ana M. V. Cavaleiro. He joined the University of Aveiro in 1992, as a training assistant, after working at Hovione - Sociedade Química during a short period (1990-1992) following his degree in Pharmaceutical Sciences at the University of Coimbra (1990). His scientific activity is centred on organic chemistry and catalysis areas. The main research interests are related to catalytic oxidative transformations of organic compounds, both under homogeneous and heterogeneous conditions. He is currently an Organic Chemistry Assistant Professor at the Department of Chemistry of the University of Aveiro and author or co-author of more than 70 scientific publications, 14 books or book chapters, more than 40 oral communications and more than 140 poster presentations.

Rapid Access to Novel Multifunctional Spirocyclic Cores for Drug Discovery

B. A. Chalyk, A. Isakov, M. V. Butko, K. Hrebeniuk, O. V. Savich, O. V. Kucher, K. S. Gavrilenko, T. Druzhenko, V. S. Yarmolchuk, O. Kirichok, A. Chernykh, D. Granat, K. Fominova, P. K. Mykhailiuk

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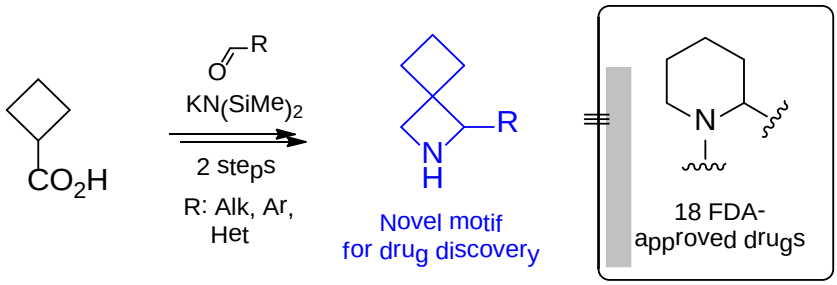
Trends in drug discovery are changing rapidly. During the past decade, terms "*Scaffold hopping*," "*Escape the Flatland*" and "*Conformational restriction*" have been introduced, and have already found huge practical application. Spiro compounds are especially interesting, because they are intrinsically both - 3D-shaped and conformationally restricted.



Scheme 1

In this work, we have rationally designed, synthesized and applied a library of novel multifunctional spirocyclic cores for drug discovery. Details of the synthesis and application of the obtained compounds will be discussed.[1-3]

References:

1. A. Kirichok, M. Kliachyna, I. Pishel, P. K. Mykhailiuk. *Angew. Chem. Int. Ed.* **2017**, *in press* (DOI: 10.1002/anie.201703801).

2. B. A. Chalyk, A. A. Isakov, M. V. Butko, K. V. Hrebeniuk, O. V. Savych, O. V. Kucher, K. S. Gavrilenko, T. V. Druzhenko, V. S. Yarmolchuk, S. Zozulya, P. K. Mykhailiuk *Eur. J. Org. Chem* **2017**, *in press* (DOI: 10.1002/ejoc.201700536).

3. B. A. Chalyk, M. V. Butko, K. S. Gavrilenko, T. V. Druzhenko, P. K. Mykhailiuk *Chem. Eur. J.* **2017**, *submitted*.

Pavel Mykhailiuk was born in Kerch, Ukraine in 1984. In 2000 he won a bronze medal at 32nd International Chemistry Olympiads, IChO (Copenhagen, Denmark). In 2008 he received PhD in Biochemistry at Technical University of Karlsruhe (KIT, Germany) after working with Prof. Anne Ulrich. Thereafter, he joined the Kyiv National Taras Shevchenko University (Ukraine), where he obtained PhD in Chemistry under the supervision of Prof. Igor Komarov. Since then Pavel holds a position Senior Scientist at this University. Independently, in 2009 he joined "Enamine LTD" company (Ukraine), where he currently holds a position of Chief Scientific Officer (CSO). Pavel´s research interests include fluorine-containing compounds, conformationally restricted molecules, 3D-shaped unnatural scaffolds and their application in medicinal chemistry. He is co-author of more than 100 research manuscripts (H=18). In 2014, he was selected as a runner up of EFMC Prize for a Young Medicinal Chemist in Industry. In 2017, Pavel received D.Sc. in organic chemistry at the Kyiv National Taras Shevchenko University (Ukraine).

Designed Aplyronine Warheads for Next-Generation Antibody−Drug Conjugates

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The aplyronines are a family of antimitotic marine macrolides isolated from the Pacific mollusc *Aplysia kurodai*.[1] They are extremely biologically active, showing highly potent antiproliferative effects at picomolar concentrations in human cancer cell lines (e.g. aplyronine A IC_{50} = 0.45 nM HeLa-S3).[2] It has been shown that aplyronine A induces an unprecedented interaction with the structural proteins actin and tubulin, destabilising the cytoskeleton and eventually leading to apoptosis (**Figure 1**).[3] This novel dual protein-targeting mechanism of action combined with their exquisite potency renders the aplyronines promising drug candidates. Importantly, recent advances in cancer chemotherapy have led us to consider conjugating the aplyronines to monoclonal antibodies to produce improved antibody-drug conjugates to target specific tumour cells.

Despite our best efforts, the scarcity and structural complexity of the aplyronines brings its own challenges in supplying material to enable these studies. Based on SAR results for the aplyronines and some related actin-binding macrolides (e.g. reidispongiolides, scytophycins, rhizopodin), we have designed simplified analogues/hybrids (**Figure 1**) with the aim of reducing the synthetic effort, whilst retaining the extraordinary potency of the natural products. Our highly convergent route has led to a substantial reduction in the step count and improved scalability. We have made methodological simplifications with attendant savings of time, effort, and resources relative to those required for the aplyronines themselves.[4] Ultimately, through this function-oriented synthetic approach and attachment of a suitable linker for bioconjugation,[5] we plan to develop a novel structural class of payload for use in next-generation antibody–drug conjugates.

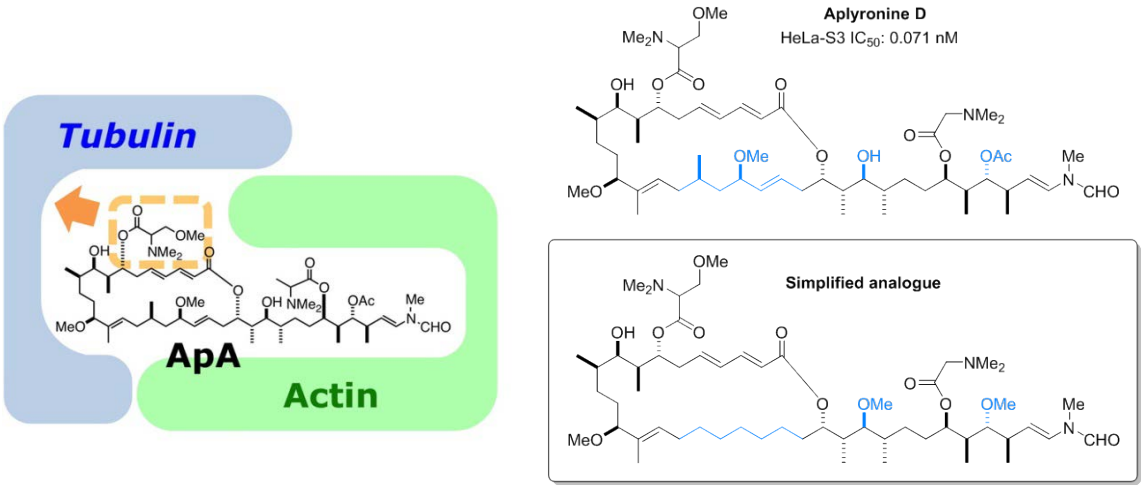
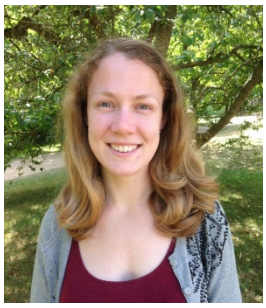


Figure 1: Heterotrimeric complex between aplyronine A, actin and tubulin;[3] structures of aplyronine D and a simplified analogue.

Acknowledgements: We thank Jeremy Parker (AstraZeneca), Simon Williams and Mike Housden for their contributions towards this project; and Trinity College (TP) and AstraZeneca (RP) for financial support.

References:

1. Yamada, K.; Ojika, M.; Ishigaki, T.; Yoshida, Y.; Ekimoto, H.; Arakawa, M. *J. Am. Chem. Soc.* **1993**, *115*, 11020.
2. Yamada, K.; Ojika, M.; Kigoshi, H.; Suenaga, K. *Nat. Prod. Rep.* **2009**, *26*, 27.
3. Kita, M.; Hirayama, Y.; Yoneda, K.; Yamagishi, K.; Chinen, T.; Usui, T.; Sumiya, E.; Uesugi, M.; Kigoshi, H. *J. Am. Chem. Soc.* **2013**, *135*, 18089.
4. Paterson, I.; Fink, S. J.; Lee, L. Y. W.; Atkinson, S. J.; Blakey, S. B. *Org. Lett.* **2013**, *15*, 3118.



Talia Pettigrew was born in Brisbane, Australia. She completed a dual Bachelor of Science (Hons I, Chemistry)/Bachelor of Arts degree at the University of Queensland. Her Honours research with James de Voss and Joanne Blanchfield focussed on isolation of natural products from medicinal herbs. She then undertook a Master of Science Communication Outreach at the Australian National University, touring to regional areas with the Shell Questacon Science Circus. In 2014, Talia began her PhD research with Ian Paterson and David Spring at the University of Cambridge. Her research interests include natural product isolation and total synthesis, as well as function-oriented modifications to natural product syntheses to create improved targets for medicinal applications.

Syntheses and Structures of Bimetallic Complexes Supported by Flexible Di(imino)pyridine-based Macrocycles

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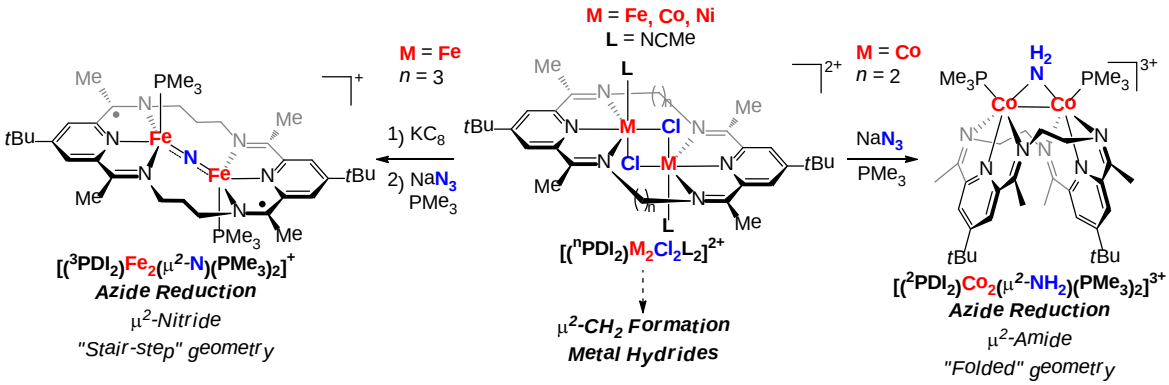
Heterogeneous metal catalysts have been applied extensively in industrial processes, however these materials have certain drawbacks, including low selectivities as well as difficulties in studying mechanistic steps and in tuning the reactivity at the surface.[1] The continuum of metal-metal bonds on the metallic surfaces generates a "sea-of-electrons" that is available for performing chemical reactions. In a similar sense, electronically flexible ligands can function as electron reservoirs, mimicking the behavior of metal atoms as ligands.[2] Thus, we are interested in developing redox-active, macrocycle-supported homogeneous metal cluster complexes to mimic the redox chemistry and small molecule activation of heterogeneous metallic surfaces. We have developed and synthesized a series of new bimetallic clusters (Fe, Co and Ni) bearing pyridyldiimine (PDI) derived macrocycles as electronically flexible ligands. The ^{n}PDI$_2$ macrocyclic ligands exhibited geometric flexibility by forming either "stair-step" or "folded" geometries, which play an important role in tuning the degree of metal-metal bonding. The dicationic, dicobalt(II) dichloride complex of ^{2}PDI$_2$ ligand was shown to reduce the azide anion and afford μ^2-phosphinimido and μ^2-amido products in good yields, suggesting the transient formation of a μ^2-nitride. Similarly, reduction of the azide anion by an isoelectronic ^{3}PDI$_2$ diiron(II) complex was achieved to form an isolable, bridging diiron(III) μ^2-nitride complex, which thermolyzes into a diiron(II) μ^2-amido complex by way of hydrogen atom transfer (HAT) involving acetonitrile. As a comparison, the reaction of the dinickel(II) complex of the ^{2}PDI$_2$ ligand with azide anion yields a dinickel(II) bis(μ^2-azido) complex. One or two electron reduction of dinickel(II) ^{n}PDI$_2$ complexes afforded mixed-valent dinickel(I,II) or dinickel(I) monohalide complexes, respectively. (**Scheme 1**)



Scheme 1: Chemistry of metal clusters supported by flexible di(imino)pyridine-based macrocycles.

Acknowledgements: We thank the University of Pennsylvania for funding.

References:

1. Muetterties, E. L. *Science* **1977**, *196*, 839.
2. Chirik, P. J.; Wieghardt, K. *Science* **2010**, *327*, 794.
3. a) Brown, S. D.; Mehn, M. P.; Peters, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 13146; b) Walstrom, A.; Pink, M.; Yang, X. F.; Tomaszewski, J.; Baik, M. H.; Caulton, K. G. *J. Am. Chem. Soc*., **2005**, *127*, 5330; c) Schöffel, J.; Rogachev, A. Y.; George, S. D.; Burger, P. *Angew. Chem. Int. Ed.*, **2009**, *48*, 4734; d) Schendzielorz, F. S.; Finger, M.; Volkmann, C.; Wurtele, C.; Schneider, S. *Angew. Chem. Int. Ed.*, **2016**, *55*, 11417.
4. C. C. H. Atienza, A. C. Bowman, E. Lobkovsky, P. J. Chirik, *J. Am. Chem. Soc.*, **2010**, *132*, 16343.

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Pd-Catalyzed C–H Functionalization Events Directed by 1,2,3-Triazoles

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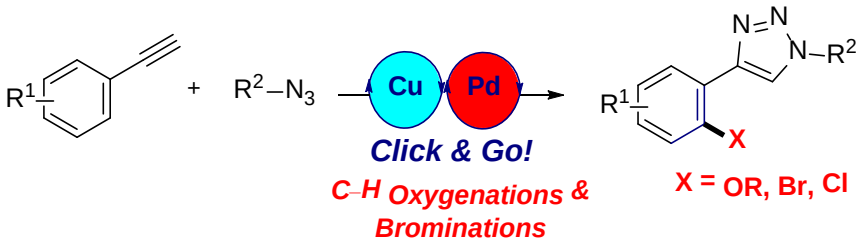
Metal-catalyzed C−H functionalizations are today established methods in the synthetic chemist's toolbox.[1] The common approach implies the use of a directing group (DG), which by coordination to a metal catalyst enables the selective activation of a proximal C−H bond through a cyclometalation process.[2] Despite the availability of a plethora of DGs, expanding the scope to other versatile motifs remains a critical challenge in modern chemistry. In this communication we will disclose our latest results on the development of unprecedented triazole-directed Pd-catalyzed C(sp^2)−H functionalization processes of arenes and certain alkenes.[3] The key feature relies on the use of simple triazoles prepared in a straightforward fashion upon "click chemistry" as practical DGs in various C−heteroatom bond-forming processes In particular, our oxygenation and halogenation protocols are distinguished by their wide group tolerance, site-selectivity and DG and substrate-controlled regioselectivity (***Scheme 1***). As a result, these procedures complement existing methodologies and represent rare examples of post-synthetic C−H functionalizations of "click" compounds.[4] Importantly, the characterization of a triazole-containing palladacycle and *in-depth* DFT studies support a mechanistic proposal involving a Pd(II)/Pd(IV) catalytic cycle.



Scheme 1: 1,2,3-Triazole-directed Pd-catalyzed C−H functionalization processes.

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References:

1. Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900.
2. a) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2015**, *112*, 5879. b) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. c) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147.
3. a) Irastorza, A.; Aizpurua, J. M.; Correa, A. *Org. Lett.* **2016**, *18*, 1080. b) Goitia, A.; Gómez-Bengoa, E.; Correa, A. *Org. Lett.* **2017**, *19*, 962.
4. For selected examples of 1,2,3-triazoles assisted C−H functionalization processes, see: a) Ye, X.; Xu, C.; Wojtas, L.; Akhmedov, N. G.; Chen, H.; Shi, X. *Org. Lett.* **2016**, *18*, 2970. b) Cera, G.; Haven, T.; Ackermann, L. *Angew. Chem. Int. Ed.* **2016**, *55*, 1484. c) Al Mamari, H. H.; Diers, E.; Ackermann, L. *Chem. Eur. J.* **2014**, *20*, 9739. d) Gu, Q.; Al Mamari, H. H.; Grazyk, K.; Diers, E.; Ackermann, L. *Angew. Chem. Int. Ed.* **2014**, *53*, 3868. e) Ye, X.; Shi, X. *Org. Lett.* **2014**, *16*, 4448. f) Ye, X.; He, Z.; Ahmed, T.; Weise, K.; Akhmedov, N. G.; Petersen, J. L.; Shi, X. *Chem. Sci.* **2013**, *4*, 3712.

Arkaitz Correa studied Chemistry at the University of the Basque Country (UPV/EHU), where he finished his PhD in 2006 under the guidance of Prof. Esther Domínguez. Along that time, he did a 3-month stay at the University of Groningen in the group of Prof. Ben L Feringa. In 2007 he joined the group of Prof. Carsten Bolm at the RWTH Aachen University (Germany) as a postdoctoral researcher for 2 years. Then, he moved to the ICIQ (Tarragona) to undertake further postdoctoral studies with Prof. Ruben Martin (2008-2014). In april 2014, he started his independent career at UPV/EHU as a Ramón y Cajal fellow and his current research interests are primarily focused on the field of C−H functionalization and heterocyclic chemistry.

Use of Branched and Dendritic Scaffolds for Controlling Selectivity in Organocatalysis

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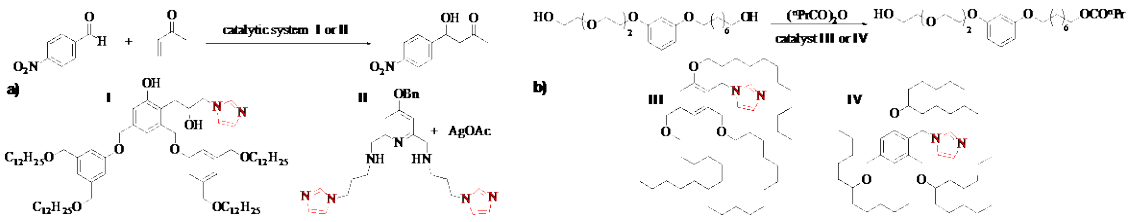
While the field of organocatalysis underwent fast development in the past decade, many organocatalytic systems still suffer from low activity or selectivity. Whereas one can counterbalance the low activity of a catalyst by increasing the reaction time or the catalyst loading, the impaired selectivity is irreparable.

The talk will mainly focus on two case studies of selectivity aspects in reactions promoted by dendritc or branched compounds equipped with an organocatalytically-active unit. In the case of the increasingly popular Baylis-Hillman reaction,[1] we found that homogeneous dendritic imidazole-based catalysts suffer from reduced chemoselectivity, as compared to their polystyrene-supported analogues. Hypothesizing that the superior chemoselectivity of the latter originates from the hydrophobic envelopment of the catalytic sites in the polymer-supported systems, we prepared and examined a series of branched/dendritic N-alkylimidazole-based catalysts with the catalytic site, partially enveloped by flexible hydrophobic tails, which demonstrated a sharp improvement of the chemoselectivity in the model reaction (e.g. catalyst **I**, Scheme 1a). Alternatively, branched organocatalysts were used in conjunction with Lewis acid additives, inducing almost perfect chemoselectivity (e.g. catalyst **II**, Scheme 1a).

Site-selective catalysis of multisite substrates opens new gateways to natural product modifications and protection-free organic synthesis. Recently, outstanding examples of such selectivity in functionalization of polyalcohol substrates were reported.[2] These were based on inducing specific interactions of the catalyst with the substrate through an intricate network of reversible covalent or supramolecular bonds, or on matching the catalyst reactivity to that of a particular site on the substrate. We hypothesized that a similar differentiation, between chemically similar reactive functionalities within a di- or a multifunctional substrate, could be achieved using compartmentalization and polarity gradient principles in dendritic catalysts. First demonstration of this principle was achieved using internally-functionalized branched and dendritic catalysts and model amphiphilic diol substrates (e.g. Scheme 1b).



Scheme 1: Branched/dendritic catalytic systems for the Baylis-Hillman (a) and acylation (b) reactions.

References:

1. a) Basavaiah D.; Veeraraghavaiah G. *Chem. Soc. Rev.* **2012**, *41*, 68. b) Wei Y.; Shi M. *Chem. Rev.* **2013**, *113*, 6659.
2. a) Ueda Y.; Kawabata T. *Top. Curr. Chem.* **2016**, *372*, 203. b) Giuliano M. W.; Miller S. J. *Top. Curr. Chem.* **2016**, *372*, 157.

Moshe Portnoy is an associate professor of chemistry in Tel Aviv University. After graduating from Tel Aviv University in 1987, he conducted his Ph.D. research (1987-1993) in the Weizmann Institute of Science under the guidance of Prof. David Milstein. After two post-doctoral fellowships, one with Prof. Itamar Willner of the Hebrew University (1994-1995) and one with Prof. Barry M. Trost in Stanford University (1995-1997), he joined the faculty of the School of Chemistry of the Tel Aviv University, where he has been promoted to his current position in 2008. His research spreads over several areas of organic chemistry, among them development of new synthetic methods, solid-phase synthesis, organocatalysis, dendrimers and their applications in catalysis and life sciences.

Organocatalysed Asymmetric Synthesis of Sulfur-Containing Heterocycles: from Tetrahydrothiophenes to 1,5-Benzothiazepines

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Organocatalytic domino reactions are fundamental modern tools in organic synthesis.[1] Chiral molecules, mainly derived from readily available amines, demonstrated to promote two or more successive chemical transformations in one reactor, driving the sequence of reactions with high stereocontrol. The importance of these methodologies is even more evident when applied to the synthesis of relevant bioactive heterocyclic compounds and pharmaceuticals.[2] In this communication, we illustrate the stereoselective syntheses of highly functionalized tetrahydrothiophenes, bearing three contiguous stereocenters, one of them quaternary, more challenging spirotetrahydrothiophenes, both obtained via a double Michael reaction promoted by a readily available amine thiourea. The first report, to produce highly enantioenriched popular drugs, i.e. the *N*-unprotected 1,5-benzotiazepines, by using only 1 mol% catalytic loading of a *Cinchona*-alkaloid derived squaramide, will be also presented (**Figure 1**).[2]

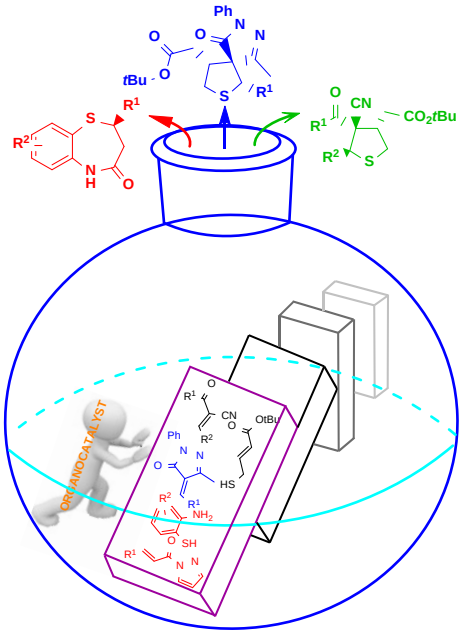

Figure 1: Asymmetric organocatalysed domino reactions leading to sulfur-containing heterocycles.

Acknowledgements: We thank MIUR for financial support and European COST Action CM0905-Organocatalysis.

References:

1. a) Grondal, C.; Jeanty, M.; Enders, D. *Nat. Chem*. **2010**, *2*, 167. b) Volla, C. M. R.; Atodiresei, I.; Rueping, M. *Chem. Rev.* **2014**, *114*, 2390. c) Tietze, L. F. *Domino Reactions: Concepts for Efficient Organic Synthesis*, Wiley-VCH, **2014**.
2. Moyano, A.; Rios, R. *Chem. Rev.* **2011**, *111*, 4703.
3. a) Meninno, S.; Croce, G.; Lattanzi, A. *Org. Lett*., **2013**, *15*, 3436. b) Meninno, S.; Volpe, C.; Della Sala, G.; Capobianco, A.; Lattanzi, A. *Beilstein J. Org. Chem.* **2015**, *12*, 643. c) Meninno, S.; Overgaard. J.; Lattanzi, A. *Synthesis*, **2017**, *49*, 1509. d) Meninno, S.; Volpe, C.; Lattanzi, A. *Chem. Eur. J.* **2017**, *23*, 4547.

Alessandra Lattanzi was born in Rome. She graduated and received her PhD from “Sapienza” University of Rome. She has been visiting scientist in the groups of Prof. V. K. Aggarwal (Sheffield, 1999-2000) and Dr. N. E. Leadbeater (London, 2001). Since 2005 she has been Associate Professor at University of Salerno. In 2013 she obtained the national italian habilitation for Full Professor in organic chemistry. Her research interests focus on the areas of chirality, stereoselective organocatalysed and metal-catalysed synthesis of heterocyclic compounds and oxidation reactions. She published over 100 papers including reviews in international journals, book chapters and coedited a book on “Asymmetric synthesis of three-membered rings (WILEY, 2017).

Origin of Lewis Acid Induced *endo*/*exo* Selectivity *Enhancement* in the Diels-Alder Reaction: Reduced Steric Penalty for *endo*

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The origin of the *enhancement* for the *endo* preference under Lewis acid (LA) catalysis in the Diels-Alder (DA) reaction has been investigated with the aid of modern reactivity models. It is understood that the *endo* preference in the *uncatalyzed* DA reaction is attributed to complex interactions in bispericyclic transition states on bifurcating reaction pathways.[1] However, the *enhancement* in the *endo* preference under LA *catalysis* has largely remained unexplained. An adapted interaction/distortion analysis[2] has been applied here which is uniquely capable of addressing molecular distortion changes and the consequences of shifts in reaction progress at the TS, caused by LA activation (**Figure 1**). The analysis reveals that the interactions which are most effected by LA activation are the steric repulsion interactions (ΔE_{steric}) as they drop off significantly with distance. LA activation induced shifts in TS reaction progress are thus predicted to reduce the steric penalty for the *endo* diastereomer. It is this reduced steric penalty, and not an enhancement in orbital interactions, in the *endo* pathway that is revealed to contribute most to the selectivity enhancement under LA activation.

Addressed in this presentation is the nature of the compensating interactions that govern the LA induced diastereoselectivity enhancement in the DA reaction. The generality of this rationalization is explored across different substrates. Furthermore, the consequences of shifts in TS reaction progress induced by LA activation on diastereoselectivity in the broader context of catalysis are briefly elaborated upon.

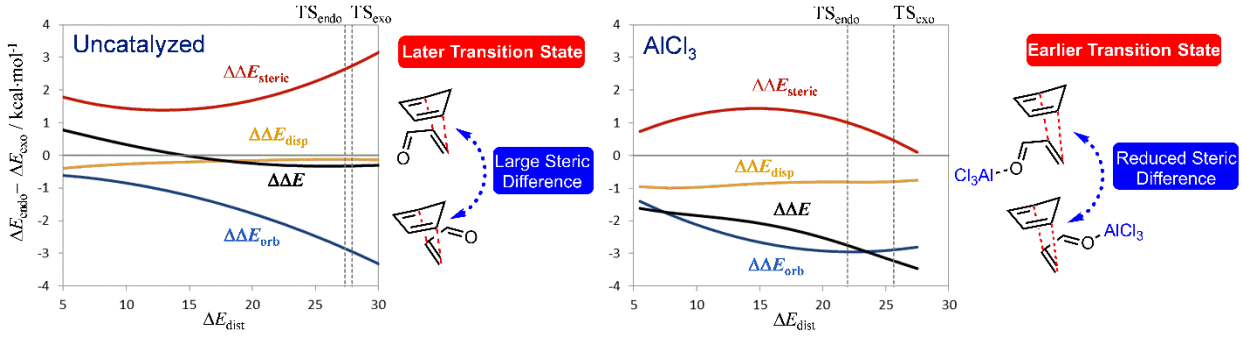

Figure 1: Interaction energy profiles of the difference between the endo and exo pathways as a function of molecular distortion (ΔE_{dist}) along their respective reaction coordinates. Left: Uncatalyzed. Right: $AlCl_3$-Catalyzed. Energy decomposition analysis was performed at the B3LYP-D3/TZVP level of theory. $\Delta\Delta E = \Delta\Delta E_{steric} + \Delta\Delta E_{orb} + \Delta\Delta E_{disp}$; $\Delta\Delta E_{steric} = \Delta\Delta E_{Pauli} + \Delta\Delta E_{elstat}$.

Acknowledgements: L. M. Wolf is grateful to UMass Lowell for financial support.

References:

1. Ess, D. H; Wheeler, S. E.; Lafe, R. G.; Xu, L.; Celebi-Olcum, N; Houk, K. N. *Angew. Chem. Int. Ed.* **2008**, *47*, 7592-7601.
2. a) Wolf, L. M.; Denmark, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 4743-4756. b) Wolf, L. M.; Thiel, W. *J. Org. Chem.* **2014**, *79*, 12136-12147.

Lawrence Wolf received his undergraduate degree in chemistry in 2006 at Drexel University and completed his Ph.D. in organic chemistry at the University of Illinois Urbana-Champaign under the guidance of Prof. Scott E. Denmark in 2012. He subsequently underwent postdoctoral research in the area of computational/theoretical chemistry at the Max-Planck-Institut für Kohlenforschung under the supervision of Prof. Walter Thiel in close collaboration with catalysis research groups. In the Fall of 2016 he joined the chemistry faculty at the University of Massachusetts Lowell as an assistant professor. His current research interests broadly include the development and application of modern reactivity models for elucidating reactivity/selectivity principles focused in catalysis as well as applying strategies in computer aided catalyst design.

Bio- and Chemo-Catalysis in the Chemistry of Lactic Acid and PLLA

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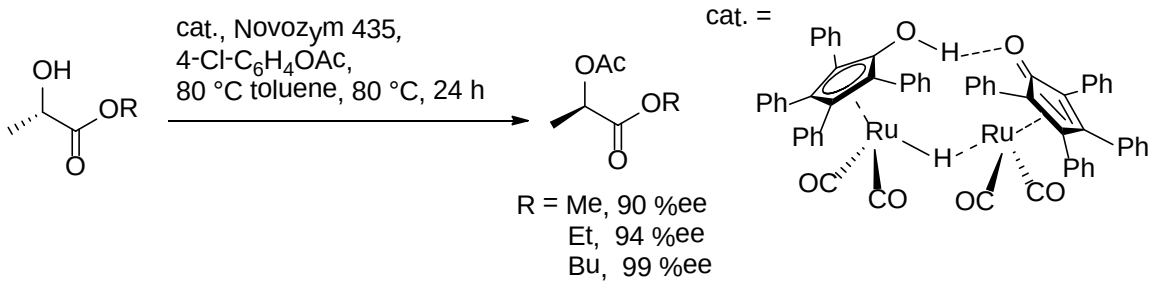
The biodegradable polymers based on lactic acids with steadily increasing applications deserve more effective methods for the manufacturing of both enantiomers of this important α-hydroxyacid. Since a couple of years, there is a large need for D-lactic acid especially as a monomer for PDLA or as a co-monomer for polymerization with L-lactic acid, since polymers containing both enantiomers show some special material properties in comparison to homochiral polylactic acid (PLA). Currently poly-L-lactic acid (PLLA) is dominating the market. Whilst L-lactic acid is readily available via fermentation of biomass in large quantities, the production of D-lactic acid is rather difficult and expensive.

Application of chemical and enzymatic catalysis opens new opportunities for the synthesis of both enantiomers of lactic acid.[1] It allows to improve the overall costs of PLLA/PDLA production by transformation of the manufacturing waste into the valuable chemicals. At the other hand it offers an attractive and scalable approach to many C3-chemicals based on renewable resources. This concept could be applied for the creation of biorefineries on the basis of lactic acid.

Number of catalytic processes such as hydrogenation and epimerisation of lactides[2,3], metal and enzyme catalyzed stereoinversion of lactic acid esters[4] (**Scheme 1**) as well as enzyme catalyzed kinetic resolution of lactides[5] were developed within this overarching concept and will be presented and discussed.



Scheme 1: Metal and enzyme catalyzed stereoinversion of lactic acid esters.

References:

1. Shuklov, I. A., Dubrovina N. V., Kühlein K., Börner A. *Adv. Synth. Cat.* **2016**, 3910**.**
2. Shuklov, I. A., Dubrovina N. V., Schulze J., Tietz .W., Kühlein K., Börner A. *Chem. Eur. J.* **2014**, 957.
3. Tietz W., Schulze J., Boerner A., Kuehlein K., Shuklov I. WO2013010618, 2013.
4. Shuklov I. A., Dubrovina N. V., Schulze J., Tietz .W., Kühlein K., Börner A. *Tetrahedron Lett*. **2012**, *53*(47), 6326.
5. Shuklov I. A., Shuklov A.D., Dubrovina N.V., Kühlein K., Börner A. *Pure Appl. Chem.* **2017**, submitted.

Dr. Ivan Shuklov graduated from Higher Chemical College of the Russian Academy of Sciences in 2002 (Moscow, Russia). He received his Ph. D. with Prof. Dr. K. Krohn in 2006 from the University of Paderborn. Currently he is working at the Leibnitz-Institute of Catalysis (LIKAT, Rostock, Germany). Over the past decade his research concentrates on the various aspects of the chemistry of lactic acid and PLA associated with industrial production. His research interests cover asymmetric catalysis, and solvent effects in organic chemistry.

Sustainable Catalytic Systems based on Acyl-Functionalized Imidazoles

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Sustainability is a key factor for the future of the society, and the development of chemistry, among other components, should be an integrated part of this process. In this context, the search for catalytic systems, both heterogeneous and homogeneous, that allow their profitability with the least impact on the environment is undoubtedly a matter of interest. In this sense, functionalized imidazoles can be employed as versatile components for catalytic systems in combination with different metals, as we have proved for a variety of organic transformations (**Figure 1**). We have employed acyl-functionalized imidazole derivatives as precursors of N-heterocyclic carbene (NHC) ligands for palladium.[1] This type of imidazoles can be also used in combination with metal salts, such as iron(III) chloride or copper(II) chloride, to produce metal-based Lewis acid ionic liquids (i.e. IBLAILs and CuBLAILs), which proved to be very verstatile catalysts in the substitution of allylic alcohols with amines. The selective preparation of different products (i.e. quinolines, 2-allylanilines and 4-allylanilines) can be achieved by modulating the reaction conditions.[2] Moreover, we have employed metal-organic frameworks (MOFs) based on imidazole dicarboxylate and copper as efficient and robust catalyst for the oxidative coupling between carboxylic acids and amides.[3] Similar calcium and barium-organic frameworks can be easily prepared providing a variety of complementary heterogeneous catalysts for different organic transformations, such as quinoline derivative synthesis. Finally, heterogeneous catalysts presented here can be easily recovered and reused. In this communication, we present our fidings in synthetic procedures with versatile and sustainable catatytic systems based on imidazole derivatives.

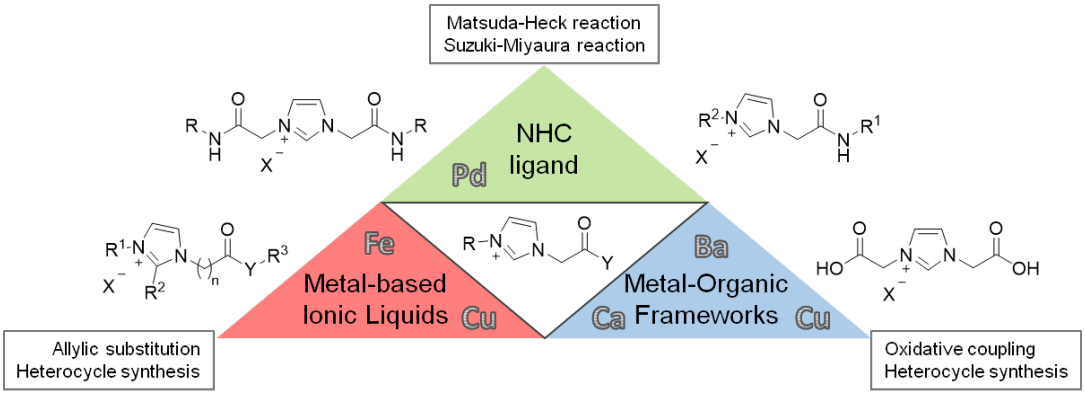

Figure 1: Versatility of catalytic systems based on acyl-functionalized imidazole derivatives.

Acknowledgements: We thank the Spanish Ministry (Ministerio de Economía y Competitividad, CTQ2015-66624-P) and the University of Alicante (VIGROB-285) for financial support. M.A.S. thanks the Spanish Ministry for a Predoctoral Fellowship.

References:

1. Allegue A.; Albert-Soriano M.; Pastor I. M. *Appl. Organomet. Chem.* **2015**, *29*, 624.
2. Trillo P.; Pastor I. M. *Adv. Synth. Catal.* **2016**, *358*, 2929.
3. Albert-Soriano M.; Pastor I. M. *Eur. J. Org. Chem.* **2016**, 5180.

Isidro M. Pastor was born in Alicante (Spain) and studied chemistry at the University of Alicante, from which he obtained B.Sc. (1996) and M.Sc. (1997) degrees. He received his doctorate in 2000 from the University of Alicante. In November 2000, he joined the research group of Prof. Hans Adolfsson at the Arrhenius Laboratory (Stockholm University, Sweden) as a postdoctoral fellow until the end of 2002. In 2003, he returned to the University of Alicante, where he was appointed as a Teaching Assistant in 2003, an Assistant Professor in 2004, a Lecturer in 2007, and an Associate Professor in 2010. His research interests are in the field of organometallic chemistry, heterocyclic chemistry, metal–organic frameworks, and catalysis.

Catalytic Reductions with Manganese N-Heterocyclic Carbenes

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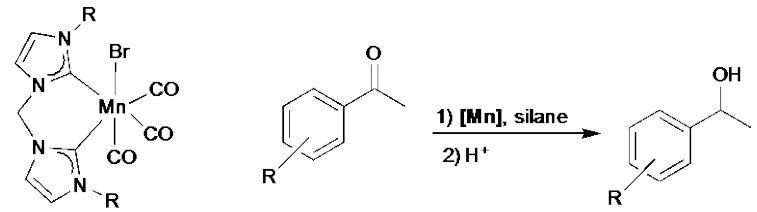
Transition metal-based catalysts are widely used in synthetic organic chemistry, but the majority of the work has been performed applying noble metals (Pd, Rh, Ir, Ru). Global efforts in sustainability, coupled with increasing prices and concerns over long term supplies of precious metals has motivated an increasing interest in developing alternative catalysts derived from abundant, non-toxic metals. Unlike noble metals, catalysts based on earth abundant first row transition metals offer not only economic and environmental advantages but also the ability to tune coordination geometry as well as oxidation and spin states to overcome challenges in substrate scope, activity, and selectivity. In particular, the use of manganese in catalysis is highly attractive, since Mn is the third most abundant transition metal in Earth´s crust, and posses a great potential redox activity due to the number of available oxidation states (-3 to +7). However, in comparison with other first-row transition metals, manganese has received much less attention in catalysis.[1] In line with our interest in developing active Earth-abundant metal-based catalytic systems for reduction reactions,[2] we have recently explored the chemistry and catalytic activity of manganese complexes bearing N-heterocyclic carbene (NHC) ligands. Herein, we present the synthesis and characterisation of a new series of Mn-NHC complexes of general type [MnBr(bis-NHC)$(CO)_3$] and their application as catalysts in transfer hydrogenation and hydrosilylation reactions (Scheme 1). We have found that complexes **1** and **2** display an excellent catalytic activity in the reduction of carbonyl groups. The scope of the reaction and the mechanistic details of these processes will be presented (**Scheme 1**). In addition, we have studied the electrocatalytic reduction of CO_2 mediated by **1** and **2**. Experimental data showed that both **1** and **2** are highly active catalysts for the reduction of CO_2 in the absence of acids. Combined UV-Vis and IR spectroelectrochemical experiments help us not only to provide mechanistic insights of the reductive pathway under inert atmosphere, but also to confirm the remarkable activity under CO_2. Preliminary results also suggest good selectivity for the conversion of CO_2 to CO.



R = Me (1), Mes (2)

Scheme 1: Catalytic hydrosilylation with Mn-NHC complexes.

Acknowledgements: We thank the Fundação para a Ciência e Tecnolgia for financial support through project UID/QUI/00100/2013 and grant fellowships SFRH/BD/52373/2013 (R.L), PD/BD/105994/2014 (M. P.), 041/BTI/2016 (S. F.) and B. R. thanks for IF/00346/2013. We are grateful to COST Action CM1205 for networking. We also thank the European Commission for the ERC-CG-2014-648304 (J. LI.-F.) and the MINECO Severo Ochoa Excellence Accreditation 2014–2018, SEV-2013-0319 (F.F.).

References:

1. Mc Garrigle, E. M., Gilheany, D. G. *Chem. Rev*. **2005**, *105*, 1563.
2. R. Lopes, M. M. Pereira, B. Royo, *ChemCatChem* **2017**, DOI: 10.1002/cctc.201700218.
3. M. Pinto, B. Cardoso, S. Barroso, A. M. Martins, B. Royo, *Dalton Trans.* **2016**, *45*, 13541.
4. J. M. S. Cardoso, A. Fernandes, B. Cardoso, M. D. Carvalho, L. P. Ferreira, M. J. C. Calhorda, B. Royo, *Organometallics* **2014**, *33*, 5670-5677.

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Powerful New Umpolung C-C and C-N Bond Forming Reactions via Enolonium Species

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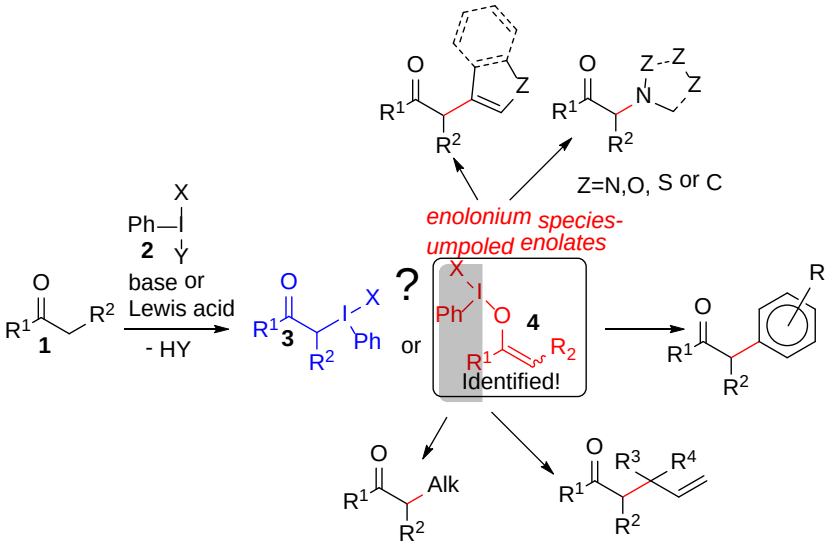
Enolonium Species derived from carbonyl compounds and hypervalent iodine reagents have been hypothesized as highly reactive intermediates in important reactions such as α-halogenation, -trifluoromethylation, -oxygenation and numerous other oxidative processes.[1] Meanwhile the actual structure, enolate-like (**4**) or ketone-like (**3**), has remained controversial since first proposed over 30 years ago. We recently reported the first characterization of these elusive species and showed them to have enolate like structure **4**.[2]

We will discuss how this mechanistic analysis and insight allowed us to design and develop a series of novel C-C and C-N bond forming reactions that rely on the unique and powerful electrophilic reactivity of enolonium species (Scheme 1). In addition to published work on the direct α-alkylation[3,4] and regioselective α-allylation of ketones.[2] We will present the unprecedented umpolung direct C-arylation of ketones (a formal C-H activation reaction) as well as novel amination reactions (Scheme 1).[5,6] The C-arylation process allows the direct coupling arylation of ketone enolates using feedstock aromatic compounds without the need to prepare functionalized aromatic starting materials of traidtional approaches.



Scheme 1: First Characterization of hypervalent Enonolnium Species and Novel Synthetic Applications.

References:

1. V. V. Zhdankin, "Hypervalent Iodine Chemistry: Preparation, Structure, and Synthetic Applications of Polyvalent Iodine Compounds", Wiley, 2013
2. S. Arava, J. N. Kumar, S. Maksymenko, M. A. Iron, K. N. Parida, P. Fristrup, A. M. Szpilman* *Angewandte Chemie Int. Ed.*, **2017**, *56*, 2599-2603.
3. O. S. Shneider, E. Piseravsky, P. Fristrup, A. M. Szpilman* *Org. Lett.*, **2015**, *17*, 282-285
4. T. A. Targel, J. N. Kumar, O. S. Shneider, S. Bar, N. Fridman, S. Maximenko, A. M. Szpilman* *Organ. Biomol. Chem.*, **2015**, *13*, 2546-2549
5. S. Maksymenko, K. N. Parida, G. Pathe, A. More, Y. Lipisa, A. M. Szpilman*, *Submitted for Publication*
6. A. More, G. Pathe, K. N. Parida, S. Maksymenko, Y. Lipisa, A. M. Szpilman*, *Submitted for Publication*

Alex M. Szpilman grew up in Hillerød, Denmark.He completed his M.Sc. at the Technical University of Denmark. He did his Ph.D. at the Weizmann Institute of Science, under the supervision of **Professor Mario D. Bachi**. Alex received a prestigious Carlsberg Postdoctoral Fellowship for his postdoctoral work which was carried out in the **Erick M. Carreira** group at the ETH. In 2009 Alex started his independent career at the Technion. From 2010 to 2012 Alex was the incumbent of the Chaya Career Advancement Chair for young faculty. In 2016, Alex moved to Ariel University. Alex's research programs include nitroxide as catalysts, and umpolung of enolates using hypervalent iodine reagents. Additional research concerns energetic materials, the biological activity of natural products and solar light induced synthetic processes.

Synthesis of Next Generation Catalysts for C_2 + N_1 Aziridinations from Organic Azides and Alkenes

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The direct synthesis of aziridines from alkenes and nitrene sources (C_2+N_1) with a wide variety of organic azides and alkenes has remained an elusive goal in catalytic organometallic chemistry. This shortcoming is seen in many distinct limitations of the reaction with the current crop of catalysts. First, alkyl azides are unreactive for almost all catalysts. Second, significant excess alkenes is normally required. Finally, many catalysts are not effective with a wide variety of functional groups on the organic azide or alkene. All of these issues are critical for preparing biologically relevant and other high value-added aziridines.

Our research has focused on developing a suite of macrocyclic tetracarbene ligands and their associated metal complexes (Figure 1). These metal and ligand combinations address the distinct problems seen in C_2 + N_1 aziridination reactions. The iron catalyst is highly effective with alkyl azides, leading to the first example of this catalysis for fully alkyl aziridination. Furthermore, bicyclic aziridines, which are critical in medicinal chemistry, can also be prepared via an intramolecular version of this reaction. Chromium catalysts are effective at lower alkene loading than the iron catalysts. More importantly, the chromium catalysts show protic functional group tolerance, which has not been previously demonstrated for this reaction.

In addition to the catalytic results, we present mechanistic insights that are derived from a combination of theoretical and experimental studies. Extensive DFT calculations allow for a comparison of the different catalytic systems and help explain why each one is preferable for different classes of azides and alkenes. Experimental product distributions elucidate the step-wise mechanism for the formation of the aziridine from the purported imide intermediate as shown in Figure 1.

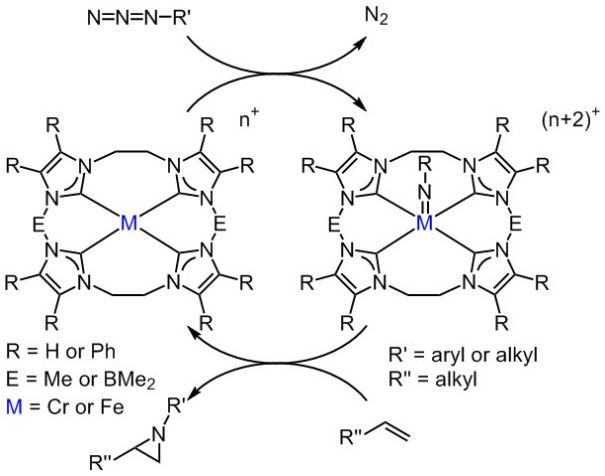

Figure 1. General C_2 + N_1 aziridination reaction catalyzed by macrocyclic N-heterocyclic tetracarbene complexes.

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Dr. David M. Jenkins completed his PhD in inorganic chemistry under the direction of Prof. Jonas Peters at the California Institute of Technology in 2005. Upon completion of his dissertation, he accepted a prestigious Miller Fellowship for Basic Research at the University of California, Berkeley where he worked with Prof. Jeffrey Long on magnetic materials. In 2008, Dr. Jenkins began his independent career at the University of Tennessee and was promoted in 2014 to the position of Mamantov Associate Professor of Chemistry. During his time at the University of Tennessee, he has won numerous university research awards, plus an NSF CAREER grant. His current research focuses on synthetic chemistry of N-heterocycles ranging for homogeneous catalysis to materials development and surface modifications for analyte detection.

In situ Generation of Gold(I) Nanoparticles as Catalyst of Solventless A^3 Coupling Synthesis of Propargylamines

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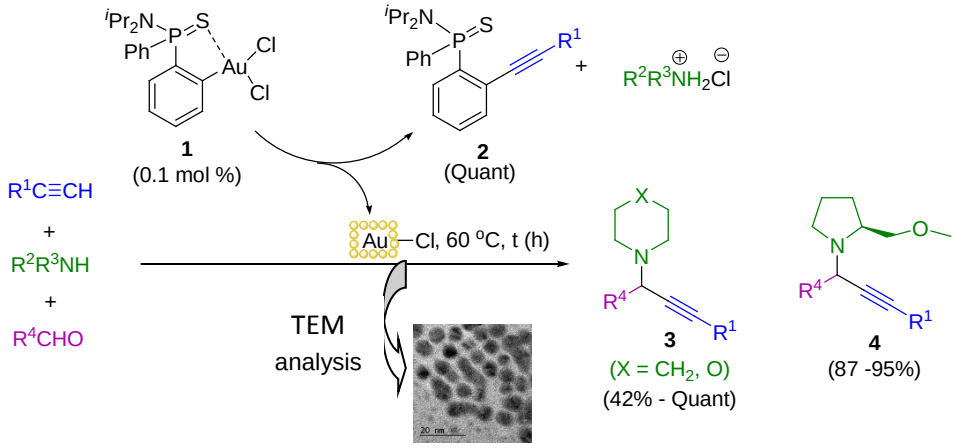
Multicomponent Coupling Reactions (MCR) under solvent-free conditions stand out as a leading force in the globalized search for environmentally-friendly protocols, not only by improving efficiency but also by preventing the formation of chemical wastes.[1] The synthesis of propargylamines via amino-acetylene-aldehyde three-component coupling (A^3) reactions fits very well within these principles. Recently, gold catalysis has become and unique tool in organic synthesis.[2] However, the use of gold as catalyst in solventless A^3-coupling processes remains almost unexplored. We have succesfully synthesized and fully characterized in solution and in the solid-state a phosphinothioic amide gold(III) metallacycle **1** through transmetallation from the corresponding chlorodimethylstannyl derivative.[3] The application of this complex to the preparation of propargylamines (**3**), showed that the target compounds were obtained with excellent conversions employing an ultralow loading of **1** (0.1 mol %) under solvent-free conditions. Moreover, very good results with diastereoselectivites up to 99:1 have been achieved with the chiral reagent (*S*)-2-(methoxymethyl)pyrrolidine (**4**, **Scheme 1**).



Scheme 1: Solvent-free synthesis of propargylamines in presence of 0.1 mol % of **1** as precatalyst.

NMR studies of the reaction revealed that **1** acts as a precatalyst of the process. The reaction begins with the transformation of **1** into the Sonogashira-type product **2** and generation of Au(I) nanoparticles (Au^{I}NPs). These Au^{I}NPs are the real catalyst and were characterized based on XPS and TEM studies. A reaction mechanism promoted by the amine has been proposed, starting with the alkyne replacing a chlorine atom in **1**, and followed by a reductive elimination which affords **2** and Au^{I}NPs.

Acknowledgements: We thank the MINECO and FEDER program for financial support (projects CTQ2011-27705 and CTQ2014-57157-P). E.B.S. thanks the MICINN for a Ph.D. fellowship.

References:

1. a) de Moliner, F.; Kielland, N.; Lavilla, R.; Vendrell, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 3758. b) Singh, M. S.; Chowdhury, S. *RSC Adv.* **2012**, *2*, 4547.
2. a) Kumar, R.; Nevado, C. *Angew. Chem. Int. Ed.* **2017**, *56*, 1994. b) Kramer, S. *Chem. Eur. J.* **2016**, *22*, 15584.
3. Belmonte-Sánchez, E.; Iglesias, M. J.; el Hajjouji, H.; Roces, L.; García-Granda, S.; Villuendas, P.; Urriolabeitia, E. P.; López-Ortiz, F. *Organometallics* **2017**, *36*, 1962.

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Bio-inspired Catalysts for Activation of Small Molecules

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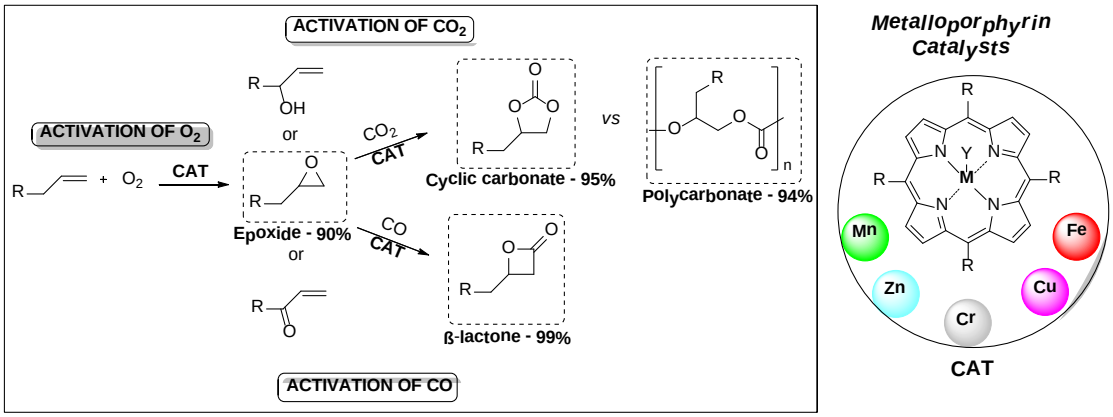
Catalytic reactions involving the activation of highly abundant small molecules, such as molecular oxygen (O_2), carbon dioxide (CO_2) and carbon monoxide (CO) are inherently 'green' processes, which comprise a great interest in current synthetic organic chemistry.[1]

In this context, metalloporphyrin complexes are among the most important biologically inspired catalysts with efficient applications in a variety of catalytic reactions, such as aerobic oxidations, carbonylations and carboxylations, since the combination of the appropriate metal with adequate functional group in the porphyrin's backbone allows the modulation of catalytic activity and selectivity for each desired reaction.[2,3]

Herein, we describe the synthesis and application of *meso*-aryl substituted metalloporphyrins as efficient catalysts for oxidation of olefins in the presence of molecular oxygen. The obtained epoxides can be further used as substrates (with or without isolation) for the successive functionalization through incorporation of CO (carbonylation) leading to biologically relevant β-lactones, or couplings with CO_2 (carboxylation), leading to high-valuable cyclic carbonates or polycarbonates (**Scheme 1**).



Scheme 1: Functionalization of small molecules *via* activation of O_2, CO_2 and CO by metalloporphyrin catalysts

The catalytic evaluation of homogeneous and/or heterogeneous metalloporphyrin catalysts is performed, and the effects of metal, axial counterion and porphyrin's *meso*-phenyl substituents in the groups are appraised in catalytic activity and selectivity.

Acknowledgements: The authors thank Fundação para a Ciência e Tecnolgia and SunStorage project for financial support to Coimbra Chemistry Centre (Pest-OE/QUI/UI0313/2014) and (SAICTPAC/0046/2015), respectively. LDD thanks CNPq (Brazil) for PhD grant 232620/2014-8/GDE. RMBC, SMAP and MJFC thanks FCT for post-doc grant SFRH/BPD/100537/2014, SFRH/BPD/84619/2012 and SFRH/BPD/99698/2014, respectively.

References:

1. a) L. Que, Jr.; W. B. Tolman.; *Nature* **2008**, 455, 333. b) Gavriilidis, A.; Constantinou, A.; Hellgardt, K.; Hii, K.K.; Hutchings, G.J.; Brett.; Kuhn, S.; Marsden, S.P. *React. Chem. Eng.* **2016**, 1, 595.
2. a) Hiroto, S.; Miyake, Y.; Shinokubo, H.; *Chem. Rev*. **2017**, 117, 2910. b) Silva, M.; Fernandes, A.; Bebiano, S.S.; Calvete, M.J.F.; Ribeiro, M.F.; Burrows, H.D.; Pereira, M.M. *Chem. Commun*. **2014**, 50, 6571.
3. a) Liu, Q.; Wu, L.; Jackstell, R.; Beller, M.; *Nature Commun.* **2015**, 6, 5933. b) C-Y. Huang, A. G. Doyle, *Chem. Rev*. **2014**, 114, 8153. c) Beller, M.; Centi, G.; Sun, Licheng.; *ChemSusChem* **2017**, 10, 6.

Maria Miguéns Pereira ibidem Mariette Pereira is Associate Professor with habilitation at the University of Coimbra since 2007. She finished the PhD in Chemistry in 1992-University of Coimbra, and later worked as Researcher at the Universities of Liverpool in 1993 and Autónoma of Barcelona in 1997-1998. She is the President of Coimbra Delegation of Portuguese Chemical Society since 2014. She is shareholder and was the Director of Chemical Research Laboratory of the pharmaceutical company Luzitin, Lda between 2010-2014. She is the Coordinator of Catalysis & Fine Chemistry Laboratory of Coimbra Chemistry Research Center since 2000. Her scientific interests are centered on the development of sustainable processes for catalytic reactions namely carbonylation and oxidation reactions for preparation of compounds with potential biological activity. She as a long-term experience on the development of innovative synthetic processes for tetrapyrrole macrocycles for biomedicinal applications, namely photodynamic therapy of cancer (PDT), microorganism inactivation (PDI) and also molecular imaging. She has published about 140 scientific papers in international scientific journals, 3 books, 5 book chapters and is the author of 4 international patents, two of them accepted in more than 30 countries.

Flash Communications

A Simple Synthetic Entryway into Palladium Cross-Coupling Catalysis

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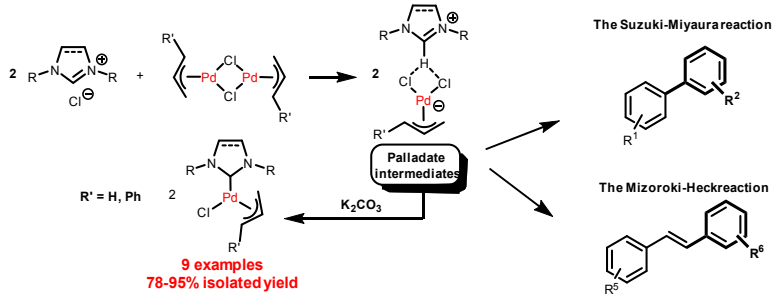
Palladium-*N*-heterocyclic carbene (NHC) complexes have been widely studied in the last decade and have been ubiquitously used in homogeneous catalysis, especially in cross-coupling chemistry.[1-3] Palladium(II) complexes of the type [Pd(NHC)(R-allyl)Cl] (R-allyl = allyl, metallyl, cinnamyl, indenyl) have shown high catalytic activity in many important C-C and C-heteroatom bond formations.[4] The manner in which these complexes are synthesised has been an interest of ours since their isolation.[4] The original synthetic approach made use of a strong base (e.g. KO^{t}Bu) to generate the free carbene followed by addition of a suitable palladium precursor such as palladium dimers [Pd(allyl)(μ-Cl)]$_2$ or [Pd(cinnamyl)(μ-Cl)]$_2$. An improved, efficient and scalable protocol for the synthesis of [Pd(NHC)(R-allyl)Cl] pre-catalysts has now been developed. The one-pot procedure involves readily available imidazolium salt and [Pd(R-allyl)(μ-Cl)]$_2$ in the presence of the inexpensive K_2CO_3, as base, and does not require the use of an inert atmosphere. A scope of this synthesis was obtained leading to Pd(II) pre-catalysts (9 examples 75-98% yield). To gain a better understanding of the reaction, the intermediate [Pd(η^3-cinnamyl)Cl$_2$][IPrH] was synthesised. The complex was unambiguously characterised by ^{1}H and {^{1}H}^{13}C NMR spectroscopy, elemental analysis and single crystal X-ray diffraction. The catalytic activity of the palladate intermediate was investigated in various cross-coupling reactions. Delightfully high catalytic activity was found for the Suzuki-Miyaura reactionand the Mizoroki-Heck reaction. Both reactions are being optimised and intensively studied in our laboratory in order to gauge the potential of the palladate intermediate in cross-coupling reactions.



Scheme 1: Synthesis and application of [Pd(R-allyl)Cl$_2$][NHCH].

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References:

1 N. Marion, S.P. Nolan, Acc. Chem. Res. **2008**, *41*, 1440.
2 G. C. Fortman and S. P. Nolan, Chem. Soc. Rev. **2011**, *40*, 5151.
3 E. A. B. Kantchev, C. J. O'Brien, and M. G. Organ, Angew. Chem. Int. Ed. **2007**,*46*, 2768; Angew. Chem. **2007**, *119*, 2824
4 a) M.S. Viciu, R.F. Germareau, S.P. Nolan, Org. Lett. **2002**, *4*, 4053; b) Marion, N.; Navarro, O.; Mei, J.; Stevens, E. D.; Scott, N. M.; Nolan, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 4101.
5 Other examples of the catalytic activity of [Pd(NHC)(R-allyl)Cl] precatalysts: a) G. Bastug and S. P. Nolan, Organometallics **2014**, *33*, 1253; b) A. Chartoire, X. Frogreux and S. P. Nolan, Adv. Synth. Catal. **2012**, *352*, 1897; c) F. Izquierdo, M. Corpet and S. P. Nolan, Eur. J. Org. Chem. **2015**,*9*, 1920.

Aryloxide-Facilitated Catalyst Turnover in Enantioselective α,β-Unsaturated Acyl Ammonium Catalysis

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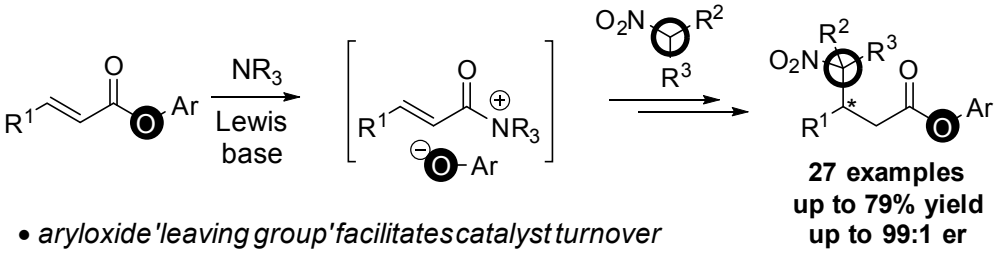
A new general concept for α,β-unsaturated acyl ammonium catalysis[1] has been developed which exploits *p*-nitrophenoxide release from an α,β-unsaturated *p*-nitrophenyl ester substrate to facilitate catalyst turnover. This method was used for the enantioselective isothiourea-catalyzed Michael addition of nitroalkanes to α,β-unsaturated *p*-nitrophenyl esters in generally good yield and with excellent enantioselectivity (27 examples, up to 79% yield, 99:1 er). Mechanistic studies including kinetic analysis, catalyst labeling and crossover studies have also been performed to deliver a fundamental understanding of this process.[2] (**Scheme 1**)



Scheme 1: Michael addition of nitroalkanes to α,β-unsaturated aryl esters using a Lewis basic isothiourea catalyst.

Acknowledgements: We thank European Research Council under the European Union's Seventh Framework Programme (FP7/2007-2013) ERC grant agreement no. 279850 (A.D.S) and the EPSRC (EP/J018139/1, A.M.). A.D.S. thanks the Royal Society for a Wolfson Research Merit Award. We also thank the EPSRC UK National Mass Spectrometry Facility at Swansea University.

References:

1. For a review see S. Vellalath, D. Romo, *Angew. Chem. Int. Ed.* **2016**, *55*, 13934-13943; *Angew. Chem.* **2016**, *128*, 14138-14148.

2. Manuscript in preparation.

Oxo-molybdenum and Oxo-rhenium Complexes as Efficient Catalysts for the Deoxygenation of Carbonyl Compounds

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During many years, high-valent oxo-molybdenum and oxo-rhenium complexes were employed as excellent catalysts for oxygen transfer reactions. Since 2003, these complexes have emerged as powerful catalysts for the activation of X-H (X = Si, B and H) bonds and for the reduction of several functional groups.[1] This new reactivity represents a complete reversal from the traditional role of these complexes as oxidation catalysts and opened a new research area for oxo-molybdenum and oxo-rhenium complexes. These oxo-complexes have also proved to be excellent catalysts for the deoxygenation of different classes of organic compounds such as sulfoxides,[2] pyridine *N*-oxides,[2] aromatic nitro compounds[3] and epoxides.[4]

This communication will highlight our recent work on the deoxygenation of carbonyl compounds to the corresponding alkane or alkene derivatives catalyzed by oxo-molybdenum and oxo-rhenium complexes using silanes or alcohols as reducing agents (Figure 1).[5]

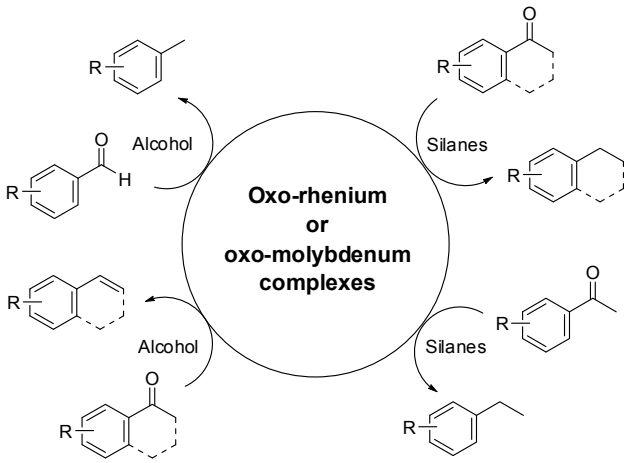

Figure 1: Deoxygenation of carbonyl compounds catalyzed by oxo-complexes

Acknowledgements: The authors thank the project UID/QUI/00100/2013 and the Portuguese NMR Network (IST–UTL Center) for providing access to the NMR facilities. ACF (IF/00849/2012) acknowledges FCT for the "Investigador FCT" Program.

References:

1. Sousa, S. C. A.; Cabrita, I.; Fernandes, A. C. *Chem. Soc. Rev.* **2012**, *41*, 5641.
2. Fernandes, A. C.; Romão, C. C. *Tetrahedron* **2006**, *62*, 9650.
3. Noronha, R. G.; Romão, C. C.; Fernandes, A. C. *J. Org. Chem.* **2009**, **74**, 6960.
4. Sousa, S. C. A.; Fernandes, A. C.*Tetrahedron Lett.* **2011**, *52*, 6960.
5. a) Bernardo, J. R.; Fernandes, A. C. *Green Chem.* **2016**, *18*, 2675. b) Fernandes, T. A.; Bernardo, J. R.; Fernandes, A. C. *ChemCatChem* **2015**, *7*, 1177. c) Fernandes, T. A.; Fernandes, A. C. *ChemCatChem* **2015**, *7*, 3503. d) Sousa, S. C. A.; Fernandes, T. A.; Fernandes, A. C. *Eur. J. Org. Chem.* **2016**, 3109.

Selective Synthesis of Spirooxindoles by an Intramolecular Heck-Mizoroki Reaction

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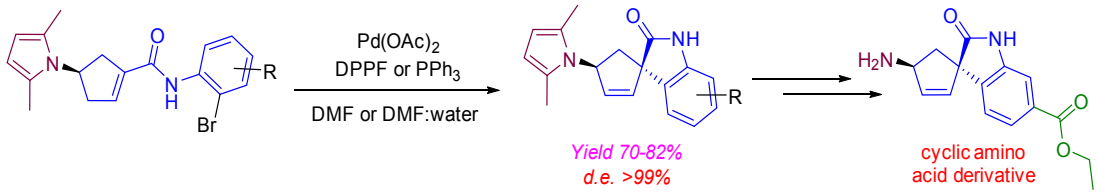
Heterocyclic spirooxindoles are present in many natural products and are important synthetic targets due to their biological activity and applications for pharmaceutical lead discovery.[1] Furthermore, unnatural five membered cyclic amino acids exhibit the potential for important biological and pharmaceutical applications. However, their synthesis with multiple stereocenters remains challenging. This is reflected by the rather limited diversity in substitution patterns both among published pharmaceuticals lead structures and drugs, and in commercially available building blocks.[2]

Herein, we report a highly diastereoselective synthesis of cyclopentene-spirooxindole derivatives via palladium(0)-catalyzed intramolecular Heck-Mizoroki reaction using aryl bromides as precursors.[3,4] The reactions were optimized towards exclusive formation of the desired product in good isolated yield (70-82%) and high diastereoselectivity (>99%). This protocol can be useful to introduce several functionalities to the aromatic nucleus of the spirooxindoles. The high diastereoselectivity of the desired product was rationalized by DFT calculations. Further, to demonstrate the potential application of the current protocol a functionalized spiroproduct was transformed into a cyclic amino acid derivative.



Scheme 1. Palladium(0)-catalyzed intramolecular Heck-Mizoroki reaction using aryl bromides.

References:

(1) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, *112*, 6104.
(2) Singh, R.; Vince, R. *Chem. Rev.* **2012**, *112*, 4642.
(3) Larhed, M.; Odell, L. *Science of Synthesis: Cross Coupling and Heck-Type Reactions 3, Metal-Catalyzed Heck-Type Reactions and C–C Cross-Coupling via C–H Activation*; Larhed, M., Ed.; Thieme, 2013.
(4) Wetzel, A.; Bergman, J.; Brandt, P.; Larhed, M.; Brånalt, J. *Org. Lett.* **2017**, 1602.

Hydroformylation of Olefins Employing Low Generation Metallodendrimers of Rh and Ru as Catalyst Precursors

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Metallodendrimers have in the last decade or so emerged as feasible alternatives to traditional catalysts based on mononuclear complexes[1]. The application of these dendritic complexes as catalyst precursors in a range of organic transformations has therefore received growing attention in recent years[2]. Here we report on the development of new low generation metallodendrimers of rhodium and ruthenium and their application as catalyst precursors in the hydroformylation of olefinic substrates. Examples of the multinuclear complexes employed in this study are shown in **Figure 1.**

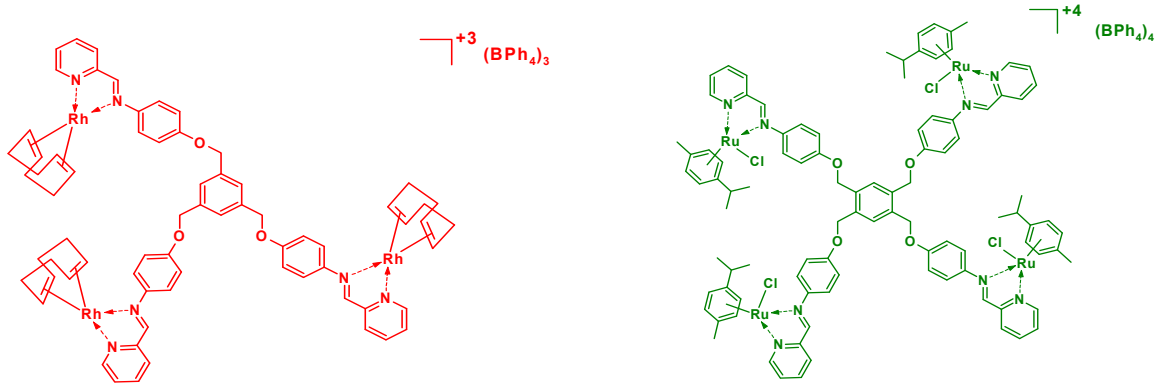

Figure 1: Some dendritic catalysts employed in olefin hydroformylation

Both the Rh and Ru dendritic systems showed good hydroformylation activity and were found to outperform simple model mononuclear analogues both in terms of selectivity and activity. Furthermore it was observed that under similar reaction conditions the Rh catalysts were substantially more active than their Ru analogues. Operating under mild reaction conditions it was found that a fair amount alkene isomerization occurred leading to the detection of reasonably high levels of internal alkenes. These subsequently undergo hydroformylation leading to the formation of a variety of branched aldehydes. The impact of a range of reaction conditions on the overall efficiency of the hydroformylation process was systematically studied and the results obtained will be presented in this talk.

Acknowledgements: NRF-DST Centre of Excellence in Catalysis, c*change., for financial support....

References:

1. A-M. Caminade, R. Laurent, A. Ouali, J-P. Majoral, *Inorg. Chim. Acta*, **2014,** *409*, 66-88.
2 S.F. Mapolie, J. L. van Wyk, *Inorg. Chim. Acta*, **2013,** *394*, 649-655

CpM(NHC) (M = Cr, Ni) Complexes: Synthesis, Electrochemistry, DFT Studies and C-C and C-O Catalytic Applications

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Transition metal complexes bearing a combination of the historically important cyclopentadienyl and stabilizing N-heterocyclic carbene ligands have become of increasing interest due to their multi-functional applicability. These include their uses as synthetic precursors, biologically active compounds, luminescent-active complexes, and highly active organocatalysts for unique transformations.[1,2] We have been investigating synthetic routes to new cyclopentadienyl Cr(III) and Ni(II) NHC complexes from the corresponding metallocenes. Facile C-H activation of imidazolium halide salts with one cyclopentadienyl ring leads to *in situ* generation and coordination of the NHC and halide ligands, with concomitant loss of one cyclopentadiene molecule. A range of structurally and electronically diverse NHC ligands have been designed with the aim of producing metal-NHC complexes that would demonstrate stability in solution, yet remain catalytically active. While the series of [CpNiBr(NHC)] complexes is formed directly from nickelocene, the series of [CpCr(Br)(Cl)(NHC)] complexes was obtained after oxidation of the sensitive [CpCrBr(NHC)] species. The electrochemistry of both series of complexes, supported by DFT calculations, was investigated (**Figure 1**). Metal- and NHC-based redox processes were observed and systematically evaluated. The electrochemistry and DFT results support the experimental catalytic efficiency of the different Ni(II)- and Cr(III)-NHC complexes, evaluated as catalysts in a range of C-C and C-O transformation reactions.[3,4] In general, the metal complexes bearing electron-donating NHCs were the most active and long-lived, and were the least susceptible to fast catalyst deactivation. Comparative stability, reactivity, catalytic, and electrochemical trends between the two series of complexes will be presented.

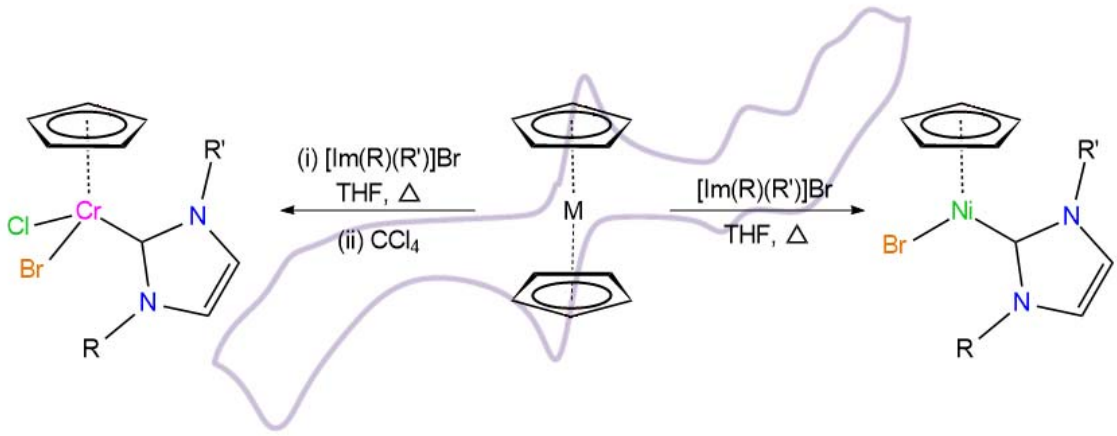

Figure 1: Synthesis and electrochemistry of potential Ni(II) and Cr(III) NHC catalysts

References:
[1] E. A. Standley, S. J. Smith, P. Műller, T. F. Jamison, *Organometallics*, **2014**, *33*, 2012–2018.
[2] Z. Wang, L. Jiang, D. B. M. Khairunnisa, J. Zhao, T. S. A. Hor, *Coord. Chem. Rev.*, **2015**, *293-294*, 292–326.
[3] F. P. Malan, E. Singleton, P. H. van Rooyen, M. Landman, *J. Organomet. Chem.*, **2016**, *813*, 7-14.
[4] F. P. Malan, E. Singleton, B. Bulling, I. Cukrowski, P. H. van Rooyen, M. Landman, *Mol. Catal.* **2017**, *432C*, 47-56

Azidoperfluoroalkanes: Synthesis and Application

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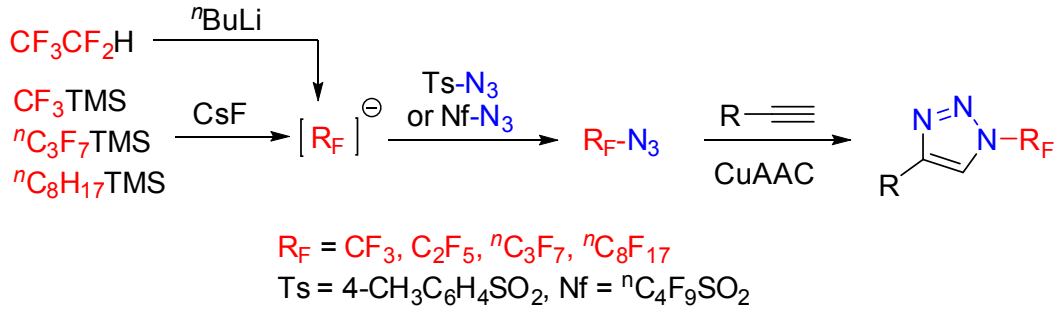
The importance of fluorinated compounds has been rapidly increasing in recent years. A plethora of methods exists for the introduction of trifluoromethyl and perfluoroalkyl motifs into various organic compounds to form carbon- and heteroatom-bound structures. However, methods for synthesizing *N*-perfluoroalkyl derivatives are still very limited and new approaches are highly sought-after.

We have recently reported an efficient synthesis of azidotrifluoromethane and longer carbon chain analogues, from the reaction of perfluoroalkyl carbanion equivalents with electrophilic azides. Azidoperfluoroalkanes can serve as fluorinated building blocks which readily underwent copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) with terminal alkynes to provide previously inaccessible *N*-perfluoroalkyl triazoles (**Scheme 1**). [1]



Scheme 1: Synthesis of azidoperfluoroalkanes and their application in CuAAC.

Acknowledgements: We thank the Czech Academy of Sciences for financial support (Research Plan RVO: 61388963).

References:

1. Z. E. Blastik, S. Voltrová, V. Matoušek, B. Jurásek, D. W. Manley, B. Klepetářová, P. Beier *Angew. Chem. Int. Ed.* **2017**, *56*, 346-349.

Pd-Catalyzed Asymmetric Addition of *N*-Heterocycles to Alkoxyallene

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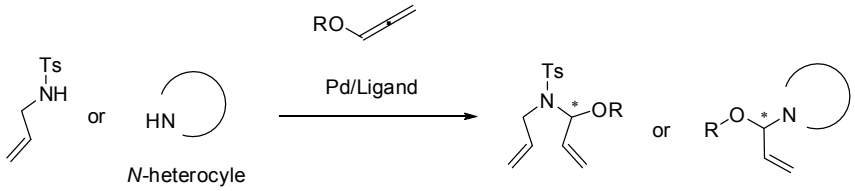
We recently reported the Pd-catalyzed asymmetric asymmetric addition of Ts-protected amines to alkoxyallene,[1-3] which provided a new synthetic protocol for azacycle and various bioactive natural products.[4,5] In addition, we developed a new and highly efficient synthetic strategy toward *N*-heterocyclic glycoside employing the catalytic asymmetric addition of heterocycles to alkoxyallene as the key event. Moreover, the stereoselective synthesis of various natural and non-natural *N*-heterocyclic glycosides with potentially new biological activities can be readily accessed by this methology. Furthermore, this reaction could be expanded for the asymmetric synthesis of several pharmaceuticals. In this presentation, the development of a new methodology and their synthetic applications will be discussed.



References:

1. Kim, H.; Rhee, Y. H. *Synlett* **2012**, *23*, 2875.
2. Kim, H.; Rhee, Y. H. *J. Am. Chem. Soc.* **2012**, *134*, 4011.
3. Kim, H.; Lim, W.; Im, D.; Kim, D.-g.; Rhee, Y. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 12055.
4. Kang, S.; Kim, D.-g.; Rhee, Y. H. *Chemistry – A European Journal* **2014**, *20*, 16391.
5. Lim, W.; Rhee, Y. H. *Tetrahedron* **2015**, *71*, 5939.

Vitamin B_{12} as a Drug Delivery Agent – a Chemical Point of View

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Delivery of an active compound to its site of action is one of the crucial issues in drug development. A promising strategy is to use naturally occurring compounds, such as vitamin B_{12} (cobalamin, Cbl) due to its unique ability to penetrate cells via a system of transport proteins.[1] In order for B_{12} to act as a carrier, its structure must be modified to allow selective coupling of biologically active compounds and at the same time high affinity to transport proteins must be retained. Selective and high-yielding functionalizations of B_{12} are highly desirable; however, the complexity of cobalamin's structure makes this extremely challenging. Our group has introduced new methods allowing to achieve this goal (**Figure 1: A**). Now, B_{12} can be selectively and directly attached to alkynes (via CuAAC),[2] acids (via amide bond formation)[3] or thiols (via disulfide bond formation).[4] Also reduction-free, direct alkynylation of vitamin B_{12} at cobalt center that leads to previously unknown heat and light stable acetylide cobalamins has been developed.[5] The selective orthogonal conjugation at both the Co center and 5'-OH group can also be achieved.[6] Recently, we have developed the method that involves modifications at previously unexplored *meso* position.[7] The idea of using cobalamin as a delivery vehicle is well documented in mammals and was applied to increase bioavailability of different therapeutics including proteins, anti-cancer drugs, fluorescent and radioisotope labels. However such approach has not been applied to bacteria yet. Thus, in our work we focus on creating a connection of B_{12} and PNA (peptide nucleic acid) that will be targeted at bacterial DNA or RNA (**Figure 1: B**).[8] The use of such short, modified oligonucleotides as inhibitors of bacterial translation seems a promising alternative for antibiotics, which are currently overused leading to fast development of bacterial resistance. We found that vitamin B_{12} transports antisense PNA into *E. coli* cells more efficiently than the most widely used cell-penetrating peptide (KFF)3K. Moreover, we have analyzed the structure and conformational dynamics of conjugates of Cbl with a PNA monomer and oligomer and B_{12} was found to increase the flexibility of PNA in a way that could be beneficial for its hybridization with natural nucleic acid oligomers.[9] The results of our study provide the foundation for considering vitamin B_{12} as a delivery tool for PNA oligonucleotides into bacterial cells.

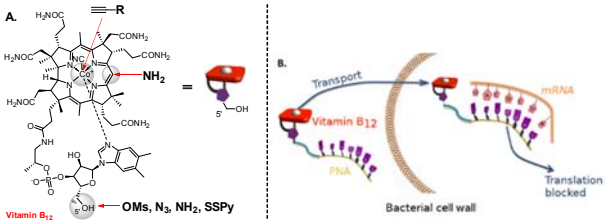

Figure 1: Sites suitable for conjugation in B_{12} (**A**). Vitamin B_{12} as a PNA transporter (**B**).

Acknowledgements: Financial support for this work was provided by the National Science Centre, grant SYMFONIA 2014/12/W/ST5/00589

References:

1. Banerjee R. *Chemistry and Biochemistry of B_{12}*, John Wiley & Sons, Inc, **1999**. 2. Chromiński M.; Gryko D. *Chem. - Eur. J.* **2013**, *19*, 5141. 3. Jackowska A.; Giedyk M.; Chromiński M.; Gryko D. *unpublished work*. 4. Wierzba A. J.; Wojciechowska M.; Trylska J.; Gryko D. *Bioconjugate Chem.* **2016**, *27*, 189. 5. Chromiński M.; Lewalska A.; Gryko D. *Chem. Commun.* **2013**, *49*, 11406. 6. Chromiński M.; Lewalska, A.; Karczewski, M.; Gryko., D. *J. Org. Chem.* **2014**, *79*, 7532. 7. Wierzba A. J.; Wincenciuk A.; Gryko D. *unpublished work* 8. Równicki M.; Wojciechowska M.; Wierzba A. J.; Czarnecki J.; Bartosik D.; Gryko D.; Trylska J. *accepted*. 9. Pieńko T.; Wierzba A. J.; Wojciechowska M.; Gryko D.; Trylska J. *J. Phys. Chem. B* **2017**, *121*, 2968.

Overcoming the Limitations of Diastereomeric Resolution

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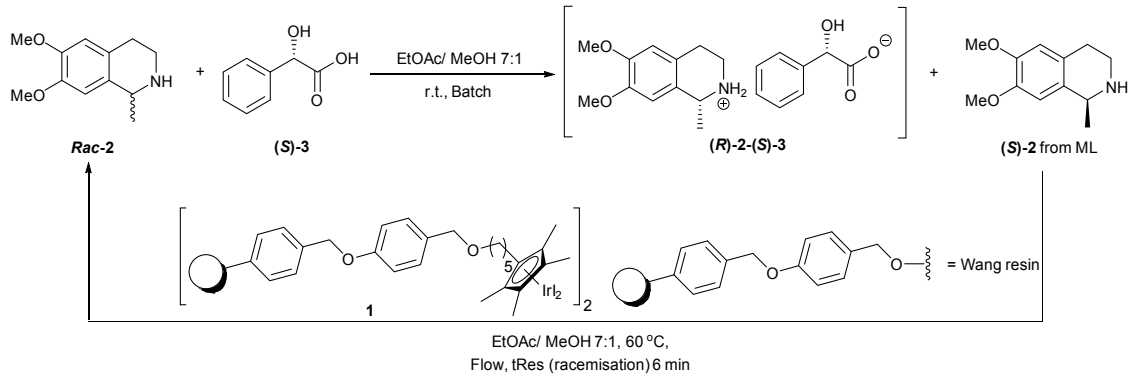
Enantiomeric resolution techniques, such as diastereomeric crystallisation, are preferred in industry over asymmetric catalytic methods because they are simple, robust and easy to operate.[1, 2] One of the main drawbacks of diastereomeric crystallisation is that a maximum yield of only 50% can be achieved. A significant improvement in productivity and reduction in waste could be achieved by recycling the mother liquor (ML) from crystallisation; and a theoretical yield of 100% could be obtained. This presentation describes the work on the synthesis of several chosen chiral amines by developing a continuous Resolution-Racemisation-Recycle (R^3) process.

Compound **2** was the first substrate chosen for development of the process. It involved diastereomeric crystallisation of *Rac*-**2** using (*S*)-mandelic acid **3** in batch;[3] whilst a continuous racemisation procedure was developed to recycle the resulting ML using C_5-tethered $[Cp^*IrI_2]_2$ **1** immobilised on Wang resin (Scheme 1). The two steps were coupled to yield a continuous resolution and recycle process, which avoids intermediate isolation and allows potential process automation. Using this R^3-process, the desired diastereomeric crystals **(*R*)-2-(*S*)-3** was obtained in 78% yield and 96% d.e. Different resolving acids, solvents, temperatures and residence times (tRes) were used in an attempt to apply the R^3-process to synthesise other chiral amines.



Scheme 1: *The R^3-process of compound **2***

Acknowledgements: I would like to thank Prof. John Blacker for his supervision and the members of the iPRD for their support. I would also like to thank Mr Martin Huscroft for his help in obtaining the chiral HPLC data of compound **2**, YProtech for providing the immobilised catalyst **1**, AstraZeneca, EPSRC and the University of Leeds for their financial support.

References:

1. Anderson N. G. *Org. Process Res. Dev.*, **2005**, *9*, 800.
2. Lorenz H. and Seidel-Morgenstern A. *Angew. Chem. Int. Ed.*, **2014**, *53*, 1218.
3. Zhu R., Xu. Z., Ding W., Liu S., Shi X. and Lu X. *Chin. J. Chem.*, **2014**, *32*, 1039.

Enantioselective Fluoroalkylation Reactions to Ketimines

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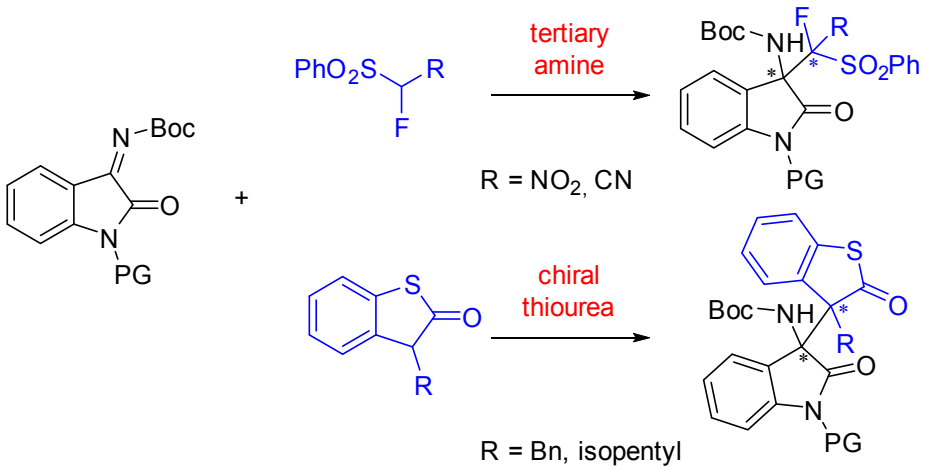
Nitrogen-containing compounds are widespread in nature and are necessary for life, because they are part of the metabolism of living cells. Nowadays about 75% of medicaments contain an amine functionality in their structure.[1] Synthesis of nitrogen-containing compounds is frequently carried out from readily available imines. The organocatalytic enantioselective reactions of imines are important reactions in terms of preparation the nitrogen compounds with a chiral quaternary carbon atom. In the area of the catalytic enantioselective fluoroalkylations using ketimines derived from isatins as substrates, there are a few examples reported to date. [2-4]

We developed enantioselective fluoroalkylation reaction of ketimines with α-fluorinated methanephenylsulfones and sulfur heterocycles (benzothiophen-2-one) catalyzed chiral tertiary amine or chiral thiourea organocatalyst. (**Scheme 1**), The reaction provides the corresponding fluoroalkylation products in good yields and moderate or excellent diastereo- and enantioselectivity.



Scheme 1: Enantioselective nucleophilic additions to ketimine.

Acknowledgements: We thank the Charles University Grant Agency (grant number 392315) and the Grant Agency of Czech Republic (grant number 16-23597S) for financial support.

References:

1. Dai,L.-X.; Lin, Y.-R.; Hou, X.-L.; Zhou, Y.-G. *Pure Appl. Chem.*, **1999**, *71*, 1033.
2. Yan, W.; Wang, D.; Feng, J.; Li, P.; Zhao, D.; Wang, R *Org. Lett.*, **2012**, *14* (10), 2512.
3. Liu, Y.-L.; Zhou, J. *Chem. Commun.*, **2013**, *49*, 4421.
4. Wang, X.-B.; Li, T.-Z.; Sha, F.; Wu, X.-Y. *Eur. J. Org. Chem.* **2014**, *4,* 739

Overview on Green Methods towards Quinoline Synthesis

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The quinoline scaffold is present in a vast number of natural compounds and pharmacologically active substances, comprising a significant segment of the pharmaceutical market. Furthermore, its derivatives have been extensively used in the pesticide, OLED and sensor industries.[1] Classical methods for the synthesis of this heterocyclic skeleton, generally from *o*-aminoacetophenones or anilines, pose serious economic and environmental concerns, requiring the use of expensive starting materials in highly acidic and/or oxidizing conditions, at high temperatures and during long reaction times.[2] Taking into account that chemical and petrochemical industries are responsible for nearly half of industrial energy use, and factoring in the consumption of natural resources and generation of large amounts of toxic waste, it is of critical importance that chemists develop chemical processes that can meet current environmental goals. As so, the discovery of new green catalysts and methods towards the synthesis of chemical entities, such as quinolines, has been in the spotlight of current research, allowing a reduction in both the cost and environmental impact of widespread chemical processes.

In this work, recent articles have been compiled and reviewed to present a broad and comprehensive view on green methods towards the synthesis of quinolines. The catalytic system and its role in the advantages and disadvantages of said methods was highlighted and its importance stated. Moreover, green metrics - Atom Economy (AE), E-factor and Effective Mass Yield (EMY) - were used to accurately determine the sustainability of distinct synthetic procedures, enabling a characterization of its toxicity, waste volume and inherent efficiency. A graphical analysis these values allowed a prompt comparison between the environmental impact of said methods **(Figure 1)**. These results allowed us to conclude that specific synthetic routes, solvents and energy supply systems have increased intrinsic sustainability and are, therefore, recommended for researchers in this field.[3]

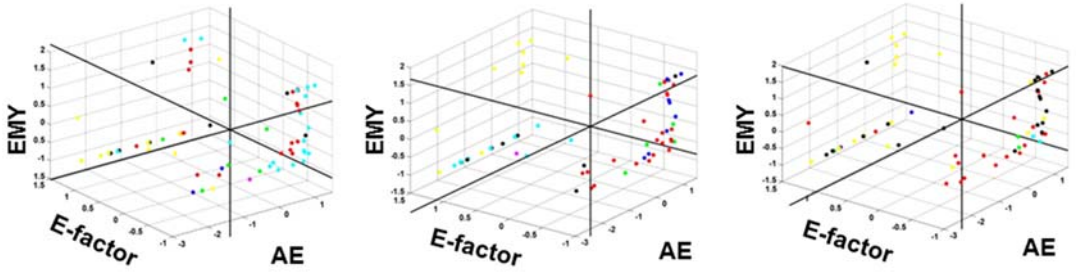

Figure 1: 3D representation of the green metrics calculated for each individual article. Color scheme represents different synthetic routes (left), solvent systems (centre) or energy sources (right).

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References:

1. Kumar S.; Bawa S.; Gupta H. *Mini-reviews in Medicinal Chemistry.* **2009**, *9 (14)*, 1648-1654.
2. Gurnos J. Quinolines: Part I. In *The Chemistry of Heterocyclic Compounds*. **1977**, 32.
3. Batista V. F.; Pinto D. C. G. A.; Silva A. M. S. *ACS Sustainable Chemistry and Engineering.* **2016**, *4*, 4064-4078.

Stereospecific Hydroxylation of C(sp^3)–H bonds: New Mechanistic Features of the *m*-CPBA Oxidant

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Selective catalytic oxidation of inert saturated hydrocarbons remains a challenge in contemporary chemistry.[1] The high energy of the C–H bond and the saturated character of alkanes foresee the use of strong terminal oxidants, such as peroxides.[1b] Among the family of peroxides, the *meta*-chloroperbenzoic acid (*m*-CPBA) stands apart due to its unusually complex oxidative behaviour. In modern organic chemistry, *m*-CPBA is an inexpensive, stable, organo-soluble, versatile oxidation reagent, routinely used in a range of processes.[2] Although *m*-CPBA is a recognized model oxidant in the metal-catalyzed alkanes oxidation, the respective research is typically aimed at the investigation of metal-containing active species formed,[3] rather than chemistry of the oxidant (*m*-CPBA).

We have found that the heterometallic complex pre-catalyst $[Co_4Fe_2O(L)_8]\cdot 4DMF\cdot H_2O$ (**1**) (Figure 1),[4] where H_2L = salicylidene-2-ethanolamine, in the presence of an acidic promoter and *m*-CPBA oxidant, affords >10^3 times reaction rate improvement of alkane oxidation (comparing to known systems), keeping >99% of retention of stereoconfiguration of model substrates, with TONs (turnover numbers) >10^4 and yields based on substrate up to 34%. A combined kinetic, spectroscopic and ^{18}O-labelling study of this system is presented. Our results reveal tertiary C–H bond hydroxylation via a competition of at least two reaction mechanisms: selective Co-mediated and non-selective free radical one. We got the evidence of a tertiary radical H abstraction by chlorobenzene radicals, originated from *m*-CPBA. Unexpectedly we also found that the incorporation of ^{18}O from $H_2{}^{18}O$ into the hydroxylation product (alcohol) can proceed via a metal-free way when *m*-CPBA is used. This contrasts with common conclusion (which comes from H_2O_2 chemistry[1b]) that such ^{18}O labelling accounts for high-valent metal-oxo C–H attacking species. We suggest that the results of ^{18}O-tests applied for alkane oxidation should be treated carefully when *m*-CPBA oxidant is used. Details of this catalytic study will be presented.

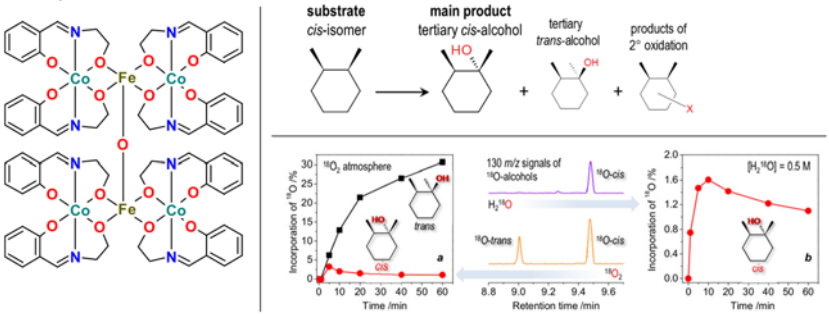

Figure 1: Molecular structure of the complex, model reaction and selected results of the ^{18}O-labelling studies.

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References:

1. a) Shul'pin, G. B. *Org. Biomol. Chem*. **2010**, *8*, 4217. b) Bryliakov, K. P.; Talsi, E. P. *Coord. Chem. Rev*. **2014**, *276*, 73. c) *Advances in Organometallic Chemistry and Catalysis: The Silver/Gold Jubilee International Conference on Organometallic Chemistry Celebratory Book*; A. J. L. Pombeiro, Ed.; Wiley, **2014**; Chapter 2.
2014; Chapters 1−3, 22.2. Hussain, H.; Al-Harrasi, A.; Green, I. R.; Ahmed, I.; Abbas, G.; Rehman, N. U. *RSC Adv*. **2014**, *4*, 12882.
3. Oszajca, M.; Franke, A.; Brindell, M.; Stochel, G.; van Eldik, R. *Coord. Chem. Rev*. **2016**, *306*, 483.
4. Nesterov, D. S.; Chygorin, E. N.; Kokozay, V. N.; Bon, V. V.; Boca, R.; Kozlov, Y. N.; Shul'pina, L. S.; Jezierska, J.; Ozarowski, A.; Pombeiro, A. J. L.; Shul'pin, G. B. *Inorg. Chem*. **2012**, *51*, 9110.

Pt(II) Coordination Complexes as Visible Light Photocatalysts

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During last years, visible light photoredox catalysis has been established as a powerful tool for the synthesis of molecules by selective activation of bonds under mild conditions.[1] The catalysts involved in most of the processes are Ru(II) and Ir(III) complexes or photoorganocatalysts such as eosyn Y or flavin. By contrast, few studies have focused on the development of photocatalysts based on other metal complexes such as iron, copper or gold, even though complexes such as the platinum organometallic complexes have been widely studied as photosensitizers in solar cells and as electrophosphorescence sensors. Very recently, our group has synthetized different coordination complexes based on platinum(II) and 8-substituted-quinoline ligands which have proved to be excellent photocatalyst in different transformations.[2]

Herein, we will present that hydroxyquinoline-Pt(II) complexes are excellent photocatalyst for the oxidation of sulfides using atmospheric O_2. The catalyst is able to oxidize a large number of sulfides containing aryl, alkyl, allyl, benzyl, as well as more complex structures such as heterocycles and methionine aminoacid, with complete chemoselectivity and without detection of other byproduct. We have also carried out mechanistic studies that suggest an electron-transfer process via oxygen radical anion as plausible mechanism.[1]

In addition, heterogenous photocatalysts have been also developed using different mesoporous silica nanoparticles functionalized with platinum complexes. All the materials have been characterized by different methods and the heterogenous photocatalysts have been applied in the dehalogenation of bromo compounds (a model reaction in pollution processes).

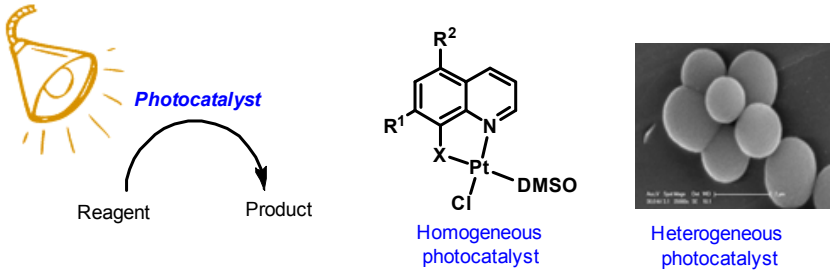

Figure 1: Homo- and heterogeneous Pt(II) photocatalyst.

Acknowledgements: We thank the European Research Council (ERC-CoG UNBICAT project number: 647550) and the Spanish Government (project number: CTQ2015-64581-R) for financial support.

References:

1. Albini A.; Fagnoni M. Handbook of Synthetic Photochemistry, WILEY-VCH, Weinheim, 2010.
2. Casado-Sánchez A.; Gómez-Ballesteros R.; Tato F.; Soriano F. J.; Pascual-Coca G.; Cabrera S.; Alemán J. *Chem. Commun.* **2016**, 9137.

Platinum and Iridium Complexes supported by the "PSi_2" Pincer-type Ligand: Synthesis, Characterization, Reactivity and Catalytic studies

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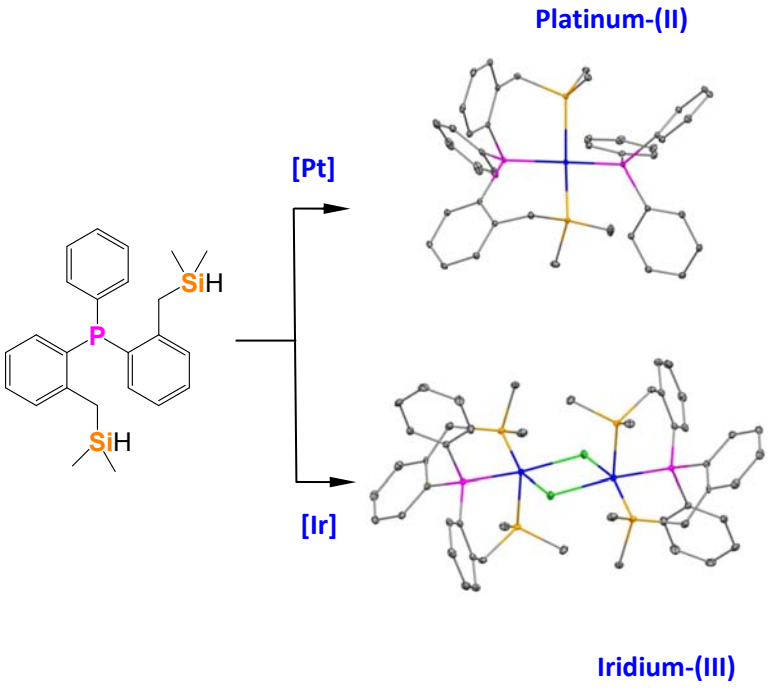
The use of multidentate ligands in transition-metal chemistry offers widespread applications due to the possibility of varying the anchoring points and thus modulating the properties of the metal center. Silicon is a strong σ donor and exerts a strong trans influence,[1] therefore makes it an excellent choice for incorporation into the skeleton of multidentate ligands.[2] As a result, attention has focused on the study of silyl pincer complexes which have been applied in a variety of chemical transformations as homogenous catalysts. For example, hydrosilylation for the production of functional silanes and silicones, and catalytic conversion of CO_2 to methanol and/or methane by platinum group metals.[3]

In the present work, we report iridium,[4] and novel platinum complexes bearing the tridentate benzylsilyl phosphine "PSi_2" ligand. Their synthesis and characterization by multinuclear NMR, in the solid and liquid state, as well as X-ray diffraction studies will be presented. Their reactivity towards small molecules, in particular H_2, will be disclosed as well as some preliminary catalytic data (hydrosilylation, CO_2 reduction ...).



Acknowledgements: We thank the CONACyT and the CNRS for financial support. We also acknowledge the French-Mexican International Laboratory (LIA-LCMMC) for support.

References:

1. Zhu, J.; Lin, Z.; Marder, T. B. *Inorg. Chem.* **2005**, *44*, 9384.
2. a) *The Chemistry of Pincer Compounds*; Morales-Morales, D.; Jensen, C. Eds. Elsevier Science: Amsterdam, **2007**. b) Corey, J. Y. *Chem. Rev.* **2016**, *116*, 11291.
3. a) Hanada, S.; Tsutsumi, E.; Motoyama, Y.; Nagashima, H. *J. Am. Chem. Soc.* **2009**, *131*, 15032. b) Troegel, D.; Stohrer, J. *Coord. Chem. Rev.* **2011**, *255*, 1440. c) Mitton, S. J.; Turculet, L. *Chem. Eur. J.* **2012**, *18*, 15258.
4. a) Corona-Gonzáles, M. V.; Zamora-Moreno, J.; Cuevas-Chávez, C. A.; Rufino-Felipe, E.; Mothes-Martin, E.; Coppel, Y.; Muñoz-Hernández, M. A.; Vendier, L.; Flores-Alamo, M.; Grellier, M.; Sabo-Etienne, S.; Montiel-Palma, V. *Dalton Trans.* **2017 DOI:** 10.1039/C7DT00727B. b) Montiel-Palma, V.; Muñoz-Hernández, M. A.; Cuevas-Chávez, C. A.; Vendier, L.; Grellier, M.; Sabo-Etienne, S. *Inorg. Chem.* **2013**, *52*,

Synthesis, Applications of Cinchona-based Organocatalysts in Aza-Markovnikov Reaction and their Recycling using Organic Solvent Nanofiltration

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It is well-known, that 1-[N-(N-heterocycle)] alkyl esters possess valuable biological activities[1] and can act as, amongst others, acaricides,[2] antimicrobials,[3] antitumor drugs.[4] Aza-Markovnikov addition of N-heterocycles to vinyl esters has recently received much attention. Such aza-Markovnikov additions were traditionally performed under harsh reaction conditions in which bases, acids and strong heating were usually used to promote the reaction. In order to avoid these disadvantages, Lin and his co-workers applied K_3PO_4 as mild base,[1] ionic liquid as reaction media and catalyst,[5] and acylases as biocatalysts.[6] In our research work our aim was to develop a new method for efficient synthesis of biological active aza-Markovnikov adducts using homogeneous catalysts which can be easily recycle after application. Three cinchona catalysts (**1–3**, see **Figure 1.**) were tested in aza-Markovnikov additions of different N-heterocycles (imidazole, benzimidazole) to esters (vinyl acetate, 4-vinyl tert-butyl benzoate). Hydroquinine (**1**) is a commercially available versatile organocatalyst. This alkaloid was converted to its amine derivative (**2**) after a mesylation, an azide formation and a catalytic hydrogenation.[7] Amine **2** was reacted with the adduct of 3,5-bis(trifluoromethyl)aniline and dimethyl squarate to give bifunctional cinchona-squaramide catalyst (**3**).[8]

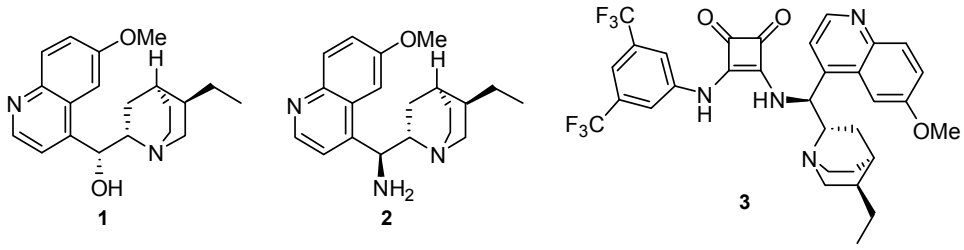

Figure 1: Three cinchona-based organocatalysts applied as aza-Markovnikov catalysts.

The feasibility of the application of these catalysts was expanded by using OSN (Organic Solvent Nanofiltration) technique. The chemically stable polybenzimidazole (PBI) membrane was used for separation of molecules. The pore size of membranes was adjusted by their preparation. With the help of OSN technique the **1–3** organocatalysts became recyclable catalysts, furthermore the products of reactions are separable from the reaction mixture.[9]

Acknowledgements: The publication of the work reported herein has been supported by ETDB at BME.

References:

1. Lin, S.-W.; Sun, Q.; Li, R.-T.; Cheng, T.-M.; Ge, Z.-M. *Synthesis* **2007**, *13*, 1933.
2. Yano, T.; Tomioka, H.; Ishiwatari, T.; Hirata, N. Jpn. Kokai Tokkyo Koho JP 03232805, 1991; *Chem. Abstr.* **1992**, *116*, 146174.
3. Bodor, N.; Kaminski, J. J.; Selk, S. *J. Med. Chem.* **1980**, *23*, 469
4. Ozaki, S.; Watanabe, Y.; Hoshiko, T.; Mizuno, H.; Ishikawa, K.; Mori, H. *Chem. Pharm. Bull.* **1984**, *32*, 733.
5. Xu, J.-M.; Liu, B.-K.; Wu, W.-B.; Qian, C.; Wu, Q.; Lin, X.-F. *J. Org. Chem.* **2006**, *71*, 3991.
6. Wu, W.-B.; Wang, N.; Xu, J.-M.; Wu, Q.; Lin, X.-F. *Chem. Commun.* **2005**, *18*, 2348.
7. Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005**, *7*, 1967.
8. Malerich, J. P.; Hagihara, K.; Rawal, V. H. *J. Am. Chem. Soc.* **2008**, *130*, 14416.
9. Großeheilmann, J.; Fahrenwaldt T.; Kragl U. *ChemCatChem* **2016**, *8*, 322

First Aziridination using Magnetically Recoverable Cu-loaded Nanoparticles

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Introduction of nitrogen atoms onto organic skeletons remains a key step for the synthesis of alkaloid bioactive molecules. Since a few years, catalytic nitrene insertion on alkenes or for C-H bond functionalization has emerged as an undeniable tool for such introduction (**Fig. 1**).[1-2] However, homogeneous catalytic systems usually used for this transformation, *i.e*. rhodium or copper complexes, present some drawbacks such as stability, toxicity and/or separation after reaction. Moreover, the recovery of the catalysts is generally eluded and their recycling not considered. Recyclable supported catalysts have then arisen as a valuable alternative to overcome this issues.[3] As part of our continued interest for the development of sustainable and ecofriendly methodologies, we designed new and efficient recoverable catalysts fitting by the way the green chemistry principles. Here, the first nitrene insertion for aziridination using a reusable copper-loaded nanoferrite as catalyst will be presented. Magnetic properties of the nanoparticles (MNP) allow an easy retrieval of those catalysts with a simple external magnet (**Fig. 1**). We will show that the catalysts could be reused for 5 times with total conversion of styrene and good yields, even after 5 runs.

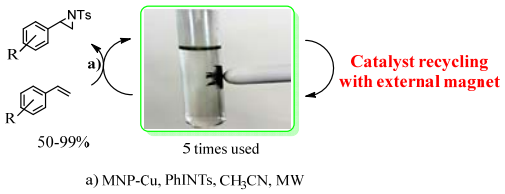

Figure 1: aziridination and catalyst recovering with external magnet

Catalysts were fully characterized by XRD, TEM, FT-IR, AAS and TGA. Investigations showed a reduction of copper loading as the runs, which can be due to a weak anchoring. This result prompts us to explore different linkers between magnetic nanoparticles and copper in order to decrease this leaching. Several linkers exhibiting different MNP-anchoring and Cu-chelating functions will be presented (**Fig. 2**). Also, the successful extrapolation of this methodology to electron-poor or electron-rich substituted styrene derivatives will be demonstrated as well as the aziridination of long chain olefins which will be exhibited.

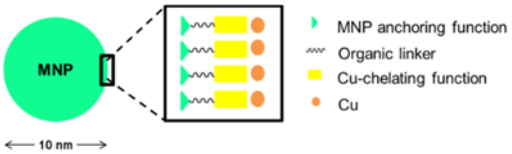

Figure 2: Surface modified Magnetic Nanoparticle (MNP) as a magnetic catalyst for aziridination reaction

Acknowledgements: We thank the Kouh Shekan SA Co. and the CNRS for financial support.

References:

1. Evans D.A.; Faul M.M.; Bilodeau M.T.; Org. Chem. **1991**, *56*, 6144-6746.
2. Dauban. P.; Saniére L.; Tarrade A.; Dodd R.H.; Am. Chem. Soc. **2001,** *123,* 7707-7708
3. Nasir Baig R. B. Varma.; R.S.; Green Chem., **2013,** *15*, 398–417

A Binuclear Cu(II) Cryptate for O_2 Activation: Potential Water Oxidation Catalyst

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Dioxygen is considered one of the primary sources for energy production in nature.[1] The activation of this molecule remains one of the main challenges in biological, synthetic and industrial processes. This activation mechanism may include different intermediates such as superoxide, peroxide, hydrogen peroxide and hydroxyl radical.[2] In cytochrome *c* oxidase a heme-copper active site reduces dioxygen to water in a four-electron-four-proton reaction and plants and algae perform the reverse process, using sunlight to oxidise water to oxygen.[1] Cu-O_2 intermediates are involved in many important reactions (e.g. oxidation, reversible O_2 binding and O_2 activation), thus it is important to study these species to fully understand these bio-relevant processes.[3] Here we explore the chemistry of binuclear Cu(II) cryptates that are able to stabilise a superoxide anion (**Figure 1**) in their cavity. This only occurs after their treatment with a reducing agent. This superoxide intermediate (**Figure 1**) can be part of the mechanism for water oxidation as previously proved for other binuclear Cu(II) complexes.[4] Computational studies (DFT) were also performed to investigate and rationalise the mechanism for superoxide formation and stabilisation. Cyclic voltammetry studies were carried out to evaluate their ability to oxidise water.

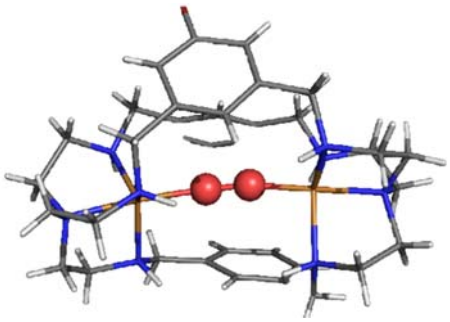

Figure 1: Single crystal X-ray structure of the Cu(II) cryptate encapsulating the superoxide anion.

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References:

1. Cao, R., Saracini, C., Ginsbach, J. W., Kieber-Emmons, M. T., Siegler, M. A., Solomon, E. I. Fukuzumi, S., Karlin, K. D., *J. Am. Chem. Soc.,* **2016**, *138*, 7055.
2. Quist, D. A., Diaz, D. E., Liu, J. J., Karlin, K. D.,. *J. Biol. Inorg. Chem.,.* **2017**, *22*, 253.
3. Saracini, C., Ohkubo, K., Suenobu, T., Meyer, G. J., Karlin, K. D., Fukuzumi, S., *J. Am. Chem. Soc.,* **2015**, *137*, 15865.
4. Su, X-J., Gao, M., Jiao, L., Liao, R-Z., Siegbahn, P. E. M., Cheng, J-P., Zhang, M-T., *Angew. Chem. Int. Ed.,* **2015**, *54*, 4909.

Molecular Docking Study of the Complex Between Novel β-Amino Acid Tripeptides Based Ligands and μ-Opioid Receptor

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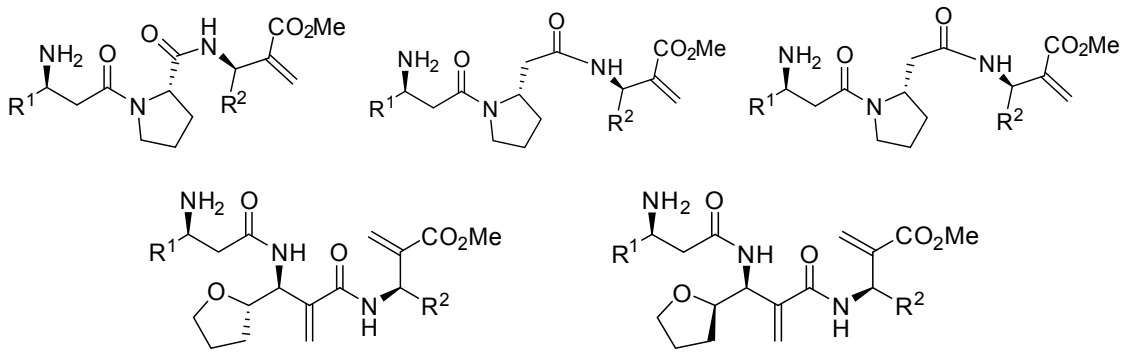
Chronic pain treatment based on morphine needs to be changed since, its use, dependency cases and even deaths are every year reported. Synthetic opioid peptides were found to act as agonist for *μ*-opioid receptor as the morphine does. By selecting peptide's structure, it is possible to get the same pharmacological effect while the side effects, which are responsible for those cases, are removed, so these features made them really interesting in new drug development(1). Despite the fact that they are less common than *α*-amino acids in nature, *β*-amino acids are proving exceptionally useful in the pharmaceutical industry because of their properties, as *β*-amino acids based peptides are able to stablish their secondary structure with fewer amino acids(2). Our group previously demonstrated that morphan derivatives were good enough in terms of opioid activity(3a)(3b). Tripeptides assayed are based on the discoveries made by Wang *et al*(4), who reported that the biological activity of amino acids based tetrapeptides were improved by an alpha double binding and an aromatic residue at the fourth position. The structures studied are shown in scheme 1 and synthetic procedure, as well as docking results, will be presented.



R1	phenyl	2-furyl	4-hydroxiphenyl	4-hydroxy-3,5-dimethylphenyl
R2	phenyl	2-furyl	(S)-2-tetrahydrofuril	(R)-2-tetrahydrofuril

Scheme 1: battery of tripeptides based in *β*-amino acids.

Acknowledgements: We thank to MINECO CTQ2015-68175-R, FEDER Junta de Castilla y León (UIC21)

References:

1. Davis; M.P., *Expert Opin. Drug Dis*. **2010**, *5*, 1007-1022.
2. Seebach, D., & Matthews, J. L., *Chemical Communications* **1997**, *21*, 2015-2022.
3a. Garrido, N. M.; Rubia, A. G.; Nieto, C.; Díez, D. *Synlett* **2010**, 587.
3b. Nieto, C. T.; Gonzalez-Nunez, V.; Rodríguez, R. E.; Diez, D.; Garrido, N. M. *European Journal of Medicinal Chemistry* **2015**, 101, 150.
4. Liu, X.; Wang, Y.; Yu J.; Ji, H.; Kai, M.; Wang, Z.; Wang, D.; Zhan, Y.; Zhao, D.; Wang, R., *Journal of Medicinal Chemistry* **2013**, *56*, 3102-3114.

Cobalt-Catalyzed Addition of Alkynes to Vinylaziridines

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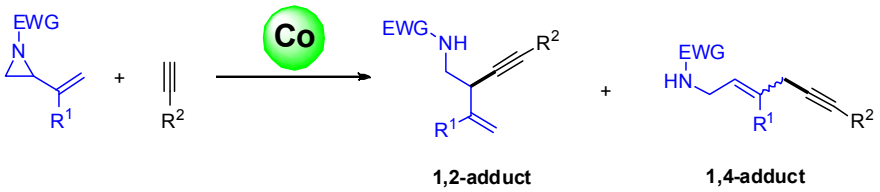
The addition of terminal alkynes to unsaturated functions, so called hydroalkynylation reaction, is one of the most straightforward methods to prepare functionalized internal alkynes which are useful blocks in organic synthesis.[1] The hydroalkynylation reactions can be catalyzed by various transition metals like Ir, Ni, Cu, Rh or Pd.[2] However, only rare examples using cobalt based catalytic systems have been reported recently. Nishimura and Hayashi described the addition of silylacetylenes across different acceptors such as α,β-unsaturated carbonyl compounds, oxa- and azabenzonorbornadienes or allenes.[3] As vinylaziridines are useful synthons in organic chemistry,[4] we were wondering if they could be a good candidates for cobalt-catalyzed addition of terminal alkynes. As depicted in **Scheme 1** either 1,2- or 1,4- addition was anticipated but both adducts are valuable molecules for further transformations.



Scheme 1: Cobalt-catalyzed addition of terminal alkynes to vinylaziridine.

It was found that a catalytic system composed from cobalt (II) acetate and bis-diphenylphosphinoethane (dppe) was able to promote the hydroalkynylation reaction with vinylaziridines. The formation of 1,2- and 1,4-addition products was observed in all cases in a 1:1 ratio. After an optimization step, high overall yields were obtained. Preliminary investigations on the mechanism led us to think that radical intermediates are involved. The reaction parameters, different scopes, and mechanistic considerations will be presented.

Acknowledgements: We thank Ministère de l'Education Nationale, de l'Enseignement Supérieur et de la Recherche (B.B. Grant) and l'École Doctorale Sciences Chimiques from Aix-Marseille University (ED 250) for financial support.

References:

1. a) Wang Z. X.; Bai X. Y.; Li B. J. *Synlett* **2017**, *28*, 509. b) Ding C. D.; Dai L. X.; Hou X. L. *Tetrahedron* **2005**, *61*, 9586. c) Ding C. H.; Dai L. X.; Hou X. L. *Synlett* **2004**, *10*, 1691. d) Trost B. M.; Taft B. R.; Masters J. T.; Lumb J. P. *J. Am. Chem. Soc.* **2011**, *133*, 8502.
2. a) Bai X. Y.; Wang Z. X.; Li B. J. *Angew. Chem. Int. Ed.* **2016**, *55*, 9007. b) Shirakura M.; Suginome M. *J. Am. Chem. Soc.* **2008**, *130*, 5410. c) Yazaki R.; Kumagai N.; Shibasaki M. *J. Am. Chem. Soc.* **2010**, *132*, 10275. d) Nishimura T.; Sawano T.; Tokuji S.; Hayashi T. *Chem. Commun.* **2010**, *46*, 6837. e) Yin J.; Chisholm J. D. *Chem. Commun.* **2006**, 632. f) Villarino L.; García-Fandiño R.; López F.; Mascareñas J. L. *Org. Lett.* **2012**, *14*, 2996.
3. a) Nishimura T.; Sawano T.; Ou K.; Hayashi T. *Chem. Commun.* **2011**, *47*, 10142. b) Sawano T.; Ou K.; Nishimura T.; Hayashi T. *Chem. Commun.* **2012**, *48*, 6106. c) Sawano T.; Ashouri A.; Nishimura T.; Hayashi T. *J. Am. Chem. Soc.* **2012**, *134*, 18936. d) Sawano T.; Ou K.; Nishimura T.; Hayashi T. *J. Org. Chem.* **2013**, *78*, 8986.
4. Ohno H. *Chem. Rev.* **2014**, *114*, 7784.

Highly Enantioselective Addition to Nitroalkenes via a Robust Activation of α-Iminoesters

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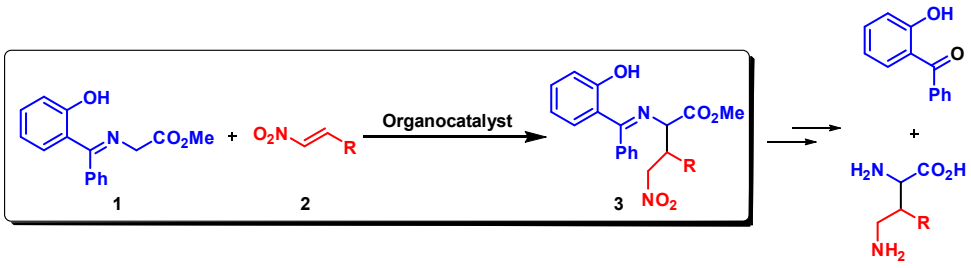
α,γ-Amino acids are very important subunits that are often found in natural products[1a] and possess powerful biological properties.[1b] They can be synthesized from *α*-iminoester derivatives following easy transformations. To date, the most common route to achieve chiral *α*-iminoesters is the use of metal-catalyzed asymmetric Michael addition of ketimine glycine derivatives to nitroalkenes.[2] Regarding the organocatalytic version of this reaction, in 2008 Takemoto's group reported the addition of a di-activated aldimine to nitrostyrenes using his thiourea catalyst. This method leads to the forñmation of the Michael adduct as an intermediate of the reaction that afterwards yields the pyrrolidine derivative in the presence of an alcohol.[3]

Herein, we describe an organocatalytic strategy for the synthesis of *α*-iminoester derivatives based on a Michael reaction of ketimine glycine derivatives **1** to nitroalkenes **2** (Scheme 1). The presence of the hydroxyl group in the ketimine causes an increase in acidity of the methylene hydrogens due to the formation of an intramolecular hydrogen bond with the nitrogen. This acidity increase is a key factor in the generation of the ylide, since a compound with smooth basic properties, such as the Takemoto bifunctional organocatalyst, is capable of affording the ylide. In addition, this hydroxyl group must also play a very important role in the control of the stereoselectivity by the formation of an additional hydrogen bond with the catalyst.



Scheme 1

This Michael reaction makes the synthesis of a large variety of α-iminoesters **3** possible in good yields (75-86%) and excellent enantiomeric excesses (89-97%). Additionally, it should be noted that the hydroxyl ketone, acting as chemical auxiliary, can be recovered once the ketimine is hydrolyzed.

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References:

1. a) O.M. Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem.* **2002**, 1877. b) Y. Huang, Q. Li, T-L. Liu, P-F. Xu, *J. Org. Chem.* **2009**, *74*, 1252.
2. K. Imae, T. Konno, K. Ogata, S. Fukuzawa, *Org. Lett.* **2012**, *14*, 4410.
3. J. Xie, K. Yoshida, K. Takasu, Y. Takemoto, *Tetrahedron Lett.* **2008**, *49*, 6910.

Iron-Catalysed Cross-Coupling of Aryl and Heteroaryl Halides with Secondary-Alkyl Grignard Reagents

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The shape of molecules is very important to their biological activity. Many potent drugs and natural products contain secondary alkyl functionality, giving them 3-dimensional structure (**Figure 1**). These groups may also offer improved physicochemical properties to pharmaceutically relevant compounds.

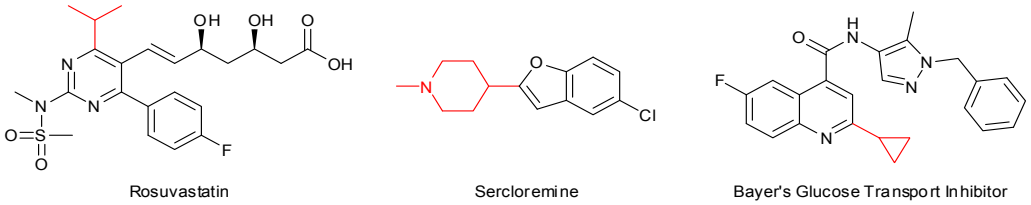
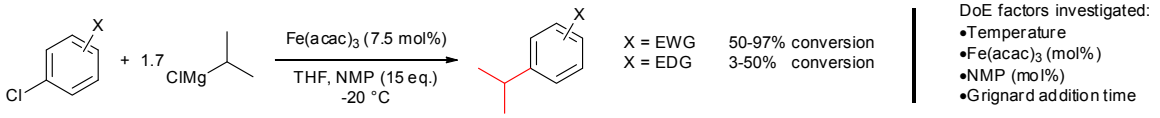


Figure 1 – Active Pharmaceutical Ingredients Containing Secondary Alkyl Groups

Historically, the coupling of alkyl nucleophiles in transition-metal catalysed cross-coupling reactions has been challenging due to undesired β-hydride elimination. Iron is known to couple primary alkyl Grignard reagents with aryl chlorides. However, there are very few reports of the iron-catalysed cross-coupling of secondary alkyl Grignard reagents – especially with *iso*-propyl or cyclopropyl nucleophiles.[1]

We have used statistical design of experiments (DoE) to optimise the iron-catalysed cross-coupling between aryl chlorides and *iso*-propylmagnesium chloride (**Scheme 1**).[2] Our conditions have allowed the successful coupling of *iso*-propylmagnesium chloride and electron deficient aryl chlorides. While electron rich substrates were found to be less reactive, the reaction was most effective with heteroaryl chlorides.



Scheme 1 – Optimised Reaction Conditions and DoE Factors Considered

Unfortunately, NMP is known to have reprotoxic effects, and its use in superstoichiometric amounts can lead to challenges with purification. We have begun a new investigation to replace NMP with catalytic quantities of readily-available ligands. Using high throughput methodology we have the tested a wide variety of well-known additives. Following initial success with a biphosphine ligand we have used principal component analysis (PCA) to study similar chemical space. This led to the selection of a further refined series of ligands, which we are currently using to carry out a focussed investigation into the scope of both heteroaryl halide and Grignard reagent.

Acknowledgements: We thank GSK and the University of Strathclyde for funding.

References

[1] Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004,** *104*, 6217-6254.
[2] Sanderson, J. N.; Dominey, A. P.; Percy, J. M. *Adv. Synth. Catal.* **2017,** *359,* 1007-1017.

Access to Spirocyclic Benzothiophenones with Multiple Stereocenters *via* Organocatalytic Cascade Reaction

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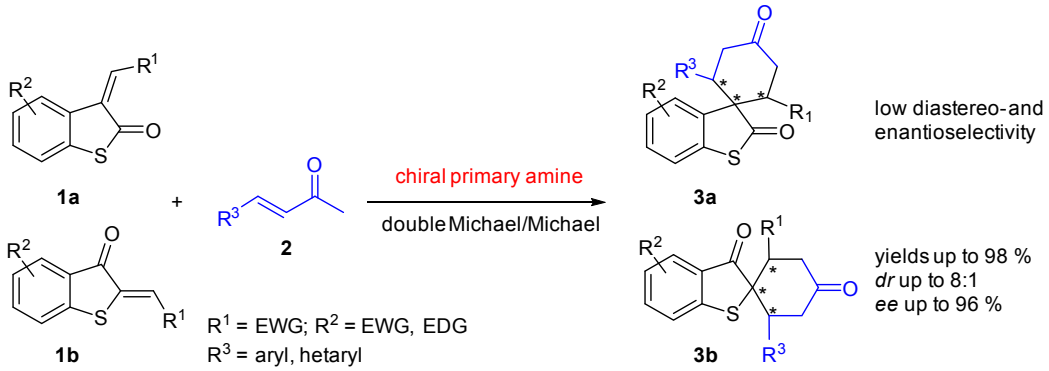
Efficient and elegant syntheses of complex organic molecules with multiple stereocenters continue to be important in both academic and industrial laboratories. In particular, catalytic asymmetric cascade reactions are highly desireable.[1] At least two steps are carried out in single operation under same reaction conditions compared to classical chemistry. In addition, protecting group manipulation and isolation of intermediates is not necessary. Use of organocatalysts in these processes allows distinct modes of activation, which can often be easily combined.[2]

Herein, we focused on the reactions of alkylidene-benzothiophenone derivatives **1** which are less explored than their nitrogen and oxygen analogues.[3] Chiral amines showed the ability to combine efficiently two activation modes (enamine/iminium catalysis) in cascade reactions of enones **2** (**Scheme 1**).

Spirobenzothiophenonic cyclohexane derivatives **3** containing three stereocenters were obtained in one-step synthesis in high yields (up to 98 %), good diastereoselectivities (about 8:1) and excellent enantioselectivities (up to 96 % ee). Scope of the reaction and further studies will be presented in details.



Scheme 1: Organocatalytic cascade reaction between alkylidene-benzothiophenones **1** and enones **2**.

Acknowledgements: We thank the Charles University Grant Agency (393615) and Czech Science Foundation (16-23597S) for financial support.

References:

1. a) Wasilke, J.-C., Obrey, S. J., Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001. b) Hahn F. E. *Angew. Chem. Int. Ed.* **2006**, *45*, 1348.
2. Enders, D., Grondal, C.; Huttl, M. R. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 1570.
3. a) Zhang, Y.; Wang, S.; Wu, S.; Zhu, S.; Dong, G.; Miao, Z.; Yao, J.; Zhang, W.; Sheng, C.; Wang, W. *ACS Comb. Sci.* **2013**, *15*, 298. b) Géant, P.-Y.; Urban, M.; Remeš, M., Císařová, I.; Veselý, J. *Eur. J. Org. Chem.* **2013**, 7979

Asymmetric Robinson Annulations in Continuous Flow: Synthesis of Key Building Blocks in Organic Synthesis

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One of the utmost importance building blocks for the synthesis of bioactive terpenoids and steroids are based on the enantiopure Wieland−Miescher and Hajos−Parrish ketone scaffolds.[1] However, the preparation of these chiral bicyclic enones through Robinson annulation has suffered from important drawbacks, such as the need for high catalyst loading, limited scope or extremely long reaction times (1-7 days).[2]

Here we present a heterogenized chiral vicinal diamine that enables the high-yield, highly enantioselective preparation of a wide range of chiral bicyclic enones under mild conditions, with reaction times as short as 60 min (batch) or residence times of 10 min (flow). The scope of the transformation has been illustrated with 14 examples bearing different cyclic scaffolds, including examples only reported previously in poorly enantioenriched or in racemic form. One of these elusive bicyclic enones has been used in enantiopure form as the starting material for a straightforward formal synthesis of the antibiotic and antifeedant sesquiterpene (−)-isovelleral. The heterogenized catalyst admits extended recycling (>10 times) and has been used to develop the first asymmetric Robinson annulations in continuous flow. The potential of the flow process is illustrated by the large-scale preparation of the Wieland−Miescher ketone (24 h of operation) and by a sequential flow experiment leading to a library of eight enantioenriched bicyclic enones (Figure 1).[2]

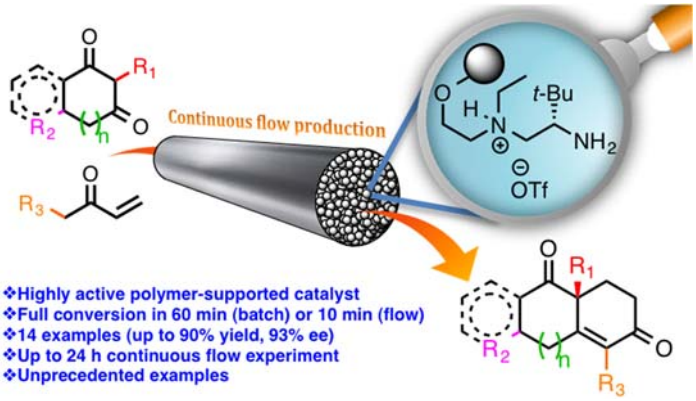

Figure 1: Representative scheme of the continuous-flow production of the building blocks obtained by a Robinson annulation.

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References:

1. For a review, see: Zeng, X.-P.; Cao, Z.-Y.; Wang, Y.-H.; Zhou, F.; Zhou, J. *Chem Rev.* **2016**, *116*, 7330 and references herein.
2. Cañellas S.; Ayats C.; Henseler A. H.; Pericàs, M. A. *ACS Catal.* **2017**, *7*, 1383.

Reductive Depolymerization of Waste Plastics and Lignin using Molecular Catalysts

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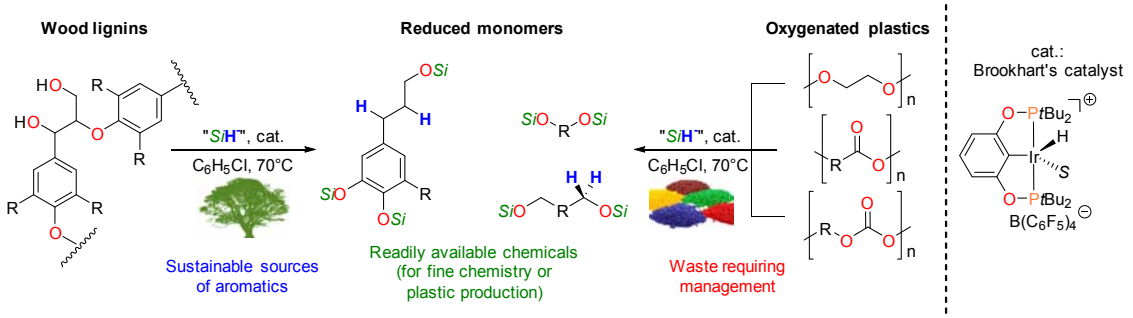
Plastics are ubiquitous in our modern society. Mainly due to their lightness, their ease to be molded and their low costs, these polymers have forced their use in various applications such as electronics, packaging, medicine, etc. It is estimated that 4-6 % of the annual production of fossil ressources are used to supply the 322 millions tons of plastics required worldwide.[1] Main recycling processes of these materials do not meet sustainable criteria since they are based on incineration and landfilling and the later causes irreversible contamination of the oceans, the soils and the fauna leading to an increasing concern in the population.
To circumvent these ecological issues, the most promising approaches consist in decoupling plastics from fossils feedstocks by producing biosourced monomers and to improve recycling at the same time as to reduce losses of organic matter.[2] In this context, we recently developed an efficient strategy for the reductive depolymerization of oxygenated polymers such as some plastics and lignin to afford pure compounds.[3] This method involves the hydrosilylation of oxygenated polymers under homogeneous catalytic conditions with tris(pentafluorophenyl)borane $B(C_6F_5)_3$. Based on this approach, we search for novel metal catalysts able to hydrosilylate strong C–O bonds and that would be more stable and selective than $B(C_6F_5)_3$ (**Scheme 1**).



Scheme 1: Catalytic hydrosilylation of wood lignins (left) and oxygenated plastics (right) with iridium(III) complex.

We found that Brookhart's iridium(III) complex supported by pincer ligands[4] is very efficient catalyst for the reduction in homogeneous conditions of model compounds and natural or manufactured polymers. This complex enables the convergent depolymerization of lignin samples from various plant species[5] as well as polycarbonates or polyesters,[6] under mild conditions (<80 °C, 0.3-3 %mol). The reactivity and the stability of this new catalytic system and its role in the reduction of C-O bonds will be presented.

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References:

1. PlasticsEurope: Plastics The Facts 2016
2. World Economic Forum, Ellen MacArthur Foundation, The New Plastics Economy – Catalysing Action, 2017
3. Feghali E.; Cantat T., *Chem. Commun*., **2014**, *50*, 862. b) Feghali E.; Carrot G.; Thuéry P.; Genre C.;Cantat T., *Energy Environ. Sci*., **2015**, *8*, 2734. c) Feghali E.; Cantat T., *ChemSusChem*, **2015**, *8*, 980.
4. Yang J.; Brookhart M.; *J. Am. Chem. Soc.,* **2007**, *129*, 12656
5. Monsigny L.; Feghali E.; Berthet J.-C.; Cantat T., manuscript submitted in Green Chemistry.
6. Monsigny L.; Berthet J.-C.; Cantat T., manuscript in preparation.

From Simple Olefins to High-Value Carbonates: Sequential Epoxidation/CO_2 Addition Reactions Catalyzed by Metalloporphyrins

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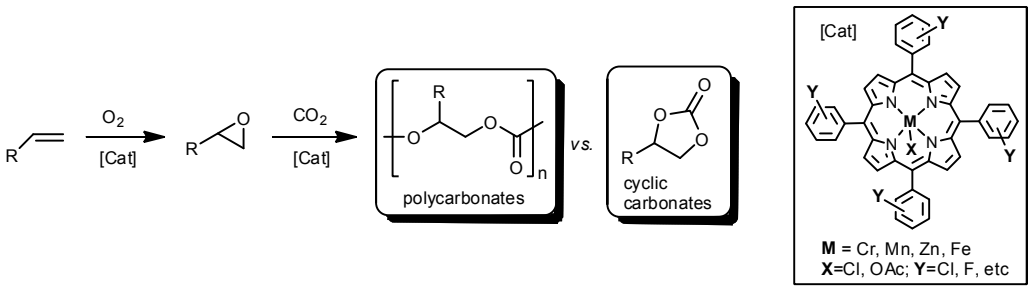
Organic carbonates are valuable synthetic targets that are widely used as raw materials for the synthesis of small molecules and polymers.[1-2] For instance, cyclic carbonates are often used as electrolytes in lithium-ion batteries, as paint strippers and also as excellent polar aprotic solvents in chemical industry.[1] On the other hand, polycarbonates are high performance and eco-efficient materials used in a large variety of relevant applications, such as sheets for roofing and glazing, optical media, medical devices, automotive goods and food contact materials, among other.[2] Regarding the search of efficient methodologies for the preparation of high-valuable cyclic carbonates and polycarbonates, the catalytic epoxidation of olefins[3] followed by coupling of the resulting epoxides with carbon dioxide (CO_2)[4] is an attractive sequential synthetic approach, due to economic and environmental benefits arising from the utilisation of renewable sources. In this context, porphyrin-based transition-metal catalysts have attracted much attention, since their aromatic heterocycle can be easily modulated by introduction of peripheral substituents and also because they are able to coordinate with a wide range of different transition metals, thus offering the possibility of increasing their catalytic activity and optimising the selectivity toward the desired product.[4]

In this communication, we present and discuss our recent achievements on the synthesis of *meso*-tetra-arylporphyrin metal complexes and their application as homogeneous or heterogeneous catalysts for epoxidation reactions of simple olefins, using O_2 as oxygen source and in the subsequent coupling reactions of epoxides (isolated or *in situ*) with CO_2, as a synthetic strategy to obtain polycarbonates and/or cyclic carbonates (Scheme 1). The effects of the catalyst structure (metal (M), electron withdrawing substituents (Y) in the *meso*-aryl porphyrins, co-axial ligand (X)) and reaction conditions are appraised, regarding their catalytic activity and selectivity for copolymers *versus* cyclic carbonates, as well as the physical/chemical properties of the carbonate products



Scheme 1: Sequential epoxidation/CO_2 addition reactions catalyzed by *meso*-aryl metalloporphirins.

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References:

1. a) Martín C.; Fiorani G.; Kleij A.R. *ACS Catal.* **2015**, *5*, 1353; b) Omae I. *Coord. Chem. Rev.* **2012**, *256*, 1384.
2. Brannigan R.P.; Dove A.P. *Biomater. Sci.* **2017**, *5*, 9.
3. Rebelo S.L.H.; Gonçalves A.R.; Pereira M.M.; Simões M.M.Q.; Neves, M.G.P.M.S.; Cavaleiro J.A.S. *J. Mol. Catal. A: Chem.* **2006**, *256*, 321.
4. Carrilho, R.M.B.; Dias, L.D.; Rivas R.; Pereira, M.M.; Claver C.; Masdeu-Bultó A.M., *Solventless coupling of epoxides and CO_2 in compressed medium catalysed by fluorinated metalloporphyrins*, *Catalysts* **2017** (*accepted paper*)

Combining Computation and Experiment in Organometallic Catalysis: From Insight to Application

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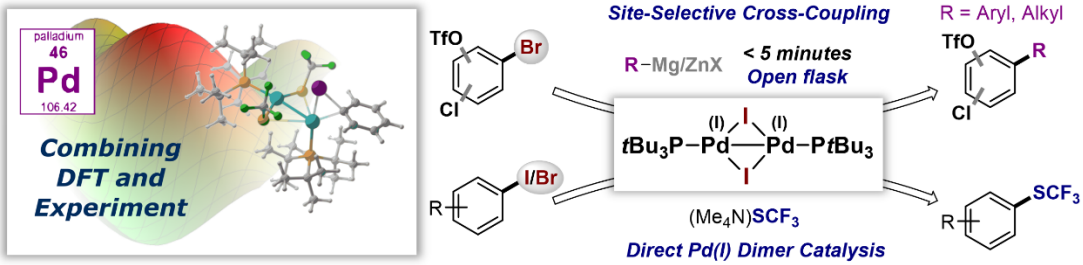
Reaching new levels of efficiency, reactivity and selectivity in chemical synthesis *via* the development of new catalytic systems is a subject of continuous efforts. Strong fundamental understanding of the processes involved is oftentimes crucial for making any further advances. Multiple possible reaction pathways, numerous potential active species and the difficulties in controlling the selectivities and reactivities are some of the challenges that burden homogenous transition metal catalysis. Fundamental studies, combining computations and experiments are a promising approach in overcoming these hurdles. In this regard, this presentation will highlight our work as a journey from initial insights of reactivity to the development of novel catalytic applications for synthesis.

The novel direct dinuclear reactivity mode of Pd(I) dimers, revealed by recent studies in our group, suggested that instead of being solely precatalysts for Pd(0), Pd(I) dimers could also react directly with aryl halides, leaving the Pd(I)-Pd(I) moiety intact.[1,2] Since then, this concept has been extended to other anions, i.e. $^{-}SCF_3$, allowing us to develop a catalytic method for the functionalization of aryl iodides and bromides.[3] The high stability of the employed Pd(I) catalyst also made it easily recoverable from the reaction, thus presenting a promising alternative to the more sensitive Pd(0) catalysis.

This Pd(I) catalyst has also allowed us to solve a long-standing problem of being able to perform reliably and predictably chemoselective cross-couplings of poly(pseudo)halogenated arenes.[4,5] The introduction of aryl, as well as alkyl groups can be performed with high convenience, with the reaction reaching full conversion within minutes under open flask conditions.



References:

(1) K. J. Bonney, F. Proutiere, F. Schoenebeck, *Chem. Sci.* **2013**, *4*, 4434.
(2) I. Kalvet, K. J. Bonney, F. Schoenebeck, *J. Org. Chem.* **2014**, *79*, 12041.
(3) G. Yin, I. Kalvet, F. Schoenebeck, *Angew. Chemie Int. Ed.* **2015**, *54*, 6809.
(4) I. Kalvet, G. Magnin, F. Schoenebeck, *Angew. Chem. Int. Ed.* **2017**, *56*, 1581.
(5) I. Kalvet, T. Sperger, T. Scattolin, G. Magnin, F. Schoenebeck, *Angew. Chem. Int. Ed.* **2017**, *DOI: 10.1002/anie.201701691*.

Valorization of Carbonic Derivatives by Hydrogenation: a Challenge for the Development of Eco-compatible Processes

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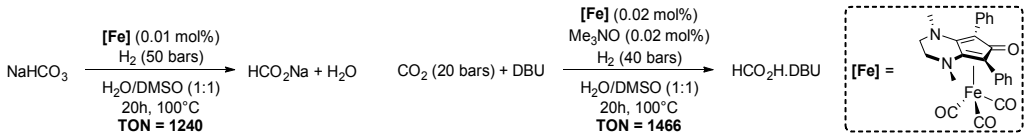
While emissions of greenhouse gases reach high levels, fossil fuels still represent 80% of global energy and 95% of our chemical commodities come from non-renewable resources. In this context, the use of CO_2 (or carbonates) such as C_1 carbon source to produce chemical platforms (methanol, formic acid) would allow its recycling. Actually, the main methods described for the reduction of carbonic derivatives involve reducing agents in stoechiometric amounts that generate toxic wastes. Catalytic hydrogenation appears to be a good alternative to these processes because hydrogen is a cheaper reducing agent and an eco-friendly agent (no by-products produced, except the catalyst, atom economy). Compared to other reduction processes, the hydrogenation of carbon dioxide suffers from little progress. However, some organometallic complexes have been developed in the last decade to achieve such a reaction and some recent reviews highlight these advances.[1] But all these efficient catalysts are mainly based on expensive noble metals such as ruthenium and iridium. Due to its abundance and its non-toxicity, iron hydride complexes[2] have been recently developed for the reduction of CO_2 into formic acid. However, even if these complexes validated the use of environmentally friendly metals in reduction of carbon dioxide, several drawbacks remained unsolved, such as quite high temperatures, high pressures of both hydrogen and CO_2 and phosphorous containing ligands. Based on a "transition metal frustrated Lewis pair" approach and on the structure/activity relationship,[3-4] we have developed a phosphine free iron complex for the reduction of both hydrogenocarbonate and carbon dioxide.[5] These results and a detailed mechanistic study will be presented.



Scheme 1: Hydrogenation of carbonic derivatives with a phosphine-free iron complex.

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References:

1. a) S. Werkmeister, K. Junge, M. Beller, *Org. Process Res. Dev.* **2014**, *18*, 289 and references therein. b) F. J. Fernández-Alvarez, A. M. Aitani, L. Oro, *Catal. Sci. Technol.* **2014**, *4*, 611. c) Y-N. Li, R. Ma, L-N. He, Z.-F. Diao, *Catal. Sci. Technol.* **2014**, *4*, 1498. f) C. Maeda, Y. Myazaki, T. Ema, *Catal. Sci. Technol.* **2014**, *4*, 1482.
2. a) Ziebart, C.; Federsel, C.; Anbarasan, P.; Jackstell, R.; Baumann, W.; Spannenberg, A.; Beller, M. *J. Am. Chem. Soc.* **2012**, *134*, 20701. b) Langer, R.; Diskin-Posner, Y.; Leitus, G.; Shimon, L. J. W.; Ben-David, Y.; Milstein, D. *Angew. Chem. Int. Ed.* **2011**, *50*, 9948. c) Bertini, F.; Mellone, I.; Ienco, A.; Peruzzini, M.; Gonsalvi, L. *ACS Catal*. **2015**, *5*, 1254.
3. a) Pagnoux-Ozherelyeva, A.; Pannetier, N.; Mbaye, M. D.; Gaillard, S.; Renaud, J.-L. *Angew. Chem. Int. Ed.* **2012**, *51*, 4976. b) Moulin, S.; Dentel, H.; Pagnoux-Ozherelyeva, A.; Gaillard, S.; Poater, A.; Cavallo, L.; Lohier, J.-F.; Renaud, J.-L. *Chem. Eur. J.* **2013**, *19*, 17881.
4. Thai T-T.; Mérel, D. S.; Poater, A.; Gaillard, S.; Renaud, J.-L. *Chem. Eur. J.* **2015**, *21,* 7066-7070.
5. Coufourier, S.; Mérel, D. S.; Thai, T-T.; Poater, A.; Gaillard, S.; Renaud, J.-L. in preparation.

Organocatalyzed Oxidation of Benzyl Alcohols by a Tetrazole-Amino-Saccharinate: A Combined Experimental and Theoretical (DFT) Study

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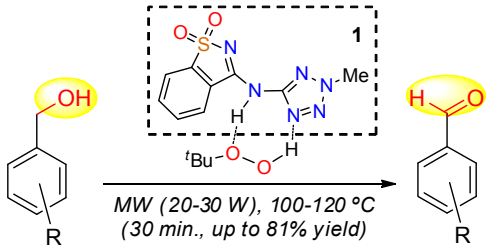
A new catalytic system for the anaerobic oxidation of benzyl alcohols using a tetrazole-amino-saccharin organocatalyst (**1**, *Scheme 1*), namely, (3-((2-methyl-2*H*-tetrazol-5-yl)amino)benzisothiazole 1,1-dioxide), has been established. In a solvent-free and microwave assisted process comprising aqueous tert-butyl hydroperoxide (TBHP) as oxidant, a variety of benzyl alcohols has been efficiently converted to aldehydes under mild conditions. Most reactions are complete within 30 minutes and the catalyst exhibits varied functional group compatibility.

Experimental evidence supported by DFT calculations indicates that the oxidation of benzyl alcohols promoted by the tetrazole-amino-saccharin derivative proceeds *via* a free radical mechanism.

DFT calculations performed for the oxidation of benzyl alcohol with and without organocatalyst show that the rate limiting steps of the whole reaction are the cleavage of the O–O bond in TBHP and the subsequent activation of the substrates by the organocatalyst which occur at the stage of H-abstracting from benzyl alcohol with consequent formation of a benzylic C-centered free radical. The amino and tetrazole functions of the organocatalyst, possibly associated to its conformational rigidity, play an important role in the main reaction steps. The simplicity, selectivity and softness of reaction conditions of the studied organocatalytic protocol suggest a great potential for extensive use in synthetic chemistry.



Scheme 1: Oxidation of Benzyl Alcohols Mediated by a Tetrazole-Amino-Saccharinate.

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References:

[1] Luís M. T. Frija, Maxim L. Kuznetsov, Bruno G. M. Rocha, Lília Cabral, M. Lurdes S. Cristiano, Maximilian N. Kopylovich, Armando J. L. Pombeiro, *submited.*

Organoboron Catalyzed Transformations of Epoxy Alcohols

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Epoxy alcohols are versatile intermediates in synthesis that can be ring opened or rearranged. Our group has demonstrated that organoboron catalysts are capable of regioselectively activating diols.[1] Recently, we expanded their utility to develop a tandem, selective and atom-economic ring-opening and protection of epoxy alcohols.[2] We now report that organoboron catalysts also enable rearrangements of epoxy alcohols to provide valuable synthetic intermediates in target-oriented synthesis. This rearrangement is proposed to occur via a pathway that is distinct from commonly used Lewis acids for these transformations.

Acknowledgements: We thank NSERC and the province of Ontario for financial support.

References:

1. Taylor, M.S. *Acc. Chem. Res.*, **2015**, *48*, pp 295–305.
2. (a) Tanveer, K.; Jarrah, K.; Taylor, M.S. *Org. Lett.*, **2015**, *17*, pp 3482–3485. (b) Garrett, G.E.; Tanveer, K.; Taylor, M.S. *J. Org. Chem.*, **2017**, *82*, pp 1085–1095.

Novel POM@MOF Materials: Improved Catalytic Performance for the Ring Opening Reaction of Styrene Oxide

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Metal-Organic Frameworks (MOFs) consist of metal centres connected by organic molecules, acting as ligands or linkers. These materials are usually obtained by conventional hydro/solvothermal methods, and this type of porous materials possess remarkably interesting applications in gas storage, catalysis and electronic chemistry, among others.[1] An emerging strategy to improve the performance of MOF materials as heterogeneous catalysts is reported: the iron-substituted polyoxometalate (POM) $TBA_4[PW_{11}Fe(H_2O)O_{39}]$ ($PW_{11}Fe$) was incorporated in to porous MOF NH_2-MIL-10(Fe), leading to a novel composite material, $PW_{11}Fe$@NH_2-MIL-10(Fe) (**Figure 1)**. In this approach[2], there is a clear increase of the catalytic performance of the MOF material for the ring opening of styrene oxide with aniline, since the conversion of the support NH_2-MIL-101(Fe) after 1 h of reaction is only 22%, instead of 100% obtained using composite $PW_{11}Fe$@NH_2-MIL- 101(Fe) catalyst. $PW_{11}Fe$@NH_2-MIL-101(Fe) also revealed to be a remarkable selective heterogeneous catalyst with 100% of selectivity to 2-phenylamino-2-phenylethanol isomer (**Figure 1**). Furthermore, high robustness and recyclability was also verified.

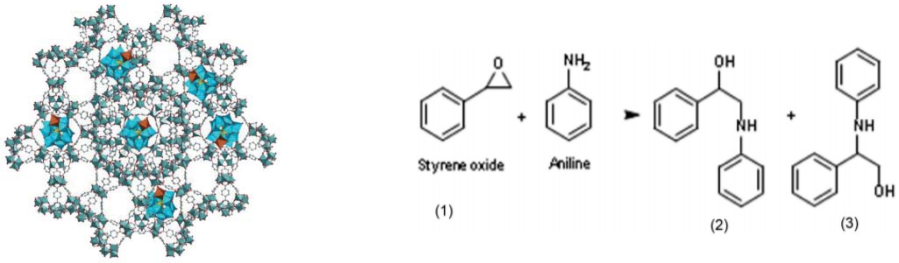

Figure 1: Representation of the composite structure (left) and the ring-opening reaction of styrene oxide with aniline.

Acknowledgements: The work co-financed by UE, FEDER - Fundo Europeu de Desenvolvimento Regional and COMPETE 2020 – Programa Operacional Competitividade e Internacionalização (POCI-01-0145-FEDER-007265) through PT 2020 and by national funds through the FCT / MCTES - Fundação para a Ciência e a Tecnologia / Ministério da Ciência, Tecnologia e Ensino Superior for the research centre REQUIMTE - LAQV (UID/QUI/50006/2013). Additional thanks to the FCT / MCTES for the PhD fellowship SFRH/BD/95574/2013 (to ADSB) and the Post-doctoral grant SFRH/BPD/111899/2015 (to LCS).

References:

1. K.K. Gangua; S. Maddilaa; S. B.Mukkamalab; S. B. Jonnalagaddaa *Inorg. Chim. Acta* **2016**, 446, 61–74.
2. Barbosa, A.D.S.; Julião, D.; Peixoto, A.F.; Freire, C.; de Castro, B.; Balula, S.S. and Cunha-Silva, L. *CrystEngComm.* **2017** in press, **DOI:** 10.1039/C7CE00528

BODIPY- Fullerene Dyads as Heavy Atom Free Singlet Oxygen Generators

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Triplet photosensitizers are widely used in photocatalytic organic reactions, photovoltaics, photodynamic therapy, and tripletetriplet annihilation (TTA) upconversion. Regarding these demand, design of efficient triplet photosensitizers showing strong absorption of visible light with long-lived triplet excited states is crucial.[1]Recently, a new generation of BODIPY based photosensitizers has been emerged that undergo efficient ISC not demanding the presence of heavy atoms on the fluorophore structure.[2]

Herein, unsubstituted, monostyryl and distyryl BODIPY- C_{60} dyads that show absorption in the visible region have been prepared via Bingel Cyclopropanation between BODIPY derivatives and fullerene C_{60} and characterized via elemental analysis, mass, ^{1}H and ^{13}C NMR spectroscopy as novel heavy atom free triplet photosensitizers to generate singlet oxygen (Figure 1). The new photosensitizers contain one and two light-harvesting antennas as well as associated different absorption wavelengths, resulting in high singlet oxygen generation. The panchromatic excitation energy harvested by the BODIPY moieties is funneled into a spin converter (C_{60}), thus ensuring intersystem crossing and population of the triplet state. We found that the BODIPY- C_{60} dyads can be used as photocatalysts that is singlet oxygen ($^{1}O^{2}$). In the photooxidation of DPBF the $^{1}O^{2}$ photosensitizing abilities of the C_{60} dyads are greater than the conventional triplet sensitizer methylene blue.[3]

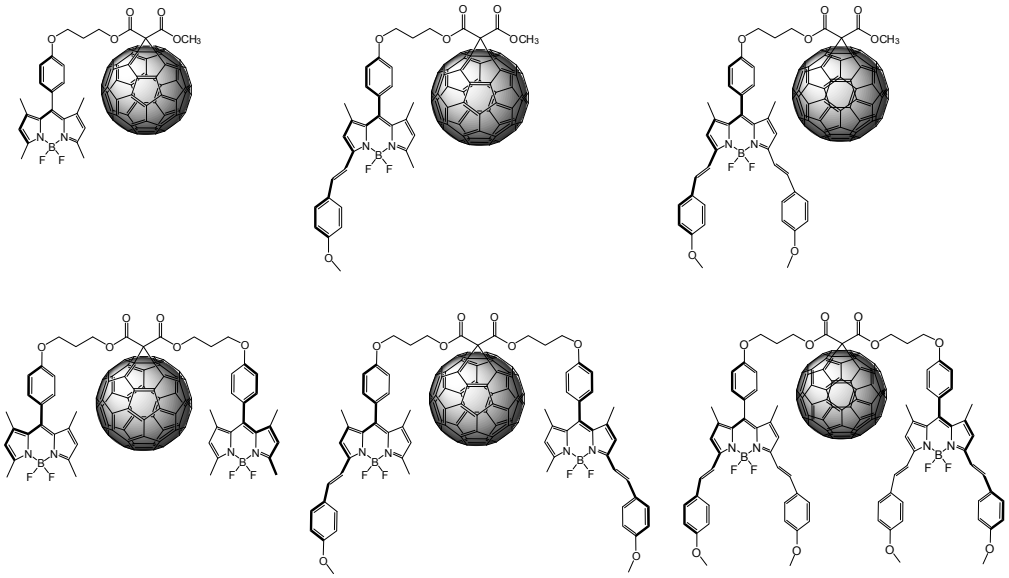

Figure 1: Molecular structures of BODIPY- C_{60} singlet oxygen generators

References:

1. Jasimuddin S.; Yamada T.; Fukuju K.; Otsuki J.; Sakai K. *Chem. Commun.* **2010**, 46, 8466
2. Li X.; Kolemen S.; Yoon J.; Akkaya E. U. *Adv. Func. Mater.* **2017**, 27, 1604053.
3. Ünlü H.; Okutan E. *Dyes and Pigments* **2017**, 142,

Various Approaches to Phosphorylation of Aromatic Compounds

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Aryl and heteroaryl phosphonates form an important class of substrates because of their broad application in medicinal chemistry, synthetic chemistry, material chemistry and catalysis. There are several methods to obtain phosphorylated aromatic and heteroaromatic substrates such as cross-coupling, nucleophilic addition or reactions catalyzed by metals. However, it should be noted that in majority of papers organic halides are used as aromatic substrates, while examples of substitution of C-H bonds where the leaving group is hydrogen are much smaller.[1]

The aim of our work was to develop simple and environmentally friendly approach to phosphorylation of aromatic and heteroaromatic compounds via electrochemical activation of aromatic C-H bonds using transition metal complexes as catalysts ($CoCl_2$bpy, $Ni(BF_4)_2$bpy, $MnCl_2$bpy, $Ni(BF_4)_2$bpy/$MnCl_2$bpy). The synthesis of arylphosphonates via direct phosphorylation of aromatic C-H bonds under electrochemical mild conditions is regarded as one of the most important approaches because it meets the generally accepted criteria of "green chemistry" such as atom-economy, short time and low waste of reaction compared to traditional approaches when organic halides are often used.[1,2]

We carried out a series of experiments to obtain phosphorylated aromatic compounds (benzene and its derivatives, coumarins, pyridine, etc.) under electrochemical oxidative conditions using bimetallic catalytic system $Ni(BF_4)_2$bpy/$MnCl_2$bpy and under electrochemical reduction conditions using $CoCl_2$bpy as catalyst. The distinctive feature of the process is an equimolar ratio of aromatic compound and phosphorylation reagent (1:1) and the room temperature. In both cases phosphorylated products were obtained in one step in good yield (up to 80%) and 100 % conversion of H-phosphonate (**Figure 1**). Although it was impossible to obtain ferrocenyl phosphonate under these conditions so we developed a non-catalytic method using Pb electrode and α-hydroxyalkylphosphonate as "masked" phosphorylating agent. Reaction proceeded at -50 °C, phosphorylated ferrocene was obtained in one step and in yield up to 90%.[2]

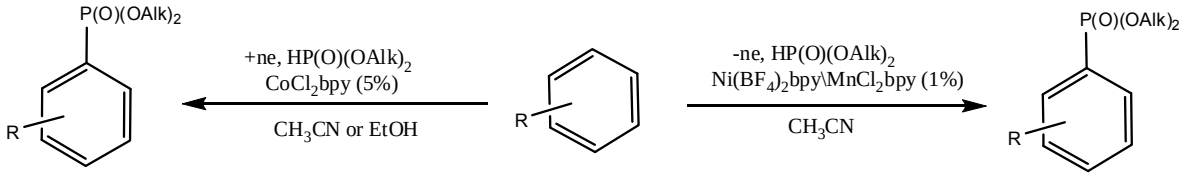

Figure 1: Electrochemical phosphorylation of aromatic compounds.

Thus new electrochemical approach to phosphorylation of aromatic compounds under mild conditions was proposed.

Acknowledgements: We thank the Russian Science Foundation, grant 14-23-00016 for financial support.

References:

1. a) Budnikova Y. H.; Sinyashin O. G. *Russ. Chem. Rev.* **2015**, *84(9)*, 917. b) Budnikova Y. H.; Gryaznova T. V.; Grinenko V. V.; Dudkina Y. B.; Khrizanforov M. N. *Pure Appl. Chem.* **2017**, *89*(3), 311.

2. a) Khrizanforov M. N.; Strekalova S. O.; Gryaznova T. V.; Khrizanforova V. V.; Budnikova Y. H. *Russ. Chem. Bull.* **2015**, 8, 1926. b) Khrizanforov M. N.; Strekalova S. O.; Kholin K. V.; Khrizanforova V. V.; Kadirov M. K.; Gryaznova T. V.; Budnikova Y. H. *Catal. Today*. **2017**, *279*, 133. c) Khrizanforov M.; Strekalova S.; Kholin K.; Khrizanforova V.; Grinenko V.; Gryaznova T.; Budnikova Y. *RSC Adv.* **2016**, *6*(48), 42701.

Multistep Organocatalytic Processes towards Stereodivergent Synthesis

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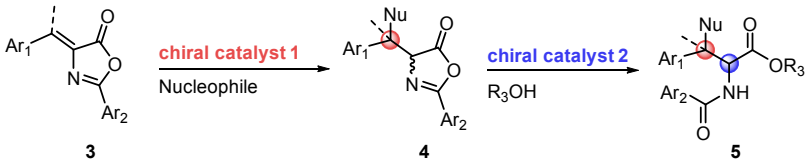
Since enantiomers of a drug candidate might display different biological properties, the preparation of all stereoisomers of a chiral product for biological evaluation has become standard procedure. Nevertheless, the development of a fully stereodivergent methodology, in order to access the complete set of stereoisomers when multiple stereocentres are present, is a great challenge in asymmetric synthesis and has recently attracted great interest.[1] On the other hand, catalytic asymmetric technologies, and in particular organocatalysis, have received great attention for the obtainment of stereodefined targets with high levels of selectivity. A class of valuable building blocks are enantiomerically pure natural and non natural α–amino acids, due to their high versatility as synthetic precursors in the obtainment of chiral drugs, peptides, chiral ligands and many other target molecules. The organocatalytic dynamic kinetic resolution (DKR) of oxazol-5-(4*H*)-ones (azlactones) by alcoholysis is a well-established methodology to obtain α–amino acid derivatives in an enantioenriched form.[2] On the other hand, the synthesis of β,β-disubstituted- α-amino acid derivatives, which also play a prominent role in the synthesis of various bioactive molecules, has received less attention. They can be synthesised from arylidene azlactones, such as **3**, exploiting a tandem Michael/ring opening reaction sequence which delivers the desired products **5**. However, arylidene azlactones have been mainly used in cycloaddition reactions[3] and there are no examples of asymmetric Michael addition reactions to arylidene azlactones **3** capable to stop at the Michael adducts **4** without proceeding to the subsequent ring-opening reaction.[4] This is generally due to the double electrophilic nature of **3**. As described in this work, the isolation of the intermediate **4** allows the development of a fully stereodivergent multi-step sequence[5] in which each catalytic step is promoted by a different chiral catalyst (Scheme 1), a scenario that enables the obtainment of all stereoisomers of the final product **5** by simple catalyst selection.



3 **4** **5**

Scheme 1

References:

1. a) Shi S.-L.; Wong Z. L.; Buchwald S. L. *Nature* **2016**, *532*, 353. b) Krautwald S.; Sarlah D.; Schafroth M. A.; Carreira E. M. *Science* **2013**, *340*, 1065. c) Zhan G.; Du W.; Chen Y.-C. *Chem. Soc. Rev.* **2017**, *46*, 1675. d) Krautwald S.; Carreira E. M. *J. Am. Chem. Soc.* **2017**, *139*, 5627.
2. a) Berkessel A.; Cleeman F.; Mukherjee S.; Müller T. N.; Lex J. *Angew. Chem. Int. Ed.* **2005**, *44*, 807. b) Berkessel A.; Mukherjee S.; Cleeman F.; Müller T. N.; Lex J. Chem. Commun. **2005**, 1898. c) Peschiulli A.; Quigley C.; Tallon S.; Gun'ko Y. K.; Connon S. J. *J. Org. Chem.* **2008**, *73*, 6409. d) Lee J. W.; Ryu T. H.; Oh J. S.; Bae H. Y.; Janga H. B.; Song C. E. *Chem. Commun.* **2009**, 7224.
3. For selected examples see: a) Jiang H.; Gschwend B.; Albrecht Ł.; Hansen S. G.; Jørgensen K. A. *Chem. Eur. J.* **2011**, *33*, 9032. b) Steurer M.; Jensen K. L.; Worgull D.; Jørgensen K. A. *Chem. Eur. J.* **2012**, *18*, 76. c) Wang D.; Wei Y.; Shi M. *Chem. Commun.* **2012**, *48*, 2764.
4. a) Geng Z.-C.; Li N.; Chen J.; Huang X.-F.; Wu B.; Liu G.-G.; Wang X.-W. *Chem. Commun.* **2012**, *48*, 4713. b) Izumi S.; Kobayashi Y.; Takemoto Y. *Org. Lett.* **2016**, *18*, 696.
5. Simmons B.; Walji A. M.; MacMillan D. W. C. *Angew. Chem. Int. Ed.* **2009**, *48*, 4349

Catalytic Cyclotrimerization of Halodiynes with Nitriles – Synthesis of 2- and 3-Halopyridines

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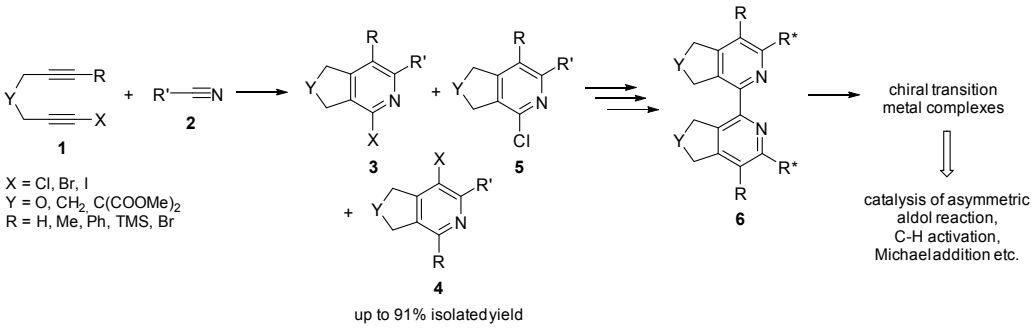
Simple or more complex substances possessing the pyridine ring are an importartant class of heteroaromatic compounds, which found application in many fields of chemistry.[1] The simplest and the most efficient method of their preparation is cyclotrimerization of alkynes with nitriles.[2]

In our work we would like to present the first example of direct synthesis of 2- and 3-halopyridines by transition-metal complex catalyzed [2+2+2] cyclotrimerization of 1-haloalkynes and nitriles.[3] We explored catalytic cyclotrimerization of 1-monohalo and 1,1'-dihalodiynes **1** (**Scheme 1**) with nitriles **2** to a mixture of 2- and 3-halopyridines **3** and **4**. The dependance of yield and regioselectivity of the reaction based on the structure of diynes **1**, nitriles **2** and reaction conditions was investigated. Creation of an unexpected third product **5** during the course of the reaction revealed a synthetically interesting halogen exchange reaction, mechanism of which was studied by NMR techniques. In addition 2- and 3-halopyridines **3** and **4** were available for further modification by e.g. cross-coupling reaction or reductive dimerization. The dimerization of 2-halopyridines **3** leads to 2,2'-bipyridines **6**. These bipyridines served as ligands for transition metal salts and the formed complexes were tested as catalysts in several organic reactions.



Scheme 1: Cyclotrimerization of halodiynes with nitriles and further transformations.

Acknowledgements: This project was supported by Czech Science Foundation (17-07707S), Grant Agency of Charles University (GAUK 243-250362) and French Embassy in Prague.

References:

1. Fache F.; Schulz E.; Tommasino M. L.; Lemaire M. *Chem. Rev.* **2000**, *100*, 2159.
2. Hill M. D. *Chem. Eur. J.* **2010**, *16*, 12052.
3. Bednarova E.; Colacino E.; Lamaty F.; Kotora M. *Adv. Synth. Catal.* **2016**, *358*, 1916.

Catalytic Activity of Dimeric Palladium Complexes bearing NHC Ligands in Suzuki-Miyaura Cross-Coupling Reaction

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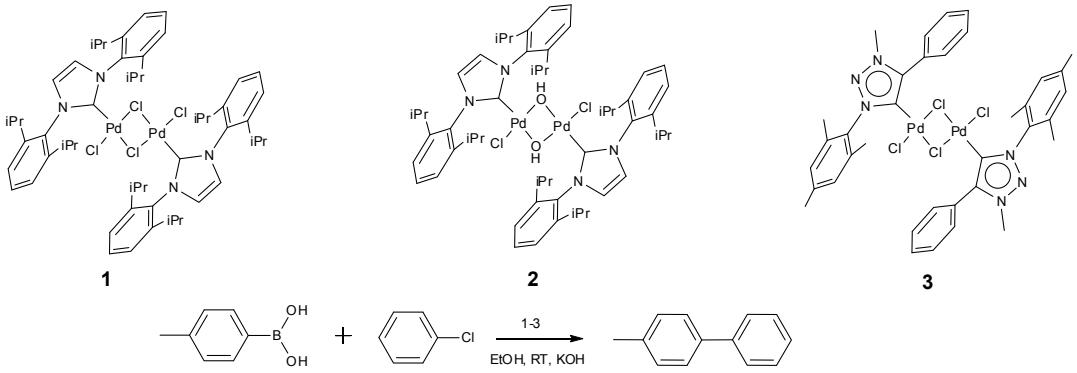
Since its introduction in 1979[1] Suzuki-Miyaura cross-coupling has become one of the most useful tool in organic sythesis[2]. Although many catalysts have been presented over the last decades, the chalange to diminish the catalyst loading at the possibly mildest reaction conditions is still the aim of many laboratories[2]. Recent progress in mechanistic studies of SM reaction indicates a key role of hydroxy moeites attached to palladium metal in the catalytic cycle[3] what inspired us to design a new effective catalyst for SM reaction[4].

In this short communication we shall disclose the cataltic activity in SM reaction of palladium dimeric complexes bearing imidazolim or triazolium carbenes as well as chloride and hydroxy anions as a μ-briged ligands (**Scheme 1**) followed by the preliminary mechanistic investgation aiming to understand the noticable difference in reactivty of presented species.



Scheme 1: Palladium dimeric complexes and their catalytic activity in SM cross coupling reaction.

Acknowledgements: The research was co-financed by the National Centre for Research and Development (NCBR) under the Project ORGANOMET No: PBS2/A5/40/2014 and National Science Centre under the project PRELUDIUM No: UMO-2015/19/N/ST5/00538.

References:

1. N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Letters* **1979**, *20*, 3437-3440.
2. "State-of-the-Art in Metal-Catalyzed Cross-Coupling Reactions of Organoboron Compounds with Organic Electrophiles": J. C. H. Lee, D. G. Hall in Metal-Catalyzed Cross-Coupling Reactions and More, Vol. 1–3 (Eds.: A. de Meijere, S. Brase, M. Oestreich),
Wiley-VCH, Weinheim, **2014**, pp. 65–132; 3
3. A. Thomas, S. Denmark, *Science* **2016**, *352*, 329-332.
4. S. Ostrowska, J. Lorkowski, M. Kubicki, C. Pietraszuk, *ChemCatChem* **2016**, *8*, 3580-3583.

Redox Trends in Cyclometalated Palladium(II) Complexes and their Application in Ligand Directed Functionalization of Aromatic C-H Bonds

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Cyclic and differential pulse voltammetry, X-ray structure analysis and quantum chemical calculations were used to study a series of binuclear and mononuclear cyclometalated palladium(II) complexes of different structure with diverse bridging groups (acetate, trifluoroacetate, chloride, phosphonate) and C^N ligand (2-phenylpyridine, benzo[h]quinoline and 1-phenylpyrazole).[1] The analysis revealed a regularity of the complexes oxidation potential on the metal-metal distance in the complexes: the larger Pd-Pd distance, the higher oxidation potentials (**Figure 1**). These results are in a good agreement with the electron density distribution in the complexes. As palladacycles are considered to be the key intermediates of ligand-directed C-H functionalization reactions, the revealed regularity might be useful to determine the optimal reaction conditions, particularly a sutable oxidant, to achieve the highest yields of the functionalized products.

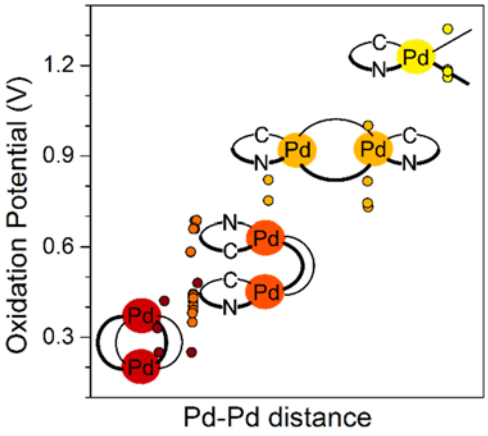

Figure 1: Dependence of palladium complexes first oxidation peak potential on Pd-Pd distance.

Acknowledgements: This work was supported by the Russian Science Foundation (grant no. 14-23-00016).

References:

1. Dudkina Yu. B.; Kholin K. V.; Gryaznova T. V.; Islamov D. R.; Kataeva O. N.; Rizvanov I. Kh.; Levitskaya A. I.; Fominykh O. D.; Balakina M. Yu.; Sinyashin O. G.; Budnikova Yu. H. *Dalton Trans*. **2017**, *46*, 165.

Monomers Containing Naturally Occurring Antimicrobials: Synthesis and Polymerization Studies for the Preparation of Highly Functional PLA-based Materials

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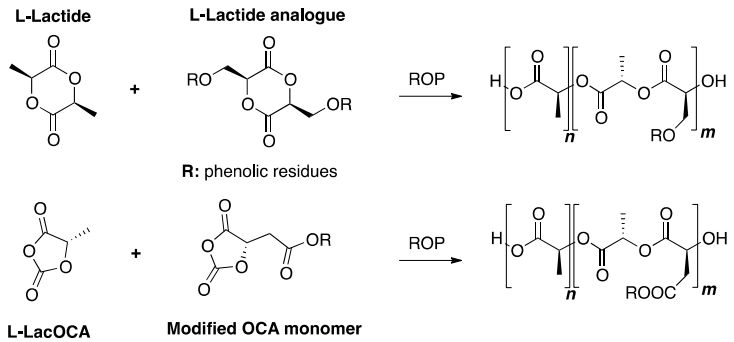
The purpose of food packaging is to preserve the quality and safety of the food it contains, from the time of manufacture to the time it is used by the consumer. In order to protect the product from physical, chemical or biological damages, the food packaging can serve as carrier of bioactive substances, such as antioxidants and antimicrobials. They can be physically mixed into formulations or, alternatively, covalently attached to the polymer, in the latter case taking care that the modification does not cause deterioration or alteration of the polymer properties. Chemical incorporation of bioactives into a biodegradable polymer backbone has multiple advantages (e.g., higher drug loading, sustained release, tunable release rates) over the aforementioned physical incorporation methods.

In recent years environmental awareness has been focused onto the replacing of traditional plastics based on petrochemical resources with alternative, more biocompatible materials. Among them, poly(lactic acid), shortly PLA, is one of the most attractive to researchers and industry, because of its good biodegradability and availability from renewable sources, such as starch and sugar beet.[1]

As part of a research project aimed to the development of improved PLA for packaging industry,[2] the main objective of the present work is to copolymerize standard L-lactide, or its equivalent the *O*-carboxyanhydride of L-lactic acid,[3] (L-LacOCA) with functionalized monomers synthesized in our laboratories, containing naturally occurring antimicrobials and antioxidants, as pendant groups (**Scheme 1**).

We report here the synthesis and the structural characterization of L-lactide analogues and OCA monomers, prepared starting from natural L-malic acid and incorporating various bioactive compounds, such as naturally occurring phenols (i.e. carvacrol, eugenol). Preliminary results on ring opening polymerization (ROP) in solution of OCA monomers will be also presented, as well as the characterization of the resulting polymers.



Scheme 1: ROP of L-lactide analogues and OCA monomers to obtain highly functionalized PLA-based polymers.

References:

1. Inkinen, S.; Hakkarainen, M.; *Biomacromolecules,* **2012**, *12*, 523-532.
2. Gazzotti, S.; Farina, H.; Lesma, G.; Rampazzo, R.; Ortenzi, M.; Silvani, A.; *Manuscript in preparation*, **2017**.
3. Vaca, B. M.; Bourissou, D; *ACS Macro Letters*., **2015**, *4*, 792-798

Secondary Phosphine Oxides as Efficient Preligands for the Generation of Active [Pd^{II}]-H: Application in Anaerobic Alcohol Oxidations

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Ligand design and synthesis are always crucial steps toward the building of highly efficient and selective catalysts[1]. On the last decade, our group developed a broad expert knowledge in Secondary Phosphine Oxides (*SPO's*)[2]. During the synthesis of new Pd^{II}-*SPO's* complexes from Pd^0(*dba*)$_2$, we noted a partial reduction of *dba*[3]. This unexpected result could be explained by the formation of a putative active and robust (*SPO*)$_2$Pd^{II}-H species from acetic acid followed by an hydride transfer from Pd to *dba* (figure 1).

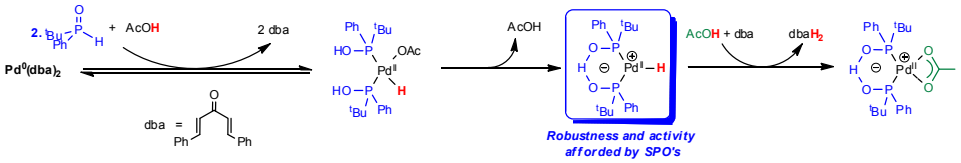

Figure 1 : *SPO*'s as efficient ligands for Pd-H stabilization

The activity and the robustness of this putative (*SPO*)$_2$Pd^{II}-H species was revisited in metal catalyzed anaerobic oxidation of alcohols by a so called "Abstracting Hydrogen Methodology"[4]. Under optimized conditions, methyl vinyl ketone (*MVK*) has proven to be the better hydride acceptor, allowing the selective oxidation of secondary alcohols bearing air sensitive moieties (figure 2)[5]. 24 examples of highly chemio- and regioselective oxidations have been done. Mechanistic aspects of this original system are still under investigations, in particular to rigorously demonstrate the key role played by water in the catalytic cycle. These encouraging results obtained about of hydride transfer could enable us to re-explore the very broad field of [Pd^{II}]-H chemistry[6].

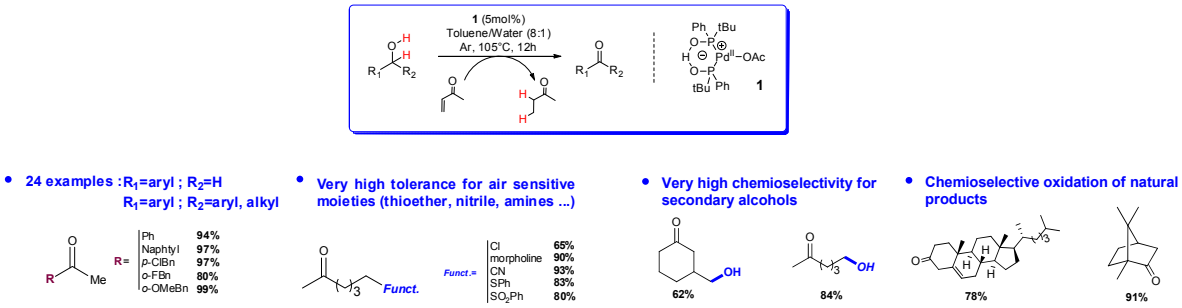

***Figure 2* : Anaerobic alcohol oxidation by "Abstracting Hydrogen Methodology"**

References :

[1] Black D. St C., Hartshorn A. J. *Coordination Chemistry Review* **1973**, *9*, 219-274

[2(a)] Leyris A., Nuel D., Giordano L., Achard M., Buono G. *Tetrahedron Letters* **2005**, *46*, 8667-8480 ;[(b)] Bigeault J., Giordano L., Buono G. *Angew. Chem. Int. Ed.* **2005**, *117*, 4831-4835 **;** [(c)] Martin D., Moraleda D., Achard T., Giordano L., Buono G. *Chem. Eur. J.* **2011**, 17, 12729-12740

[3] Gatineau D., Moraleda D., Naubron J. V., Burgi T., Giordano L., Buono G. *Tetrahedron Asymmetry* **2009**, *20*, 1912-1917

[4 (a)] Nishimura T., Onoue, T., Ohe, K., Uemura S. *J. Org. Chem.* **1999**, *64*, 6750-6755 ;[(b)] Muzart J., *Chem. Asian. J.* **2006**, *1*, 508-515 ; [(c)]Ding B., Zhang Z., Liu Y., Sugiya M., Imamoto T., Zhang W. *Org. Lett.* **2013**, *15*, 3690-3693

[5] Membrat R., Vasseur A., Gatineau D., Tenaglia A., Nuel D., Giordano L. *Chem. Cat. Chem.* **2017**, *9*, 728-732

[6] For a comprehensive review see :[(a)] Grushin V. V. *Chem. Rev.* **1996**, *96*, 2011-2034 ; For recent works see : [(b)] Vyas D. J., Larionov E., Besnard C., Guénée L., Mazet C. *J. Am. Chem. Soc.* **2013**, *135*, 6177-6183

Earth-Abundant Metal Catalysis Made Easy

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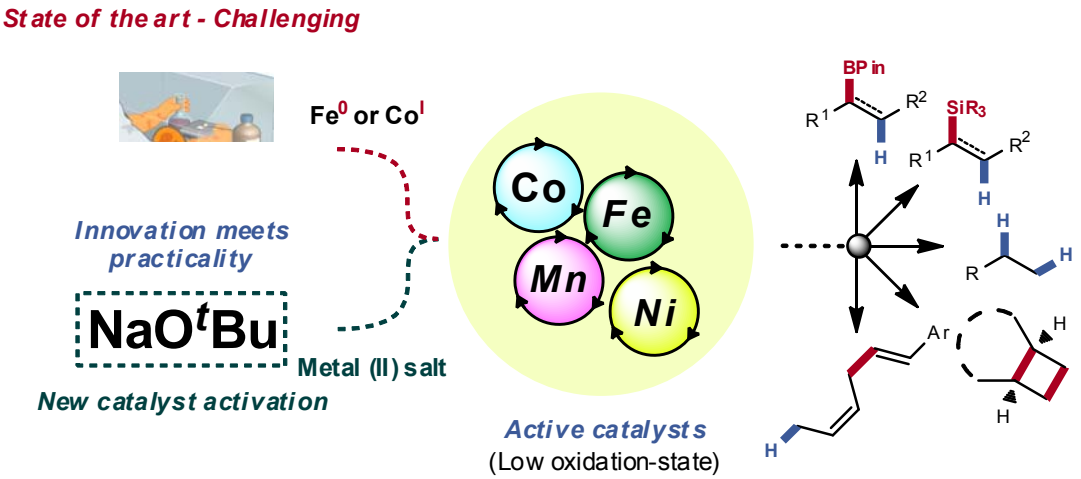

A sustainable future lies in the use of first row, low cost, low toxicity, Earth-abundant metals. Despite this, the metals that are most abundant have yet to be widely adopted by the global community.

Why is this?

Why does the synthetic chemist not instinctively use iron, manganese or cobalt?

Why do expensive metals such as; platinum, palladium and rhodium dominate?

The simple answer:

The non-expert chemist is simply not equipped to try.

Most of these powerful synthetic methods rely on the use of air- and moisture-sensitive pre-catalysts or reagents, which are challenging to handle, store and transport. In the ideal scenario, all reagents and pre-catalysts would be air- and moisture-stable solids that are easily handled, and applicable in large-scale processes with minimal associated hazards.

We have developed a simple pre-catalyst activation protocol using a safe and easily handled reagent (NaO^{t}Bu) with wide commercial availability. This has allowed generic access to sustainable first-row transition metal (Fe, Co, Mn, Ni) low oxidation-state catalysis across a wide range of reductive alkene and alkyne functionlisation reactions (hydroboration, hydrosilylation, hydrogenation, hydrovinylation and [2π+2π] cyclisation reactions).

1. J. H. Docherty, J. Peng, A. P. Dominey and S. P. Thomas. ***Nature Chemistry***, 9, 595-600 (2017). DOI: 10.1038/nchem.2697 *Highlighted in: Chemistry World, ACS The Nexus & Phys.org*

Iron-Catalyzed Chemoselective Hydrogenation of α,β-Unsaturated Carbonyl Compounds

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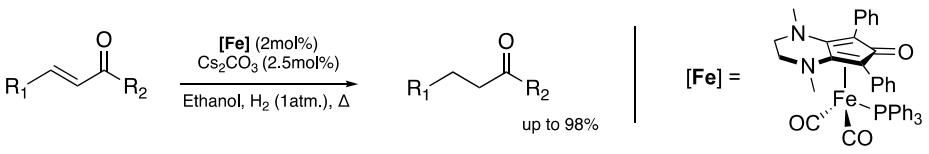
In molecular chemistry, carbon-carbon double bond reduction remains challenging compared to polarized C=X bond (X=O, N), and find its importance within common organic synthesis.[1] When C=C and C=X are entailed on a same molecule, the difficulty to reduce one beside the other becomes even more challenging, more importantly when they are both conjugated. Over the past decade, catalytic hydrogenation was brought as efficient and clean system in homogeneous catalysis. Most of the catalytic system carrying this transformation involved late transition metal such as rhodium, ruthenium, iridium and palladium.[2] Literature furnished a plethora of examples which are efficient for carbonyl reduction of an α,β-unsaturated ketone. Unfortunately, only few toward selective carbon-carbon hydrogenation have been reported so far.[3] Recently, we discussed about a bifunctional iron complex for ketone alkylation under mild conditions.[4] DFT calculations have provided interesting aspects about the reactivity of the complex, and lead us to investigate further in its chemoselectivity towards conjugated carbonyl compounds.[5] (Scheme 1)



Scheme 1: Hydrogenation of carbonyl derivatives catalyzed by iron bifunctional complex.

Acknowledgements: We gratefully acknowledge financial support from the "Ministère de la Recherche et des Nouvelles Technologies", Normandie Université, the "Centre National de la Recherche Scientifique", the "Région Normandie", Ademe agency, and the LABEXSynOrg (ANR-11-LABX-0029).

References:

1. a) Klingler, F. D. *Acc. Chem. Res.* **2007**, *40*, 1367. b) Hems, W. P.; Groarke, M.; Zanotti-Gerosa, A.; Grasa, G. A. *Acc. Chem. Res.* **2007**, *40*, 1340. c) Johnson, N. B.; Lennon, I. C.; Moran, P. H.; Ramsden, J. A. *Acc. Chem. Res.* **2007**, 40, 1291. d) Shimizu, H.; Nagasaki, I.; Matsumura, K.; Sayo, N.; Saito, T. *Acc. Chem. Res.* **2007**, *40*, 1385. e) Guo, N.; Hu, M.-Y.; Feng, *Org. Chem. Front.* **2015**, *2*, 692. f) Bart, S. C.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 13794. g) Yu, R. P.; Darmon, J. M.; Hoyt, J. M.; Margulieux, G. W.; Turner, Z. R.; Chirik, P. J. *ACS Catal*. **2012**, *2*, 1760.
2. Wang, D.; Astruc, D. *Chem. Rev.* **2015**, *115*, 6621−6686
3. a) Jurcik, V.; Nolan, S. P.; Cazin, C.S.J. *Chem. Eur. J.* **2009**, *15*, 2509-2511. b) Shimizu, H.;, Nagano, T.; Sayo, N.; Saito, T.; Ohshima, T.; Mashima, K. *Synlett*, **2009**, *19*, 3143-3146. c) Ding, Z.; Zhang, Z.; Liu, Y.; Sugiya, M.; Imamoto, T.; Zhang, W. *Org. Lett.* **2013**, *14*, 3690-3693. d) Broggi, J.; Jurčík, V.; Songis O.; Poater, A.; Cavallo, L.; Slawin, A.M.Z.; Cazin, C.S.J. *J. Am. Chem. Soc.* **2013**, *135*, 4588–459. e) Li, W.; Wu, X.-L. *Chem. Eur. J.* **2015**, *2*, 331-335. f) Noyori, R.; Umeda, I.; Ishigami, T. *J. Org. Chem.* **1972**, *37*, 1542-1545. g) Chirik, P.J. *Acc. Chem. Res.* **2015**, *48*, 1687−1695
4. a) Thai T-T.; Mérel, D. S.; Poater, A.; Gaillard, S.; Renaud, J.-L. *Chem. Eur. J.* **2015**, *21,* 7066-7070. b) Seck, C; Mbaye, M. D.; Coufourier, S.; Lator, A.; Lohier, J.-F.; Poater, A.; Ward, T. R.; Gaillard, S.; Renaud, J.-L. **2017**, *submitted*
5. Lator, A.; Coufourier, S.; Fillion, E.; Ward, T. R.; Gaillard, S.; Renaud, J.-L. *manuscript in preparation*

Palladium-Catalyzed Regioselective Direct Arylation of Benzofurazans at C4 Position

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Benzofurazan skeleton especialy C4 or/and C7 (hetero)aryl benzofurazans are advantageous as fluorophore due to their palanar strucutre. They are also used as conventional acceptor in the design of electron donor–acceptor type organic semiconductors.[1] The most common way to access these derivatives is through palladium cross coupling reactions using an organometallic or boron reagents.[2] In this work, the access to 4-arylbenzofurazans and 4,7-diarylbenzofurazans throught palladium catalyzed regioselective C-H bond arylation using phosphine-free palladium acetate as the catalyst and potassium acetate as an inexpensive base in the presence of aryl bromides as coupling parteners were invistageted.[3] A wide range of functions on the aryl bromide are tolerated. Some sterically hindered aryl bromides, and sulfur or nitrogen containing heteroaromatic substrates have also been successfully employed. The use of a larger amount of aryl bromide allowed the palladium-catalyzed one-pot C4,C7-diarylation of benzofurazan. Finaly the synthesis of some quinoxalines were invistigated from arylated benzofurazans, throught an opening of the furazan unit of the benzofurazans in the presence of ethanolamines under acidic conditions.

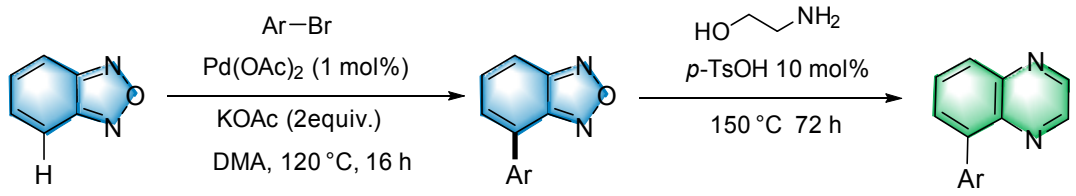

Figure 1: Palladium catalyzed direct arylation of benzofurazan and their ring opening.

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References:

1. a) B.Behramand, F.Molin, H.Gallardo, Dyes and Pigments, **2012**, 95, 600-605. b) L. Wang, W. Huang, R. Li, D. Gehrig, P. W. M. Blom, K. Landfester, K. A. I. Zhang, Angew. Chem. Int. Ed. **2016**, 55, 9783-9787.
2. a) C. Song, Y. Ling, L. Jin, M. Zhang, D.-L. Chen, Y. He, DaltonTrans. **2016**, 45, 190-197. b) H.-C. Ting, Y.-T. Yang, C.-H. Chen, J.-H. Lee, J.-H. Chang, C.-I. Wu, T.-L. Chiu, C.-F. Lin, C.-L. Chung, K.-T. Wong, ChemSusChem **2016**, 9, 1433-1441.
3. I.Idris, F.Derridj, J.-F. Soulé, H. Doucet, Adv. Synth. Catal. **2017** (Accepted Author Manuscript)

Synthesis of 5-Bromo-4-Thio-2'-Deoxyuridine-5'- Triphosphate

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One of the leading causes of death today is cancer and its most common treatment is photo / radiotherapy. To increase the efficiency of these modalities one usually uses sensitizers that make cancer cell more sensitive to UV and/or ionizing radiation. Modified nucleosides with high electron affinity, prone to dissociative electron attachment are the examples of such compounds.[1]

The current project was aimed to obtain a modified, radiosensitive DNA. For that purpose we synthesized the 5'-trifosphosphate of 5-bromo-4-thio-2'-deoxyuridine (5-Br-4SdUTP) and incorporated it into DNA using the chemically-enzymatic method.[4] Hence, 5-Br-4SdUTP was obtained by thiolation of 5-BrdU, followed by phosphorylation with tributylammonium pyrophosphate and phosphoryl oxychloride.[3] The triphosphate was then incorporated into DNA fragment. In order to reach this goal we used a chemically synthesized single-stranded template (oligonucleotide, ss30compl – see Fig. 1) and two shorter complementary oligonucleotides (ss14, ssP15 – see Fig. 1) one of them phosphorylated at its 5'-end. After annealing a double stranded oligonucleotide with a one nucleotide gap is formed as shown in Fig. 1. Afterwards, the nick in double-stranded DNA is filled in with the 5-Br-4SdUTP using a BSU DNA Polymerase –Large Fragment. Finally T4 DNA ligase repairs the remaining single stranded break. The obtained oligonucleotide was purified with HPLC and its mass was confirmed with LC-MS method.

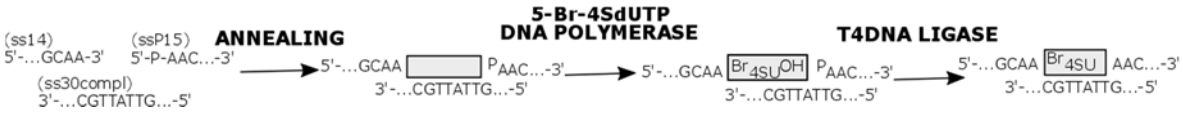

Figure 1. Enzymatic synthesis of double-stranded oligonucleotide labelled with 5-Br-4SdU.

Acknowledgements: We thank the Polish National Science Centre for financial support (Grant Number: 2014/14/A/ST4/00405)

References:

1. Rak J.; Chomicz L.; Wiczk J.; Westphal K.; Zdrowowicz M.; Wityk P.; Żyndul M.; Makurat S.; Golon Ł. *J. Phys. Chem.,* 2015, 119, 8227–8238.
2. Xu Y.-Z.; Zhang X.; Wu H.C.; Massey A.; Karran P. **2004**, *Bioorg. Med. Chem. Lett. 14,* 995–997.
3. Tauraite D.; Jakubovska J.; Dabužinskaite J.; Bratchikov M.; Meškys R. **2017,** *Molecules* 672-688.
4. Westphal K.; Zdrowowicz M.; Zylicz-Stachula A.; Rak J. **2017**, *J. Photochem. Photobiol B:,* 228–235.

Poster Communications

Experimental and DFT Studies on the Pd-Catalyzed Synthesis of 4-Allyl- isochromen-1-imines from 2-Alkynylbenzamides

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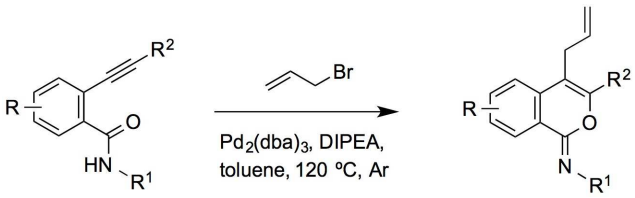
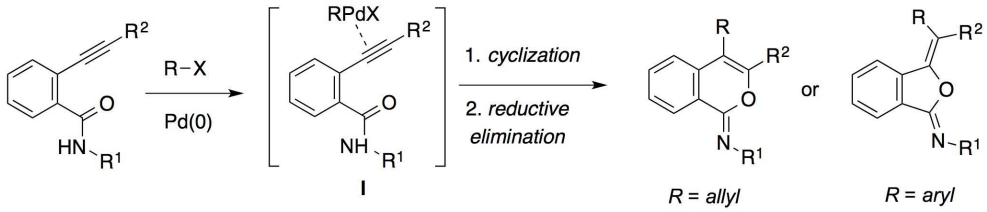
The palladium-catalyzed heterocyclization reactions of 2-alkynylbenzamides have enjoyed increased attention in recent years, particularly in the case where cyclization is followed by a C-C coupling in a cascade process.[1] Usually, products derived from either a 5-*exo*- or a 6-*endo*-O-cyclization are obtained with high selectivity. However, these regiochemical preferences have not been rationalized. We have now extended the applicability of these cyclization-coupling reactions of 2-alkynylbenzamides with the use of allyl bromide as coupling reagent, and report that the corresponding *O*-cyclization-allylation process proceed with high regioselectivity to afford 4-allyl-isochromen-1-imines (**Scheme 1**). These products are formally the result of a 6-*endo*-cyclization of the starting alkynylbenzamide.



Scheme 1. Pd-catalyzed preparation of 4-allyl-isochromen-1-imines from 2-alkynylbenzamides

DFT calculations have been performed on this reaction and the related arylation,[2] that affords the alternative 5-membered isobenzofuranimines under similarly Pd(0)-catalyzed conditions. A possible rationalization for the observed regiochemical divergence is offered in a unified mechanism proceeding via alkynylpalladium complexes **I** (Scheme 2).



Scheme 2. Computed mechanistic hypothesis

Acknowledgements: We thank the Spanish Ministerio de Economía y Competitividad (MEC) (grant number CTQ2015-68794-P), Fondos Europeos para el Desarrollo Regional (FEDER), and the Universidad del País Vasco (PES12/32 and fellowship Y. M. "*Ayuda para la Contratación de Doctores Recientes*") for financial support. SGIker UPV/EHU is thanked for technical support (NMR facilities). We are grateful to the Centro de Supercomputación de Galicia (CESGA) for generous allocation of computing resources.

References:

1. (a) Madich, Y.; Álvarez, R.; Aurrecoechea, J. M. *Eur. J. Org. Chem.* **2014**, 6263; (b) Madich, Y.; Alvarez, R.; Aurrecoechea, J. M. *Eur. J. Org. Chem.* **2015**, 6298, and references cited therein.
2. Yan, Z. Y.; Tan, C. M.; Wang, X.; Li, F.; Gao, G. L.; Chen, X. M.; Wu, W. S.; Wang, J. J. *Synlett* **2011**, 1863.

Synthetic Aproaches to 8-Deoxyheronamide C

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8-Deoxyheronamide C belongs to a family of natural polyene macrocyclic lactams isolated from the culture broth of *Streptomyces* sp.[1] All the members of this family feature a highly unsaturated macrocyclic system that can engage into pericyclic reactions. The structure was deduced by spectroscopic analysis.[2] We report here different approaches to the total synthesis of 8-deoxyheronamide C, based on convergent scheme involving Pd-catalyzed cross coupling reactions to elongate the polyene system, a *cis* selective Julia-Kocienski reaction of an allylic sulfone and an amidation reaction. This strategy would establish the basis for the preparation of other members of the same family and the study of their (bio)synthetic relationship (**Figure 1)**.

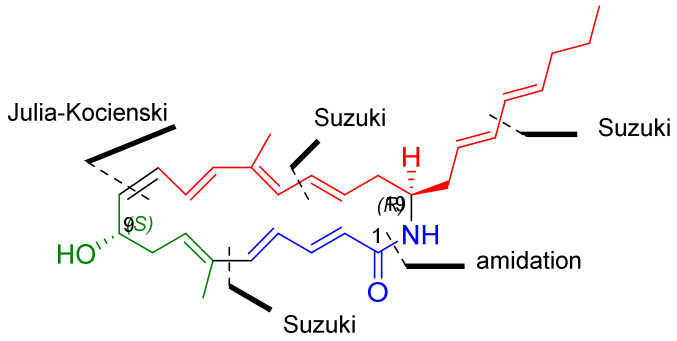

Figure 1: Structure of 8-deoxyheronamide C.

Acknowledgements: We thank the Spanish MINECO (SAF2013-48397-R, FEDER), Xunta de Galicia (Grant 08CSA052383PR from DXI+D+i; Consolidación 2006/15 from DXPCTSUG; INBIOMED-FEDER "Unha maneira de facer Europa") for financial support.

References:

1. Sugiyama R.; Nishimura S.; Matsumori N.; Tsunematsu Y.; Hattori A.; Kakeya H. *J. Am. Chem, Soc.* **2014**, *136*, 5209.
2. Raju R.; Piggott A. M.; Conte M. M.; Capon R. J. *Org. Biomol. Chem.* **2010**, *8*, 4682.

Synthesis of Dehydrotryptophans by Methal Catalyzed Cyclization-Heck Cascade Reactions

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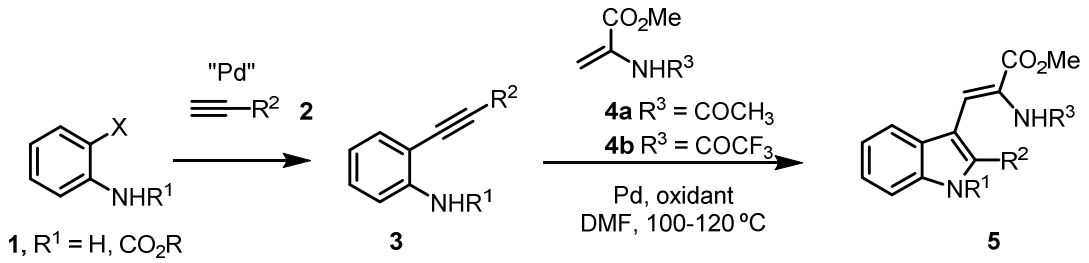
The indole ring represents a very common framework both in natural product and important bioactive molecules currently used as drugs.[1] Therefore, all the efforts towards the development of efficient synthetic strategies to the simple preparation of this scaffold are of high interest. Based on our previously reported strategy to prepare benzofuran-, indole- and 1*H*-isochromen-1-imine- type derivatives following a heterocyclization-oxidative Heck cascade strategy,[2] we envisioned the use of dehydroalanine derivatives in the form of α-acetamidoacrylate esters (**4**) as components of the Heck reaction. Thus, starting from simple aniline substrates, dehydrotryptophan derivatives can be prepared through a Pd-driven cascade event (**Scheme 1**). The optimization of the reaction conditions and the development of a one-pot three-component version of this process will be discussed.



Scheme 1: Stepwise Sonogashira-cascade cyclization-oxidative coupling from haloanilines, alkynes and α-acetamidoacrylate esters.

Acknowledgements: We thank the Spanish *Ministerio de Economía y Competitividad* (Grant CTQ2012-37734, FEDER) for financial support.

References:

1. Taylor, R.D; MacCoss, M; Lawson, A. D. G. *J. Med. Chem.* **2014**, *57*, 5845.

2. Álvarez, R.; Martínez, C.; Madich, Y.; Denis, J. G.; Aurrecoechea, J. M.; de Lera, Á. R. *Chem. Eur. J.* **2010**, *16*, 12746; corrected in *Chem. Eur. J.* **2012**, *18*, 13894.

In Sılıco Analysıs of Inhıbıtıon Effect of Protoporphyrın IX Derıvatıves on Quorum Sensıng System of Pseudomonas Aeruginosa

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Pseudomonas aeruginosa (PA) is a Gram negative organism which is responsible for many human infections. Some studies suggest that failure to remove disease might be caused by biofilm form of PA resistant to antibiotics. Biofilm is a complex that bacteria forms, in which they communicate by Quorum Sensing (QS) when they reach a certain population and show increased resistance. There are QS systems in PA, The las systems and the RhI system. LasI system consists of the LasR transcriptional regulator and the LasI synthase protein. It could be helpful targeting lasI and lasR to inhibit the QS activity in this organism. Some potential lasR inhibitory compounds were also reported to various studies such as furanones. Anti-bacterial activity of Gallium(III)protoporphyrin IX (GaPPIX) on PA has been investigated recently(1) and studies on several human cells showed that GaPPIX does not show cytotoxicity at concentrations below 128 µM (2). The aim of this study to investigate the inhibition effect of protoporphyrin IX (M-PPIX) derivatives on las systems of PA *in silico*.

In this study, we have investigated inhibition effect of M-PPIX derivatives on the QS system in PA *in silico*. Conformational analysis and geometry optimization of M-PPIX derivatives (M= Zn, Co,Cu etc) was performed using Gaussian software by quantum mechanical DFT/wb97xd/6-31G (d,p) calculations. The crystal structure of lasI protein (PDB ID 2UV0) and lasR protein (PDB ID 1RO5) were subjected to protein preparation. PPIX derivatives was docked with the lasI and lasR proteins and docking studies were carried out by AutoDock Vina software based on scoring function. The same method was also applied to M-PPIX derivatives and results were compared in terms of binding energies of docked complexes.

Results of docking studies showed that M-PPIX derivatives bind to both proteins of Las system with very similar binding energies (≈-8.7 kcal/mol). Therefore we proposed that these compounds can be used as possible candidate drugs for inhibiting of QS systems of PA. It is clear that these compounds should be subjected to in vitro studies also.

References

1. Hijazi S., Visca P., Frangipani E. “Gallium(III)protoporphyrin IX Inhibits Pseudomonas Aeruginosa Growth by targeting Cytochromes”, *Frontiers in Cellular and Infection Microbiology*, 7, (2017)

2. Chang, D., Garcia, R. A., Akers, K. S., Mende, K., Murray, C. K., Wenke, J. C., et al.. “Activity of gallium meso-and protoporphyrin IX against biofilms of multidrug-resistant Acinetobacter baumannii isolates”. *Pharmaceuticals* 9:16 (2016)

Solvothermal Alcoholysis Routes for Recycling Polylactide Waste as Lactic Acid Esters

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In recent years there has been growing interest in the use of biomass as the feedstock for the production of chemical intermediates, because this is an attractive alternative to the use of traditional fossil-fuel-derived materials. Much attention has focused on lactic acid and its alkyl esters, which are produced commercially from a range of agricultural residues and food byproducts. Alkyl lactates (ALs) are important eco-friendly chemicals, referred to as green solvents; and have a number of industrial and commercial applications: e.g., as solvents or diluents for polymeric resins, dyes, paints, inks and pigments, low-temperature lubricants, components of cleaning, agriculturally or cosmetically useful compositions. Ethyl lactate is particularly useful and is one of the most promising green chemicals used in a multitude of mechanical and microelectronic applications.[1]

Currently, bulk production of lactate esters is based on esterification of lactic acid with the appropriate alcohol in the presence of acid catalysts. The process is technologically complicated because the presence of water affects the reaction equilibrium and limits conversion or self-esterification of lactic acid under prolonged heating. The use of excess alcohol, catalysts, and separation processes is therefore essential for efficient AL synthesis.[2]

The recent significant increase in industrial applications of bioplastics has also increased interest in the development of alternative processes based on chemical recycling of polylactides (PLAs) to produce a range of industrially useful lactic acid esters. We have developed a simple and convenient solvothermal alcoholysis method for large-scale recycling of PLA resins or residues from disposable packaging in the presence of the appropriate alcohol under catalyst-free or catalytic conditions. The results show that the best catalytic activities involve magnesium and calcium alkoxides synthesized in situ from organometallic or metallic precursors and an alcohol (**Figure 1**). We determined the crystal structure of the chiral mononuclear postcatalyst $[Ca(LAc)_2(EL)_2]$ (LAc = lactic acid anion, EL = ethyl lactate), obtained directly from the reactor. Particular emphasis is placed on the operating conditions and high activity of the catalyst used. Key factors that affect the catalytic activity and reaction mechanism are also highlighted.[3]

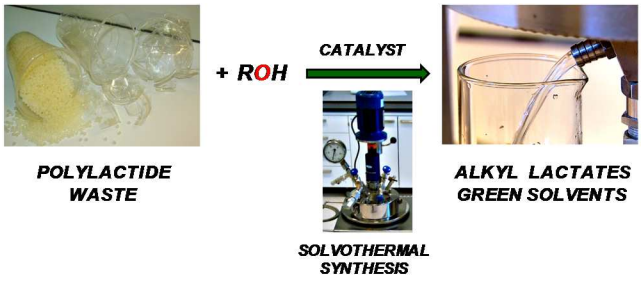

Figure 1: Solvothermal alcoholysis method for recycling of PLA resins as lactic acid esters.

References:

1. a) Nikles S. M.; Piao M.; Lane A. M.; Nikles D. E. *Green Chem*. **2001**, *3*, 109. b) Henneberry M. *PCI Magazine* **2002**, *18*, 84.
2. Pereira C. S. M.; Silva V. M. T. M.; Rodrigues A. E. *Green Chem*. **2011**, *13*, 2658.
3. Petrus R.; Bykowski D.; Sobota P. *ACS Catal.* **2016**, *6*, 5222.

Electrochemical Behavior of Consumable Graphite Electrodes for the Production of Hydrogen and Synthetic Fuels

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Water electrolysis is a well known process for the production of hydrogen[1] as well the utilization of carbon-based catalysts in electrocatalytic applications. In this work, it was envisaged to obtain an innovative electrochemical process for the production of hydrogen and synthetic fuels.

Low temperature electrolysis in alkaline media using graphite consumable anodes, from which syngas was obtained[2], has been conducted using two different sources of graphite, Schunk and Electroerosion quality (GR_{EQ}), pursuing higher efficiency in the production of hydrogen and synthetic fuels. Due to the better results obtained for the production of the desired gases, Electroerosion graphite was selected.

The electrochemical oxidation of the graphite proceeded at near room temperature with the production of gases CO_2, CO and H_2. Traces of CH_4 and C_2H_6 were also detected by gas chromatography analysis. Sectional voltammetry studies with increments of 250 mV in the interval between -1V and 3V, at different scan rates, suggest the formation of oxidation species that will be discussed in this work (Fig. 1).

Cyclic voltammetry and polarization curves were used to establish optimum operational conditions and to study the electrodes aging degradation. Morphological studies carried out by scanning electronic microscopy (SEM) allowed verifying the evolution of the graphite electrodes during the aging process. Typical results are shown in Fig. 2.

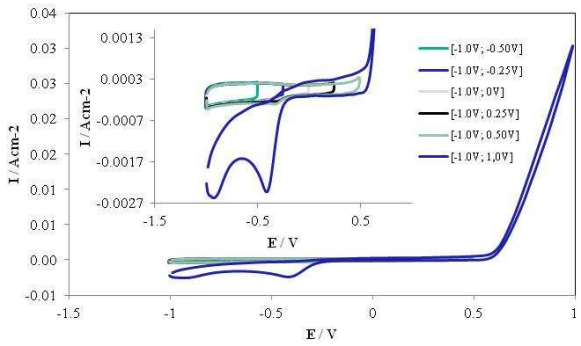
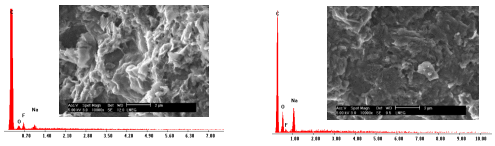


Fig. 1 - Sectional cyclic voltammetry studies at room temperature, scan rate 50 mVs^{-1} with increments of 250 mV in the interval between -1V and 1V, using an aqueous solution of NaOH, 0.4M and Ag/AgCl as reference



(a) (b)

Fig.2 – Scanning electronic microscopy (SEM) images and respective EDX spectrum of electroerosion graphite particles before (a) and after (b) being electrochemically oxidized.

References

1. Zeng, K., Zhang, D., *Recent progress in alkaline water electrolysis for hydrogen production and applications*, Progress in Energy and Combustion Science, **2010**, *36*, 307-326.
2. J. Rodrigues, Portuguese Patent 106779 T: Obtenção de gás de síntese por eletrólise alcalina da água, 2013.02.13

Selective Stripping of C-supported Metal Catalysts from Aqueous to Organic Phases by Supercritical (sc-)CO_2

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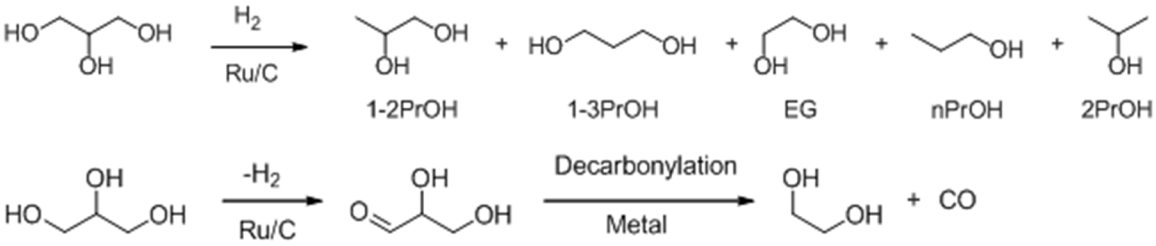
Multiphase systems (MPs) composed of an organic solvent, water, and an ionic liquid (IL), have been extensively used to run organic reactions in the presence of heterogeneous metal-based catalysts.[1,2] Although this configuration allows an efficient recovery of catalysts and products, it may often limit the activity of catalysts, thereby requiring harsher conditions to push reactions to completion. Not to mention the contamination by residual salts derived from the IL. With the aim of investigating solutions to these issues, we were able to develop a simple and effective procedure for the selective stripping of C-supported metal catalysts from an aqueous to an organic (hydrocarbon-based) phase, by using sc-CO_2. As an example, starting from a bi-phasic water-isooctane system, model reactions such as the hydrogenolysis of glycerol have been explored in the presence of a Ru/C catalyst. At different pressures of H_2 and CO_2 (up to 30 and 50 bar, respectively), not only the reaction occurred in the aqueous phase by producing the expected diols, alcohols and hydrocarbons (through both hydrogenolysis and C-C bond breaking pathways, Scheme 1), but also the metal catalyst could be selectively transferred in the isooctane phase (Figure 1, right). Otherwise, in the absence of CO_2, Ru/C was partitioned between the two immiscible (aq./org) media (Figure 1, left). A plausible explanation for the observed behaviour takes into consideration the effect of compressed carbon dioxide as a liquid expanding agent, for which a variety of mechanisms have been proposed.[3]



Scheme 1. The aqueous phase hydrogenolysis of glycerol catalysed by Ru/C.

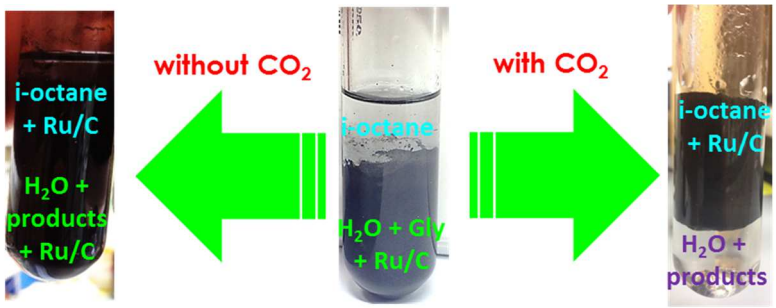


Figure 1: picture of multiphase hydrogenolysis of glycerol. Centre: start of the reaction; Right: the final mixture when sc-CO_2 was used; left: the final reaction mixture in the absence of CO_2.

References:

1. A. Perosa, P. Tundo, *Chem. Soc. Rev.*, **2007**, *36*, 532-550.
2. M. Selva, M. Gottardo, A. Perosa, *ACS Sustainable Chem. Eng.*, **2013**, *1*, 180-189
3. G. R. Akien, M. Poliakoff, *Green Chem.*, **2009**, *11*, 1083–1100.

Ruthenium – Catalyzed, Phthalimide Directed C(sp2)-H bond Alkenylation by Alkynes

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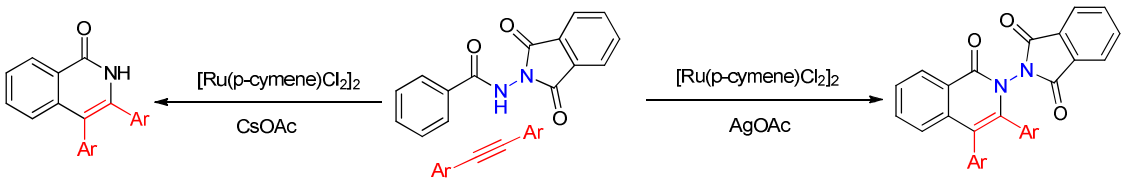
A pthalimide directed ruthenium-catalysed C(sp2)-H functionalization with alkyne has been doveloped. The cyclization of substituted N-(1, 3-dioxoisoindolin-2-yl)benzamides with alkynes in the presence of easily available ruthenium complex [(RuCl2(p-cymene)]2 and CsOAc provides isoquinolone[1] derivatives in good to excellent yields. Whereas N-N intact product also formed in the presence of ruthenium complex and AgOAc condition with good to excellent yields.

Scheme



Acknowledgements: We thank University Grants Commission, India for financial support and IIT Mandi for instrumental facility.

References:

1. (a) N. Guimond, C. Gouliaras and K. Fagnou, Journal of the American Chemical Society, 2010, 132, 6908;
(b) N. Guimond, S. I. Gorelsky and K. Fagnou, Journal of the American Chemical Society, 2011, 133, 6449.

2. P. S, Sagara, P.C. Ravikumar, P.F. Siril (Manuscript under preparation)

Palladium Nanoparticles on Temperature Responsive Microgels for Hydrogenation

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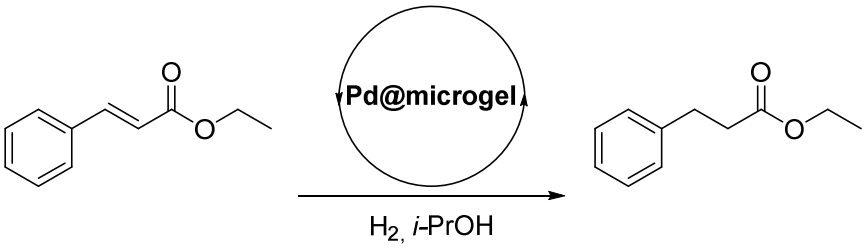
Transition metal catalysis has been established as one of the most powerful tools in organic synthesis.[1] Considering the importance of recycling and reusing catalysts, due to the increasing prices of the metal salts the recovery is placed in the spotlight. Immobilization of catalysts on suitable supports is one of the favored methods to improve recovery and efficiency of catalysts.[2] The most used solid supports for transition metal compounds are carbon, alumina, silica and zeolites, but all these heterogeneous supports show some limitations in terms of accessibility of the active species and lower diffusion properties, leading to lower activities compared to homogeneous catalysis.
In the last years stimuli-responsive polymers, colloids and polymer materials attracted considerable interest. In particular microgels are getting into the focus of research. Microgels are soft polymer networks synthesized of crosslinked polymer chains.[3] The interesting part of microgels is the ability of changing size, softness and surface by varying pH, light, solvent or temperature.[4] This ability makes microgels interesting systems for immobilizing catalysts, since they provide a quasi-homogeneous environment. We describe the development of a new stimuli microgel-based colloidal catalyst system. The palladium-nanoparticles can be recycled for ten reaction cycles without losing reactivity (**Scheme 1**).



Scheme 1: Hydrogenation of ethyl cinnamate with palladium nanoparticles on an ethyl acrylate-based microgel (0.1 wt%).

Acknowledgements: We thank the SFB 985 for financial support.

References:

1. a) M. Rueping, R. M. Koenigs, R. Borrmann, J. Zoller, T. E. Weirich, J. Mayer *Chem. Mater.* **2011**, *23*, 2008. b) Q. Wu, H. Cheng, A. Chang, X. Bai, F. Lu, W. Wu *Chem. Commun.* **2014**, *50*, 14217.
2. a) E. Guibal *Prog. Polym. Sci.,* **2005**, *30*, 71. b) N. Madhavan, C.W. Jones., M. Weck *Acc. Chem. Soc. Res.,* **2008**, *41*, 1153.
3. F. A. Plamper; W. Richtering *Acc. Chem. Soc. Res.* **2011**, *50*, 131.
4. A. Pich; W. Richtering *Adv. Polym. Sci.* **2010**, *234*, 1.

De Novo Synthesis of Rare Pyranosugars Based on Sequential Metal Catalysis

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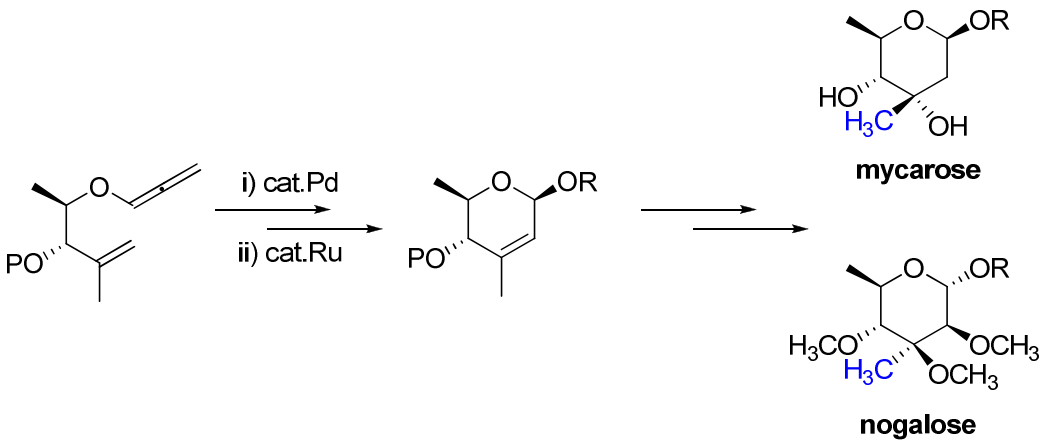
Rare sugars are found as a key fragment in numerous natural products. Thus, the efficient synthesis of rare sugars represents a synthetic challenge. Conventional methods require multi-step transformations that rely heavily on protective group strategy. In addition, the conventional synthesis of the oligosaccharides containing rare sugars suffer from problems associated with the O-glycosidic bond formation.

De novo synthesis based upon catalytic asymmetric synthesis is becoming a very powerful alternative. In this context, we recently reported a highly efficient synthesis of apiofuranoside. The key event is the sequential metal catalysis consisting of Pd-catalyzed asymmetric hydroalkoxylation of alkoxyallene and the subsequent Ru-catalyzed ring-closing metathesis. [1] In this presentation, we wish to report our recent result that expands the scope of this reaction to the rare C3-methylated pyranosugars as an anomerically well-defined cyclohexyl glycoside. Optimization process as well as the application to the synthesis of nogalose and mycarose will be discussed.



References:

1. a) Lim, W.; Kim, J.; Rhee, Y. H., *J. Am. Chem. Soc.* **2014**, *136*, 13618. b) Kim, M.; Kang, S.; Rhee, Y. H., *Angew. Chem. Int. Ed.* **2016,** *55*, 9733.

Kinetic Study of Friedel-Crafts Acylation Reaction Over Hierarchical Y Zeolite Prepared Through Surfactant Mediated Technology

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One of the most important routes for the synthesis of aromatic ketones that are intermediates in manufacturing fine and speciality chemicals are the Friedel-Crafts acylation and related rearrangements. Several studies show that zeolites are promising catalysts as an alternative to homogeneous ones such as $AlCl_3$ and $FeCl_3$ that are harmful to the environment. However, the microporous nature of zeolites limits its application, especially when larger molecules are involved. To overcome this limitation efforts have been made to incorporate mesopores in zeolites, thus creating hierarchical materials. In the present work Y zeolite (FAU structure) was submitted to alkaline treatment with NH_4OH in the presence of surfactants, under autogenous pressure, according to Garcia-Martinez et al[1]. The influence of several parameters such as: the pH of the suspensions (10 or 11), the type of surfactant cetyl trimethylammonium bromide (CTAB) or dodecyl trimethyl ammonium bromide (DTAB) and the duration of the treatment (12 or 24 h) were studied. The samples were characterized by X-ray powder diffraction, N_2 adsorption isotherms at -196 ºC and pyridine adsorption followed by IR spectroscopy. The catalytic behaviour was investigated in Friedel-Crafts acylation of heteroaromatics using furan as substrate and acetic anhydride as acylating agent (molar ratio 1:5) at 60ºC. Samples of the reaction mixture were periodically separated from the catalyst and analysed by GC. A simplified Langmuir-Hinshelwood model was used to calculate kinetic parameters[2] and turnover frequencies (TOF) were also determined. **Figure 1** shows the evolution of product yield as a function of time.

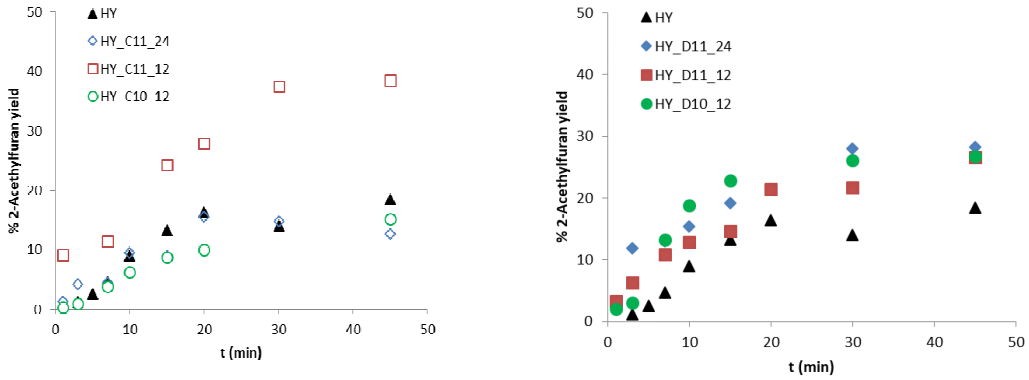

Figure 1: Evolution of 2-acethylfuran yield (selectivity > 99%) as a function of time. **Sample designation:** C=CTAB, D=DTAB surfactants, followed by the pH (10 or 11) and the duration of the treatment (12 or 24 h)

As can be observed, the pH of the suspensions and the duration of the treatment originate distinct catalytic behaviors that depend on the type of surfactant used (CTAB or DTAB), evidencing that multiple factors are involved in this methodology to prepare hierarchical catalysts.

Acknowledgements: We thank FCT for financial support: UID/MULTI/00612/2013 and PEst-OE/QUI/UI0612/2013.

References:

1. Garcia-Martinez J., Johnson M., Valla J., Li K.H., Ying J.Y., **2012** *Catalysis Science & Technology, 2*(5), 987.
2. Aleixo R, Elvas-Leitão R, Martins F, Carvalho A.P., Brigas A., Martins A., Nunes N., **2017** *Molecular Catalysis*, *434*, 175.

Transition Metal Free α-Arylation of Ketones via Enolonium Species

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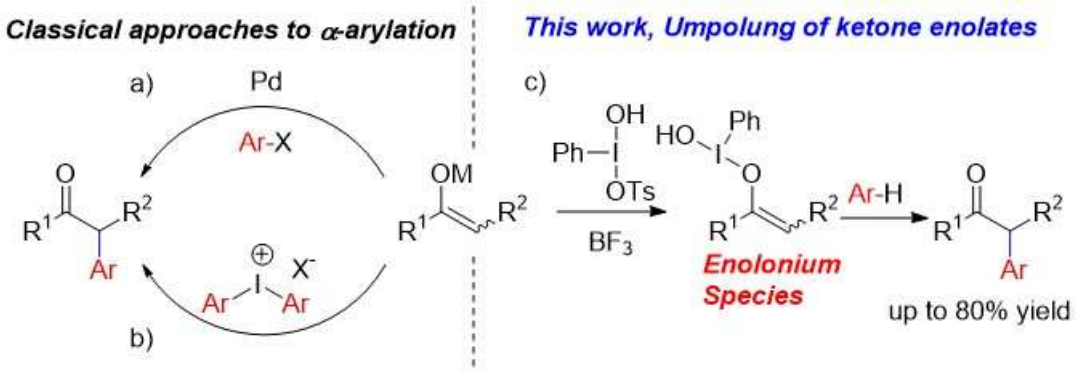
Arylation of ketones is an important transformation in organic synthesis. It has seen numerous applications in the synthesis of medicinal compounds as well as in the total synthesis of natural products. It is generally carried out by the transition metal catalyzed reaction of enolates with aryl halides (**Scheme 1a**). An alternative is the reaction of enolates with an electrophilic aryl reagent such as diaryliodonium salt (**Scheme 1b**). A common factor in these approaches is the use of a functionalized aryl donor.

We report a novel transition metal-free direct arylation of ketone enolates that does not require such a functionalized aryl donor, but allows the use of feedstock heteroaromatic and aromatic compounds. This unprecedented reaction proceeds via the umpolung of a ketone enolate into an electrophilic enolonium species by the action of a hypervalent iodine reagent (**Scheme 1c**). [1] The reaction is of broad scope with respect to heteroaromatic compounds and allows reaction with electron-rich benzene derivatives. It should prove useful for applications both in industry and academia.



Scheme 1

References:

1. a) P. S. Baran, J. M. Richter, J. Am. Chem. Soc., **2004**, *126*, 7450–7451 b) P. S. Baran, J. M. Richter, D. W. Lin, *Angew. Chem. Int. Ed.* **2005**, *44*, 609 –612.

Synthesis and Toxicological Evalution of Cocaine Analogues

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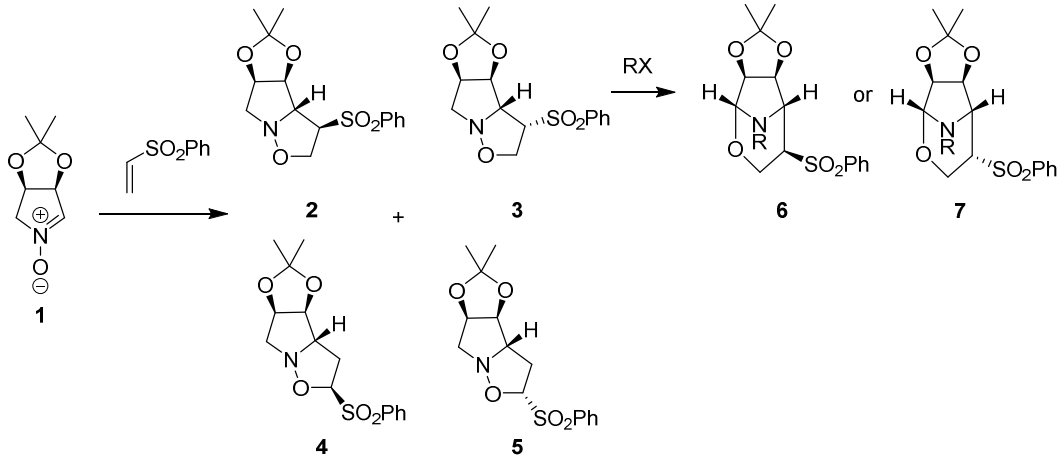
Cocaine is an alkaloid derived from *Erythroxylon coca* plant. Dopamine transporter (DAT) is the primary target for cocaine's action. DAT mediates reuptake of dopamine from the synaptic cleft and thereby controls the termination of dopaminergic signaling. Cocaine is a high-affinity inhibitor of DAT and it is thought that its binding to DAT causes a rapid increase in extracellular dopamine levels that produce the reinforcing effects leading cocaine abuse.[1]

Development of compounds that block the binding of cocaine to DAT and present low addictive power could be used as pharmacological treatments for cocaine abuse. These compounds should be cocaine analogues that avoid abrupt elevations of dopamine in the synaptic space.[2]

Our research group has been working in the last years in the reactivity of sulfones and nitrones for the synthesis of isoxazolidines (**2**-**5**) by 1,3-dipolar cycloaddition reaction.[3] In this communication it will be described a new procedure based on the rearrangement of chiral isoxazolidines into bicyclic system with two heteroatoms analogues of cocaine as compounds **6** and **7** by treatment with reactive organic bromides (**Scheme 1**). In addition, a toxicological evaluation of cocaine analogues was carried out using zebrafish embryo as model.



Scheme 1. Synthesis of bicyclic system with two heteroatoms analogues of cocaine starting from nitone 1

Acknowledgements: Financial support: Junta de Castilla y León co-financed by the Fondo Social Europeo (BIO/SA59/15.), University of Salamanca (KAS7) and MINECO (CTQ2015-68175-R).

References:

1. Beuming, T.; Kniazeff, J.; Bergmann, M. L.; Shi, L.; Gracia, L.; Raniszewska, K.; Newman, A. H.; Javitch, J. A.; Weinstein, H.; Gether, U.; Loland, C. J. *Nat. Neurosci.* **2008**, *11*, 780-789.
2. Velázquez-Sánchez, C.; Ferragud, A.; Murga, J.; Cardá, M.; Canales, J. J. *Eur Neuropsychopharm* **2010**, *20*, 501-508.
3. a) Flores, M.; García, P.; Garrido, N. M.; Nieto, C. T.; Basabe, P.; Marcos, I. S.; Sanz-González, F.; Goodman, J. M.; Díez, D. *Tetrahedron: Asymm.* **2012**, *23*, 76-85. b) Flores, M.; Garcia-Garcia, P.; Garrido, N. M.; Marcos, I. S.; Sanz, F.; Diez, D. *RSC Adv.* **2012**, *2*, 11040-11048.

Synthesis and Antitumor Activity of Alkyl Ether Phospholipids Analogs of Edelfosine.

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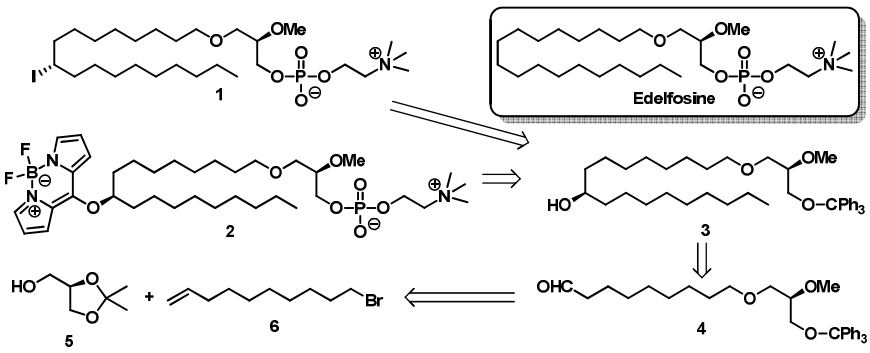
The so-called alkylphospholipid analogs (APLs) constitute a family of synthetic antitumor compounds that target cell membrane. The alkyl ether phospholipid edelfosine has been considered the prototype of these antitumor agents and promotes apoptosis in tumor cells by a selective way, while sparing normal cells.[1] Lipid rafts are membrane microdomains enriched in sphingolipids and cholesterol wich are more ordered than the surrounding lipid bilayer. Lipid rafts are crucial for the compartmentalization of signaling processes in the membrane, mostly involved in cell survival and apoptosis.[2] It has been proved that APLs act as antitumor drugs at the cell membrane level, specifically in lipid rafts domains.[1]

In this work, we report the stereoselective synthesis of two analogs of edelfosine; compound **1**, that has a iodine atom in C9 of the alkyl chain of edelfosine, and compound **2**, that has a BODIPY-type fluorescent label at the same carbon. Retrosynthesis of compounds **1** and **2** are shown in **Scheme 1**.

It has been proved that iodine analogs of edelfosine are highly active as antitumor agents and, in addition, they are better incorporated into tumor cells.[3] BODIPY (4,4-difluor-4-bora-3a,4a-diazo-*s*-indacene) dyes have been used for PET (Positron Emission Tomography)/FMT (Fluorescence Molecular Tomography) imaging in order to obtain *in vivo* tumor images.[4] That should be usefull in cancer therapeutics and diagnosis.[5] Antitumor activities of these compounds and other edelfosine analogs are being carried out in Dr. F. Mollinedo's laboratory.



Scheme 1: Retrosynthesis of compound **1** and **2** from *R*-solketal and 1-bromodec-9-ene.

Acknowledgements: We thank the Spanish Ministerio de Economía y Competitividad (SAF2014-59716-R) for financial support, and A. M. R. thanks the Spanish Ministerio de Educación, Cultura y Deporte for a FPU fellowship.

References:

1. Gajate C; Mollinedo F. *Anticancer Agents Med. Chem.* **2014**, *14*, 509.
2. Gajate C; Mollinedo F. *J. Leukocyte Biol.* **2015**, *98*, 739.
3. Gil-Mesón A. Tesis Doctoral, *Universidad de Salamanca*, **2013**.
4. Hendricks JA; Keliher EJ; Wan D; Hilderbrand SA; Weissleder R; Mazitschek R. *Angew. Chem. Int. Ed.* **2012**, *51*, 4603.
5. (a) Flores-Rizo JO; Esnal I; Osorio-Martinez CA; Gomez-Duran CF; Banuelos J; Lopez Arbeloa I; Pannell KH; Metta-Magana AJ; Pena-Cabrera E. *J. Org. Chem.* **2013**, *78*, 5867. (b) Kowada T; Maeda H; Kikuchi K. *Chem. Soc. Rev.* **2015**, *44*, 4953.

From C-H Activation to Fuel Cells: a Ruthenium Story

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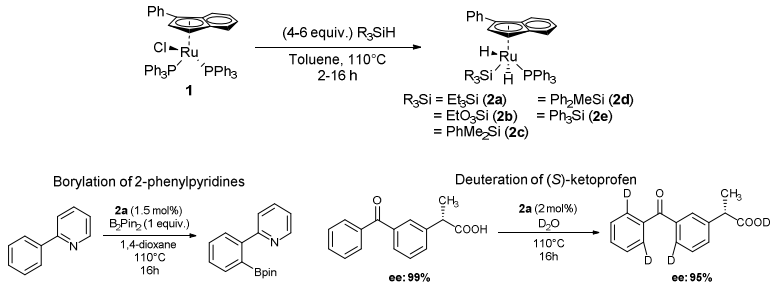
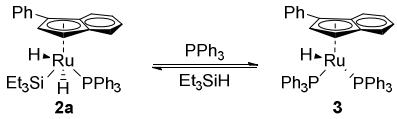
σ-Complexes are species where one of the ligands is bound to the metal center through the donation of 2 σ-electrons in an L-type fashion.[1] In recent decades, they attracted much attention due to their role in the activation of C-H bonds. We contributed to this area of research with a family of easily prepared ruthenium complexes (**2a**-**2e**). Of this series, the triethylsilane-based complex (**2a**) showed remarkable activity in the borylation of 2-phenylpyridines[2] and in the H-D exchange of different organic moieties.[3] In addition, the deuteration of the enantiopure (*S*)-Ketoprofen led to the incorporation of three deuterium atoms with retention of molecular chirality.



While studying the formation of compound **2a**, it was found that this complex was in equilibrium with the hydrido species **3**.



Complex **3** has already been reported, showing poor activity in transfer hydrogenation reactions.[4] However, we recently discovered that it could be effectively used in the decomposition of formic acid[5]. Indeed, complexes containing Ru-H bonds have shown interesting catalytic activities in the decomposition of formic acid to H_2 and CO_2.[6] Hydrogen has lately gained much attention for its growing use in fuel cell technology[7] and formic acid is considered one of the most promising compounds for the generation of hydrogen, due to its high mass content of hydrogen and ease of storage.[8] The *in-situ* generated H_2 was employed in the hydrogenation of alkenes, such as *trans*-stilbene and cinnamic acid, and in the production of electricity *via* a fuel cell.

References:

1. R. Crabtree, *The organometallic chemistry of the transition metals*, John Wiley & Sons, Hoboken, NJ, Fourth Edi., 2005; R. Crabtree, *Angew. Chemie Int. Ed.*, 1993, **32**, 789–805.
2. J. A. Fernández-Salas, S. Manzini, L. Piola, A. M. Z. Slawin, and S. P. Nolan, *Chem. Commun*. , 2014, **50**, 6782–6784.
3. L. Piola, J. A. Fernández-Salas, S. Manzini and S. P. Nolan, *Org. Biomol. Chem.*, 2014, **12**, 8683–8688.
4. S. Manzini, C. A. U. Blanco and S. P. Nolan, *Adv. Synth. Catal.*, 2012, **354**, 3036–3044.
5. L. Piola, J. A. Fernández-Salas, F. Nahra, A. Poater, L. Cavallo, and S. P. Nolan, *Molecular catalysis,* manuscript accepted.
6. T. Koike and T. Ikariya, *Adv. Synth. Catal*., 2004, **346**, 37-41; C. P. Casey, S. W. Singer and D. R. Powell, *Can. J. Chem*., 2001, **79**, 1002-1011; G. A. Filonenko, R. van Putten, E. N. Schulpen, E. J. M. Hensen and E. A. Pidko, *ChemCatChem*, 2014, **6**, 1526-1530.
7. A. B. Züttel, A. and L. Schlapbach, *Hydrogen as a Future Energy Carrier*, Wiley, 2008.
8. J. Graetz, *Chem. Soc. Rev*., 2009, **38**, 73-82.

Straightforward Asymmetric Syntheses of Orthogonally Protected Aspartic Acid by Oxidation of *β*-amino Acids.

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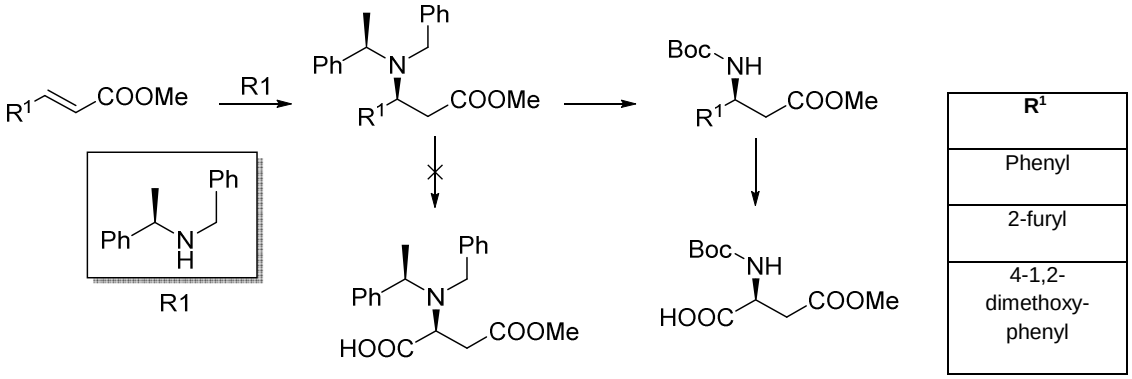
Natural *α*-amino acids are very commonly used in the current pharmacology research. However, new study areas in medicinal chemistry and genetic fields are being discovered due to the properties presented by their synthetic analogs[1,2]. As an example, these chiral *α*-amino acids are found in current drug skeletons; such as carbapenems, penicillins or cephalosporins[1]. Furthermore, secundary and terciary peptide structure propierties have been able to be demostrated by placing unnatural chiral *α*-amino acids in their structure[3].

Our team previously studied the reactivity of a chiral lithium amide, which is able to induce chirality to prochiral substrates. This sthereochemical conformation is produced by the intermediate state of the reaction[4]. We demonstrate here the extension of the methodology in order to obtain chiral orthogonally protected aspartic acid derivatives.

At the last synthesis step, $RuCl_3$ and $NaIO_4$ were used as oxidant and cooxidant in order to turn the aromatic group into a carboxilic acid. While this reaction was succesfully managed when the amine gruop was conveniently protected, it was observed that the reaction did not take place if more than one aryl group were found in the molecule.



R¹
Phenyl
2-furyl
4-1,2-dimethoxy-phenyl

Scheme 1: Methodology used in syntheses of aspartic acids derivatives.

This procedure allows to obtain the orthogonally protected aspartic acid as a powerfull building block in organic synthesis, from which we can extend the synthesis of α or β-amino acids by selective transformation of a proper functional group, as well as interesting β-amino tetrahydrofuryl derivatives that will be discussed within the meeting.

Acknowledgements: We thank to MINECO CTQ2015-68175-R, FEDER Junta de Castilla y León (UIC21)

References:

1. Gupta, A.; Halve, A. K. *Int. J. Pharm. Sci. Res.* **2015**, *6*, 978.
2. Lang, K.; Chin, J. W. *Chemical Reviews* **2014**, *114*, 4764.
3. Lyu, P. C.; Sherman, J. C.; Chen, A.; Kallenbach, N. R. *Proceedings of the National Academy of Sciences* **1991**, *88*, 5317.
4. Nieto, C. T.; Díez, D.; Garrido, N. M. *Journal of Computational Chemistry* **2014**, *35*, 1846.

Synthesis of Chiral Bis-(1,2,3-Triazol-1,4-Disubstituted) Compounds using Enabling Technologies

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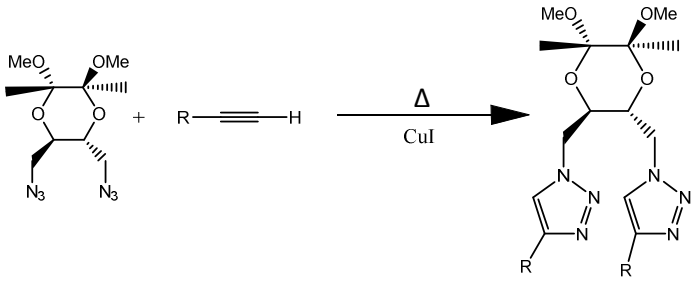
Known since the late nineteenth century, 1,2,3-triazoles units have been present in various biologically active synthetic substances and commercial pharmaceutical compounds.[1] These units have much interest due to their applications in several areas, especially in pharmaceutics, in which they exhibit key biological activities like anticancer, anti-HIV, antibacterial, etc.[2]

Recently there has been a notable additional interest in these compounds due to the discovery of the copper-catalyzed alkyne/azide cycloaddition reaction (CuAAC) which has become very popular as a "click" reaction.[3] In this communication we report the synthesis of novel chiral bis-(1,2,3-triazol-1,4-disubstituted) compounds with potential application in medicinal chemistry or in asymmetric catalysis using enabling technologies (**Scheme 1**).



Scheme 1: Our CuAAC reaction

Acknowledgements: We thank the Fundação para a Ciência e a Tecnologia (FCT) through grant UID/QUI/0619/2016 (contributed to CQE-UE) for supporting this work.

References:

1. Singhai N.; Sharma P.K.; Dudhe R.; Kumar N. J. Chem. Pharm. Res., **2011**, 3, 126.
2. Liang, L.; Astruc, D. *C. Chem. Rev.*, **2011**, 255, 2933.
3. Melo, J.; Donnici, C.; Augusti, R.; Ferreira, V.; Souza, M.; Ferreira, M.; Cunha, A. *Química Nova* ***2006***, 29, 569.

Enantioselective Fluoroalkylation Reactions to Ketimines

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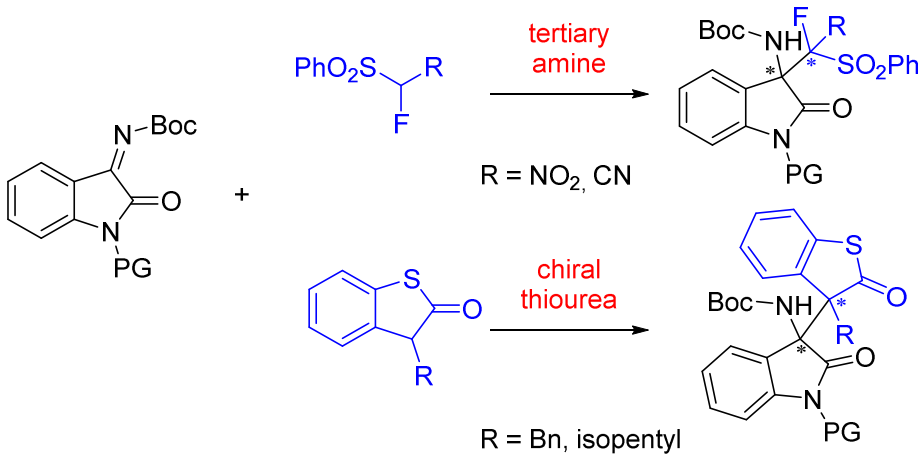
Nitrogen-containing compounds are widespread in nature and are necessary for life, because they are part of the metabolism of living cells. Nowadays about 75% of medicaments contain an amine functionality in their structure.[1] Synthesis of nitrogen-containing compounds is frequently carried out from readily available imines. The organocatalytic enantioselective reactions of imines are important reactions in terms of preparation the nitrogen compounds with a chiral quaternary carbon atom. In the area of the catalytic enantioselective fluoroalkylations using ketimines derived from isatins as substrates, there are a few examples reported to date. [2-4]

We developed enantioselective fluoroalkylation reaction of ketimines with α-fluorinated methanephenylsulfones and sulfur heterocycles (benzothiophen-2-one) catalyzed chiral tertiary amine or chiral thiourea organocatalyst. (**Scheme 1**), The reaction provides the corresponding fluoroalkylation products in good yields and moderate or excellent diastereo- and enantioselectivity.



Scheme 1: Enantioselective nucleophilic additions to ketimine.

Acknowledgements: We thank the Charles University Grant Agency (grant number 392315) and the Grant Agency of Czech Republic (grant number 16-23597S) for financial support.

References:

1. Dai,L.-X.; Lin, Y.-R.; Hou, X.-L.; Zhou, Y.-G. *Pure Appl. Chem.*, **1999**, *71*, 1033.
2. Yan, W.; Wang, D.; Feng, J.; Li, P.; Zhao, D.; Wang, R *Org. Lett.*, **2012**, *14* (10), 2512.
3. Liu, Y.-L.; Zhou, J. *Chem. Commun.*, **2013**, *49*, 4421.
4. Wang, X.-B.; Li, T.-Z.; Sha, F.; Wu, X.-Y. *Eur. J. Org. Chem.* **2014**, *4,* 739.

Titanium Salan Complexes: Synthesis and Reactivity

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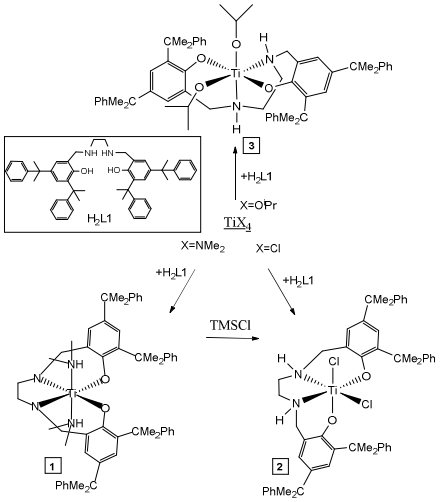
Diamine bisphenolate ($N_2O_2^{2-}$) ligands are important scaffolds in transition metals (TM) and lanthanides (Ln) chemistry.[1] In this area, we have been interested in the chemistry of early TM and Ln complexes displaying tripodal diamine bisphenolate ligands.[2] Applications in polymerization catalysis, using Ti and Zr complexes,[3] in radical process such as O_2 activation and C-C coupling, using Ti and V complexes,[4a] and oxidation catalysis, as epoxidation and sulfoxidation, using Ti, V, Mo, and W complexes,[4b, c] were reported.

The work presented here explores the reactivity of Ti complexes supported by a different type of diamine bisphenolate ligands, usually identified as salan ligands. **H2L1** is a very bulky ligand precursor that was prepared by current procedures. Using different titanium starting materials, it was possible to obtain complexes **1**, **2**, and **3**, shown in Scheme 1. Complex **1** presents one unique C_2 isomer that displays trans-phenolate ligands and was structurally characterised by NMR and X-ray diffraction. Differently, **2** revealed 4 isomers that were identified by NMR as C_1-cis-dichloro complexes, which result from the stereoisomerism (R or S) of the nitrogen atoms and the coordination isomerism of the ligand. The molecular structure of one of the isomers of **2** was determined by single crystal X-ray diffraction. Interestingly, the reaction of $\mathbf{H_2L_1}$ with $Ti(NMe_2)_4$ is accompanied by H^+ transfer from the ethylenediamine fragment to the dimethylamido ligands, with **Scheme 1:** Synthesis of Salan-Titanium(IV) Complexes.formation of a tetraanionic diamido bisphenolate ligand. The coordination sphere of the titanium is completed by the bonding of 2 dimethylamine ligands that are mutually *trans*. Upon reaction of **1** with TMSCl, complex **2** is obtained, showing that the ethylenediamido fragment can be protonated, coming back to the original dianionic form of the ligand. An analogous process, namely the intramolecular migration of 2 protons from coordinated dimethylamine to the tetraanionic ligand occurs upon reaction of **1** with CO_2 that inserts in the Ti-NMe_2 bonds. The non-innocent behaviour of the ligand, that corresponds to the equilibrium $(N_2O_2^{2-})/(N_2O_2^{4-})$ is remarkable because, contrarily to most cases described in the literature, the ligand does not present extended conjugation in any of its forms.



The proton exchange is merely an acid/base intramolecular and reversible process.The reaction of **2** with $KHBEt_3$ follows a reductive path and originates a Ti(III) salan species. Catalytic applications of the latter complexes in radical coupling are under way.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (SFRH/BD/114399/2016, SFRH/BD/87679/2012, SFRH/BPD/86815/2012, SFRH/BPD/7394/2010 and UID/QUI/00100/2013).

References:

1. Tzubery, A.; Tshuva, E. Y. *Inorg. Chem.* **2012**, *51*, 1796-1804;
2. Barroso, S.; Coelho, A. M.; Gómez-Ruiz, S.; Calhorda, M. J.; Žižak, Z.; Kaluđerović, G. N.; Martins, A. M. *Dalton Trans.* **2014**, *43*, 17422–17433;
3. Adao, P.; Avecilla, F.; Bonchio, M.; Carraro, M.; Pessoa, J.C.; Correia, I. *Eur. J. Inorg. Chem.* **2010**, 5568-5578;
4.a) Barroso, S.; Adão, P.; Duarte, MT.; Meetsma, A.; Pessoa, JC.; Bouwkamp, MW. ; Martins, A. M. Eur. J. *Inorg. Chem. 2011, 27,* 4277-4290*;* b) Barroso, S.; Adão, P.; Coelho, A. M.; Pessoa, J. C.; Martins, A. M. *J. Mol. Cat. A: Chem.* **2016**, *412*, 107-116; c) Barroso, S., Madeira, F., Calhorda, M. J., Ferreira, M. J., Duarte, M. T., Martins, A. M. *Inorganic Chemistry*, **2013**, *52*, 9427–9439.

Synthesis of New Oxidative Stress Protective Agents

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Alzheimer (AD) is a cronic neurodegenerative disease, the main cause of dementia of the world. The principal syntoms of diagnosed patients are: motor insuficency, memory decrease and confussion that worsens over time and ends with the loss of self-reliance. Desregulation and disfunction of metabolic processes induce an increase of the concentration of ROS (reactive oxygen species) and crecent metabolic stress inducing cell death of neuronal cells[1-3]. One strategy of enhance cell survival and delay the acute effects of AD is reducing this oxidative stress in neuronal cells by incorporation of antioxidative agents. The potential therapeutic application of antioxidative strategy for AD and other neurodegenerative disorders have been intesively studied for safranal in the last years, despite shows moderate toxicity[4]. In this work, we present a new option for the antioxidative treatment of AD by using of 1,3-cyclohexadienals, that have been demonstrated to be potent antioxidative agents with low toxicity profile. The synthesis of the cyclohexadyenals (Figure 1) have been developed in our laboratories using organocatalysis, by the estereochemically controlled reaction of α,β-unsaturated aldehyde, **I**, with β-substituted-α,β-unsaturated aldehydes, **II**, in presence of Hayashi-Jørgensen catalyst[5].

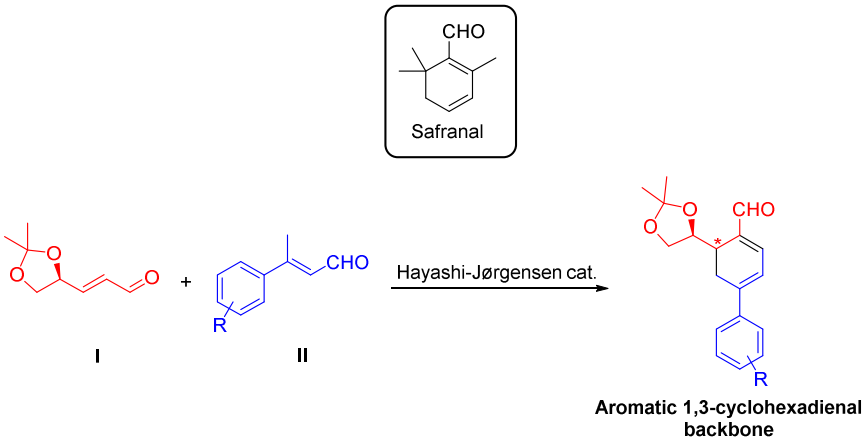

Figure 1: General procedure of organocatalyzed obtention reaction of 1,3-cyclohexadienals

Acknowledgements: The authors gratefully acknowledge the help of J. Rodilla of University of Beira Interior and A. Lithgow (NMR) and C. Raposo (MS) of University of Salamanca. Financial support of this work was provided by MINECO CTQ2015-68175-R, FEDER Junta de Castilla y León (UIC21) and University of Salamanca.

References:

1. De-Paula, V. J.; Radanovic, M.; Diniz, B. S.; Forlenza, O. V.: Alzheimer's Disease. In Protein Aggregation and Fibrillogenesis in Cerebral and Systemic Amyloid Disease; Harris, J. R., Ed.; Springer Netherlands: Dordrecht, 2012; pp 329-352.
2. Buendia, I.; Michalska, P.; Navarro, E.; Gameiro, I.; Egea, J.; Leon, R. Nrf2-ARE pathway: An emerging target against oxidative stress and neuroinflammation in neurodegenerative diseases. Pharmacology & therapeutics 2016, 157, 84-104.
3. Kisler, K.; Nelson, A. R.; Montagne, A.; Zlokovic, B. V. Cerebral blood flow regulation and neurovascular dysfunction in Alzheimer disease. Nature reviews. Neuroscience 2017.
4. Ziaee, T.; Razavi, B. M.; Hosseinzadeh, H. Saffron Reduced Toxic Effects of its Constituent, Safranal, in Acute and Subacute Toxicities in Rats. Jundishapur Journal of Natural Pharmaceutical Products 2014, 9, 3-8.
5. Urosa, A.; Tobal, I. E.; de la Granja, A. P.; Capitán, M. C.; Moro, R. F.; Marcos, I. S.; Garrido, N. M.; Sanz, F.; Calle, E., Díez, D. Diastereoselective Synthesis of Chiral 1,3- Cyclohexadienals. Manuscript accepted, under revision. PLoS One, may 12th, 2017

Oxidation of Cyclohexane Catalyzed by Copper(II) Complexes of Arylhydrazone in Ionic Liquids

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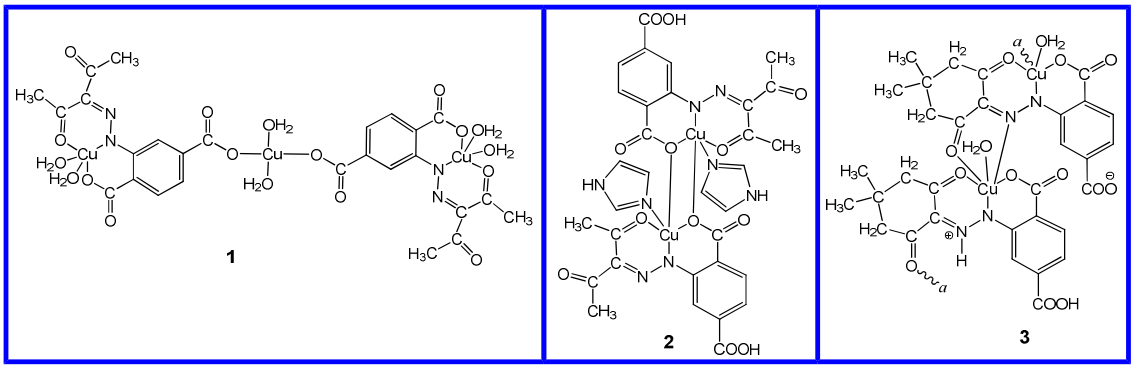
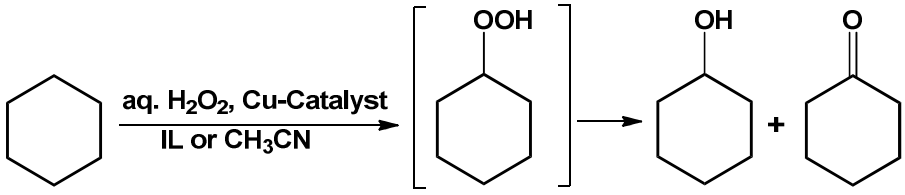
Several known copper(II) complexes of arylhydrazone of β-diketone were synthesized (Scheme 1)[1] and applied as catalysts for cyclohexane oxidation (Scheme 2). The reaction was carried out in microwave and using an organic solvent (acetonitrile) or an ionic liquid. The effect of reaction time, in the presence of acidic additive, will be discussed. The difference in catalytic behavior due to the presence of the ionic liquid will be addressed. The different structures of the complexes (Scheme 1) will also be related with the experimental results of the reaction.



Scheme 1. Schematic representations of **1**–**3**.



Scheme 2. Peroxidative oxidation of cyclohexane (without a defined stoichiometry) catalyzed by **1**–**3**.

Acknowledgements: This work supported by the Foundation for Science and Technology (FCT), Portugal (UID/QUI/00100/2013). G.A.O.T is also thankful to the CATSUS doctoral FCT program for his PhD fellowship.

Reference:

1. R. Jlassi, A. P. C. Ribeiro, M. F. C. Guedes da Silva, K. T. Mahmudov, M. N. Kopylovich, T. B. Anisimova, H. Naili, G. A. O. Tiago, A. J. L. Pombeiro, *Eur. J. Inorg. Chem.*, **2014**, 4541-4550.

Iron-(Amino-Acid) Complexes in the Oxidative Coupling of 2-Naphthol

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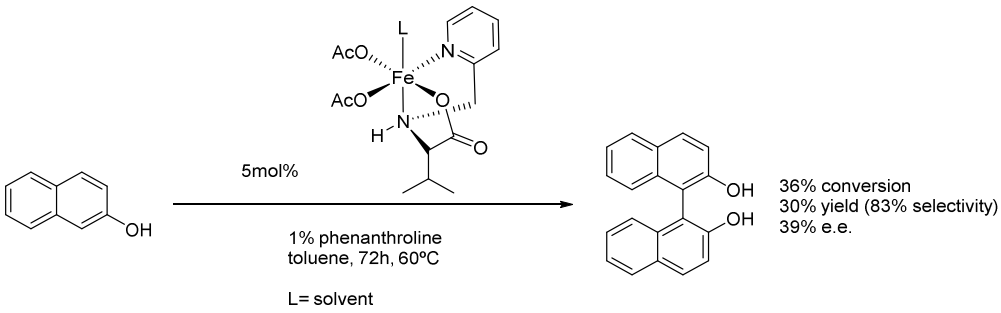
Coupling reactions have demonstrated a crescent role since 1970's till nowadays in the synthesis of many relevant fine chemicals such as polymers, active pharmaceutical ingredients, natural products, dyes and pesticides, among others. Despite the great influence and importance of palladium- and nickel-mediated coupling methodologies, in order to reduce the negative environmental impact and chemical waste treatment expenditures of many processes in the chemical industry, the preparation and application of more sustainable and efficient transition-metal catalysts as gained relevance in the last years. Iron compounds have emerged, in the last 2 decades, as an excellent example of these alternatives, and the subject of our study is the synthesis and application of iron amino-acid-based complexes as catalysts for C-C coupling reactions, as well as in oxidation transformations, using environmentally-friendly conditions.

Herein we describe the synthesis of two iron (III) complexes derived from chiral amino acid-based ligands and their application as homogeneous catalysts for the asymmetric oxidative coupling of 2-naphthol[1,2] (**Scheme 1**). Adding proper organic bases to the reaction medium, in specific amounts, these structurally simple iron complexes can be used as catalysts in the development of mild and environmentally-friendly enantioselective procedures for the oxidative coupling of 2-naphthol.



Scheme 1: General procedure for the oxidative coupling of 2-naphthol mediated by Fe-(amino acid) complexes.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia/MCTES (Portugal), projects UID/QUI/00100/2013, RECI/QEQ-QIN/0189/2012 and RECI/QEQMED/0330/2012, PD/BD/106078/2015 and CATSUS PhD Programme (Portugal) for the financial support.

References:

1. Adão, P., Barroso, S., Carvalho, M. F. N. N., Teixeira, C. M., Kusnetzov, M. L., Costa Pessoa, J. C., *Dalton Trans.*, **2015**, *44, 1612*;
2. Egami, H., Katsuki, T., *J. Am. Chem. Soc.*, **2009**, *131, 6082*.

Preparation and Catalytic Application of Molybdenum(II) Organometallic Phenanthroline Complexes

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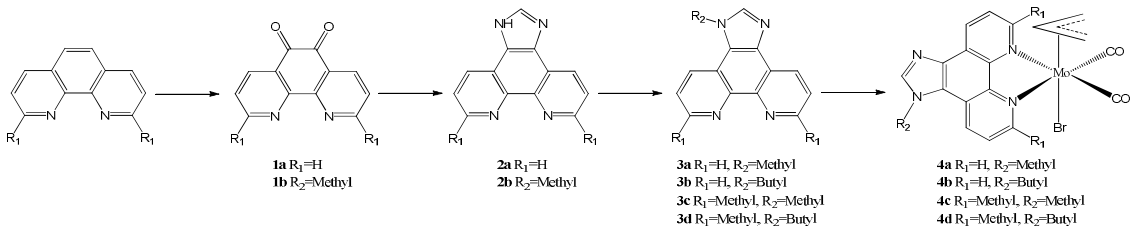
A set of phenanthroline derivatives were synthesized from 1,10-phenanthroline and 2,9-dimethyl-1,10-phenanthroline as shown in **Scheme 1**[1]. These ligands were reacted in inert atmosphere and at room temperature with the precursor complex $[MoBr(\eta^3\text{-}C_3H_5)(CO)_2(CH_3CN)_2]$ resulting in the formation of the new family of molybdenum(II) organometallic complexes $[Mo(\eta^3\text{-}C_3H_5)Br(CO)_2(1\text{-}R_1\text{-imidazo}[4,5\text{-f}]\text{-}R_2\text{-}[1,10]\text{phenanthroline})]$ (R_1=butyl, methyl, R_2=dimethyl, H)[2]. All the ligands and complexes prepared were characterized by FTIR, ^1H and ^{13}C NMR. The new complexes prepared were used as homogeneous catalysts for the oxidation of cyclooctene, styrene, cis-3-hexen-1-ol, trans-2-hexen-1-ol, R-limonene, geraniol and 1-octene with TBHP (tert-butyl hydroperoxide) as the oxidant. The data were collected through GCMS. The effects of reaction time, temperature and amount of catalysts were discussed.



Scheme 1: Synthesis of the Molybdenum(II) organometallic complexes.

Acknowledgements: Support for this work was provided by FCT through UID/MULTI/00612/2013, PEst-OE/QUI/UI0612/2013, UID/QUI/00100/2013 (CQE), PTDC/QEQ-ERQ/1648/2014 and PTDC/QEQ-QIN/3967/2014. APCR acknowledges FCT for SFRH/BPD/90883/2012, JW for PD/BD/114397/2016, and MSS for Grant SFRH / BPD / 88082 / 2012.

References:

1. Alyssa A. Webster, Shyamal K. K. Prasad, Justin M. Hodgkiss, John O. Hoberg, Dalton Trans. 44(2015) 3728-3736.
2. Marta S. Saraiva, Susana Quintal, Fátima C.M. Portugal, Telma A. Lopes, Vitor Félix, José M.F. Nogueira, Margarida Meireles, Michael G.B. Drew, Maria José Calhorda, J. organomet. Chem. 693 (2008) 3411–3418.

Asymmetric Synthesis of 2,3,6-Trisubstituted Piperidines via Methyl Acrylate and *p*-Benzyloxybenzaldehyde

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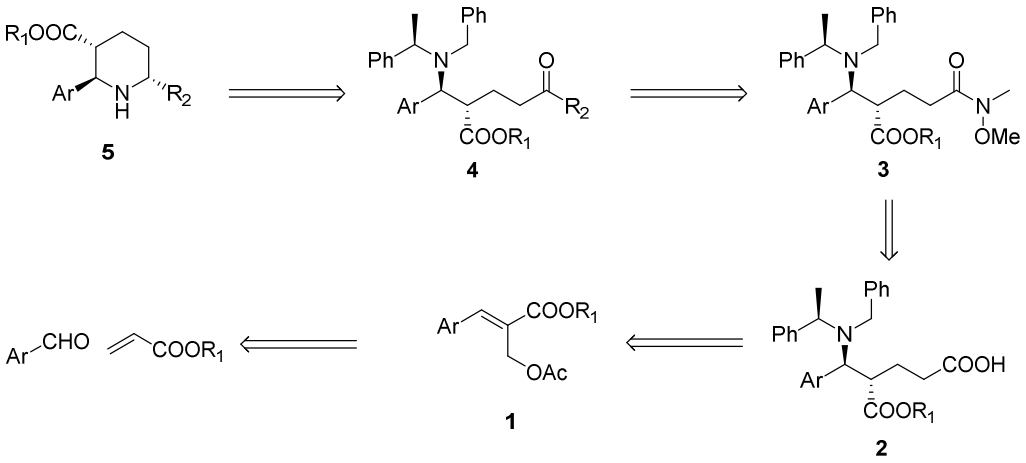
Piperidine rings are prevalent in the core structure of many naturally occurring alkaloids and drugs.[1] Substituted piperidines, particularly, 2- and/or 2,6-disubstituted piperidines are synthetically very important[2] and exhibit a wide spectrum of biological activities such as antibacterial,[3] antifungal[4], anti-tuberculosis,[5] anticancer, antioxidant, anti-inflammatory. For this reason, significant efforts have been made to synthesize the derivatives of piperidine or piperidone and to investigate the stereochemistry. Recently, our group has communicated the strategies of the reaction domino: that includes allyl acetate and estereoselective Ireland-Claisen rearrangements followed by an asymmetric Michael addition.[6] This methodology allows us to obtain δ- amino acids **3** directly by treatment of aducts of Baylis-Hillman **2** with quiral lithium amide(*R*)-**1** and has been applied to the synthesis of biologically actives piperidines.[7]

Here we communicate the asymmetric synthesis 2,3,6-trisubstituted piperidines. The preparation of the ketone **3** is carried out by Weinreb's method. This amide is treated with a Grignard reagent to give the correspondent ketone **4**. The next stage is remove benzyl groups by hydrogenolysis and reductive amination to yield the trisubstituted piperidine.



Scheme 1: Retrosynthetic scheme proposed for piperidine obtention.

Acknowledgements: We thank to MINECO CTQ2015-68175-R, FEDER Junta de Castilla y León (UIC21) and Junta de Castilla y León, (SA162A12-1), for financial support.

References:

1. Mochizuki, A.; Nakamoto, Y.; Naito, H.; Uoto, K.; Ohta, T. Bioorganic & Med Chem Lett, 2008, 18, 782.

2. Ghorai, M. K.; Halder, S.; Das, R. K. J Org Chem 2010, 75, 7061; Ganellin, C. R.; Spickett, R. G. W. J Med Chem 1965, 8, 619.

3. Ramalingan, C.; Park, Y. T.; Kabilan, S. Eur J Med Chem, 2006, 41, 683;

4. Rameshkumar, N.; Veena, A.; Ilavarasan, R.; Adiraj, M.; Shanmugapandiyan, P.; Sridhar, S. K. Biological and Pharmaceutical Bulletin, 2003, 26, 188.

5. Aridoss, G.; Amirthaganesan, S.; Ashok Kumar, N.; Kim, J. T.; Lim, K. T.; Kabilan, S.; Jeong, Y. T. Bioor & Med Chem Lett, 2008, 18, 6542.

6. Garrido, N. M.; García, M.; Díez, D.; Sánchez, M. R.; Sanz, F.; Urones, J. G. Org Lett, 2008, 10, 1687.

7. Garrido, N. M.; Rosa Sánchez, M.; Díez, D.; Sanz, F.; Urones, J. G. Tetrahedron: Asymmetry 2011, 22, 872.

Asymmetric Synthesis of 3-Alkyl-PDA via Domino/Tandem Reaction

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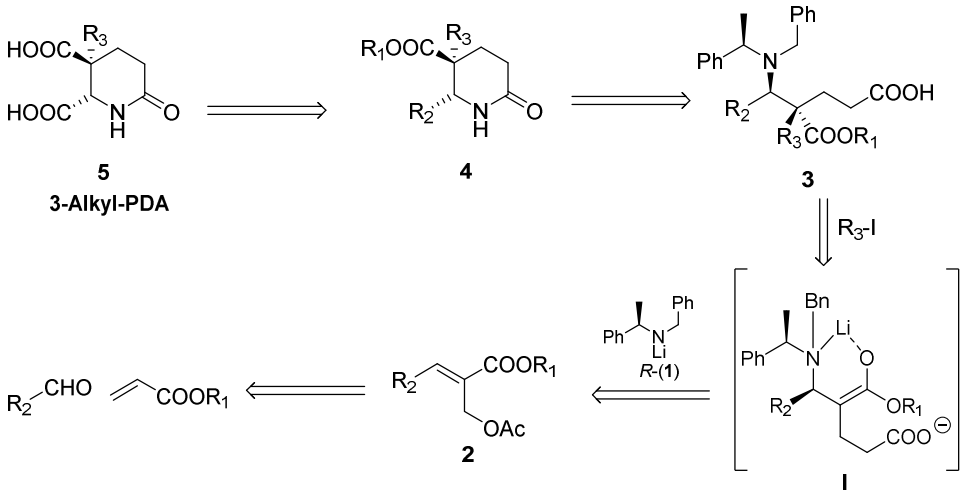
Modulation of the (EAA)[1] receptors seems to be implicated in several neurological disorders such as Huntington's chorea, Alzheimer disease and epilepsy.[2] It is known that glutamic and aspartic acids are the major excitatory neurotransmitters and their receptor complexes are pharmacologically characterized by their affinities for *N*-methyl-*D*-aspartic acid (NMDA), kainic acid, α–amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) and *trans*-1-aminocyclopentyl-1,3-dicarboxylic acid (ACPD). The NMDA receptor has been the most studied and the synthesis of NMDA analogues constitutes an active area of investigation. Some of these restricted analogues are *cis*- and *trans*-2,3-piperidine dicarboxylic acids (PDA). Thus we propose 2-alkyl PDAs as valuable compound with an interesting quaternary stereogenic center for SAR studies. Recently, we have demonstrated[3] a novel domino reaction: allylic acetate rearrangement, stereoselective Ireland-Claisen rearrangement and asymmetric Michael addition. A protocol starting from Baylis-Hillman adducts **2** (Scheme 1) using chiral lithium amide (*R*)-**1** to afford δ-aminoacids, that can be transformed to homoquiral *cis* and *trans*-PDA.[4]



Scheme 1: Retrosynthetic scheme proposed for 3-alkyl-PDA obtention, indicating the domino/tandem reaction.

In order to demonstrate further the versatility of this methodology, here we communicate the asymmetric synthesis of homochiral 3-alkyl-piperidinedicarboxylic derivatives by using the aforementioned domino methodology followed by tandem alkylation of the asset enolate **I**, that will provide the proper 3,3-disubstituted-δ-aminoacid **3**, which upon hydrogenolisis the piperidinone **4** is obtained as useful tool for stereochemistry determination. The enantioselective synthesis of 3-alkyl-PDA **5** will be undertaken as in the reported work.[4]

Acknowledgements: We thank to MINECO CTQ2015-68175-R, FEDER Junta de Castilla y León (UIC21) and Junta de Castilla y León, (SA162A12-1), for financial support.

References:

1. Moloney, M. G.; *Nat. Prod. Rep.* **1998**, 205-219.
2. Whitten, J. P.; Muench, D.; Cube, R. V.; Nyce, P. L.; Baron, B. M.; McDonald, I. A. *Biorg. Med. Chem. Lett.* **1991**, *1*, 441-444.
3. Garrido, N. M.; García, M.; Díez, D.; Sánchez, M. R.; Sanz, F.; Urones, J. G. Org Lett, **2008**, 10, 1687.
4. Garrido, N. M.; Rosa Sánchez, M.; Díez, D.; Sanz, F.; Urones, J. G. Tetrahedron: Asymmetry **2011**, 22, 872.
5. Tietze, L.F. Chem.Rew. **1996**, 96, 115-136

Access to Spirocyclic Benzothiophenones with Multiple Stereocenters *via* Organocatalytic Cascade Reaction

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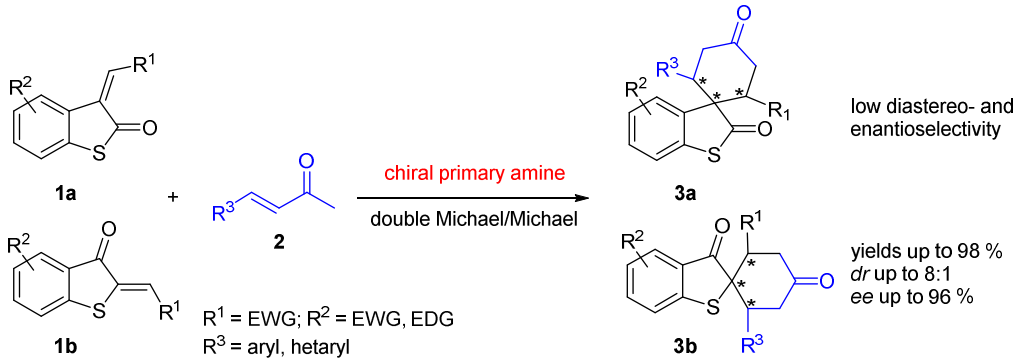
Efficient and elegant syntheses of complex organic molecules with multiple stereocenters continue to be important in both academic and industrial laboratories. In particular, catalytic asymmetric cascade reactions are highly desireable.[1] At least two steps are carried out in single operation under same reaction conditions compared to classical chemistry. In addition, protecting group manipulation and isolation of intermediates is not necessary. Use of organocatalysts in these processes allows distinct modes of activation, which can often be easily combined.[2]
Herein, we focused on the reactions of alkylidene-benzothiophenone derivatives **1** which are less explored than their nitrogen and oxygen analogues.[3] Chiral amines showed the ability to combine efficiently two activation modes (enamine/iminium catalysis) in cascade reactions of enones **2** (**Scheme 1**).
Spirobenzothiophenonic cyclohexane derivatives **3** containing three stereocenters were obtained in one-step synthesis in high yields (up to 98 %), good diastereoselectivities (about 8:1) and excellent enantioselectivities (up to 96 % ee). Scope of the reaction and further studies will be presented in details.



Scheme 1: Organocatalytic cascade reaction between alkylidene-benzothiophenones **1** and enones **2**.

Acknowledgements: We thank the Charles University Grant Agency (393615) and Czech Science Foundation (16-23597S) for financial support.

References:

1. a) Wasilke, J.-C., Obrey, S. J., Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001. b) Hahn F. E. *Angew. Chem. Int. Ed.* **2006**, *45*, 1348.
2. Enders, D., Grondal, C.; Huttl, M. R. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 1570.
3. a) Zhang, Y.; Wang, S.; Wu, S.; Zhu, S.; Dong, G.; Miao, Z.; Yao, J.; Zhang, W.; Sheng, C.; Wang, W. *ACS Comb. Sci.* **2013**, *15*, 298. b) Géant, P.-Y.; Urban, M.; Remeš, M., Císařová, I.; Veselý, J. *Eur. J. Org. Chem.* **2013**, 7979.

Polylactide/Cellulose Nanocrystals: the *in situ* Polymerization Approach to Improved Nanocomposites

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Poly(lactic acid), shortly PLA, is one of the most attractive biopolymer, both to researchers and industry, since it proved not only to possess good physical properties, but also appeared to be cost competitive against common packaging plastics (such as PET). In addition, it is biodegradable and its monomer can be extracted from renewable sources. However, alongside with these good properties, PLA still suffers some drawbacks (poor thermal and mechanical resistance, poor barrier properties and low flexibility) which significantly limit its applicability. Among possible alternatives to overcome some of these limitations, the preparation of nanocomposites has emerged as the most promising suitable solution.[1] Aiming to produce fully organic bionanocomposites, we decided to focus our attention onto cellulose nanocrystals (CNCs). CNCs are the crystalline nanometric domains in cellulose fibers and they can be extracted from cellulosic matrices through acidic or oxidative hydrolysis[2] reactions. What is interesting about CNCs comes from their outstanding chemical (many free hydroxyl surface groups that can be functionalized in different ways) and physical (extremely high young modulus, low density and high aspect ratio) properties, and also from the fact that they can be extracted from biomass residues.[3]

On the basis of our related experience on preparation of PLA nanocomposites containing nanosilica (NS)[4] or modified montmorillonite (MMT)[5] fillers, we looked at PLA-CNCs nanocomposites via the *in situ* polymerization of L-lactide in the presence of various amounts of CNCs. It is well established that *in situ* polymerization in the presence of fillers provides distinct advantages when compared to other nanocomposite synthesis techniques, appearing more appropriate in providing excellent dispersion of the nanoparticles, which should have a greater impact on achievable properties. To the best of our knowledge, no *in situ* polymerization strategies employing CNCs have been described for the preparation of PLA nanocomposites.

In this study, the *in situ* polyaddition of L-lactide was performed with different loading ratios of CNCs, prepared by acidic hydrolysis of cotton linters. The protocol exploits the alcoholic moieties of CNCs as initiators in ring opening polymerization reaction of L-lactide. Molecular weight, morphology, thermal, mechanical and crystallization properties of the obtained nanocomposites were evaluated. Some of them exhibited enhanced thermal stability compared with pure PLA and with conventional PLA-CNCs blends, introducing for the first time the *in situ* polymerization strategy as a valuable approach for the preparation of improved PLA-CNCs nanocomposites.

References:

1. Raquez, J.M.; Habibi, Y.; Murariu, M.; Dubois, P.; *Progress in Polymer Science* **2013**, *38*, 1504-1542.
2. Rampazzo, R.; Alkan, D.; Gazzotti, S.; Ortenzi, M.A.; Piva, G.; Piergiovanni, L.; *Packaging Technology and Science* **2017**.
3. Ioelovich, M.; *BioResources;* **2008**; *4*; 1403.
4. Basilissi, L.; Di Silvestro, G.; Farina, H; Ortenzi, M.A.; *J. App. Polym. Sci.* **2013**, 1575-1582.
5. Sabatini, V.; Farina, H.; Basilissi, L.; Di Silvestro, G.; Ortenzi, M.A.; *Journal of Nanomaterials* **2015**, 1-16.

Sequential Multicomponent Approach for the Synthesis of Densely Functionalised Spirooxindole-fused Thiazolidines

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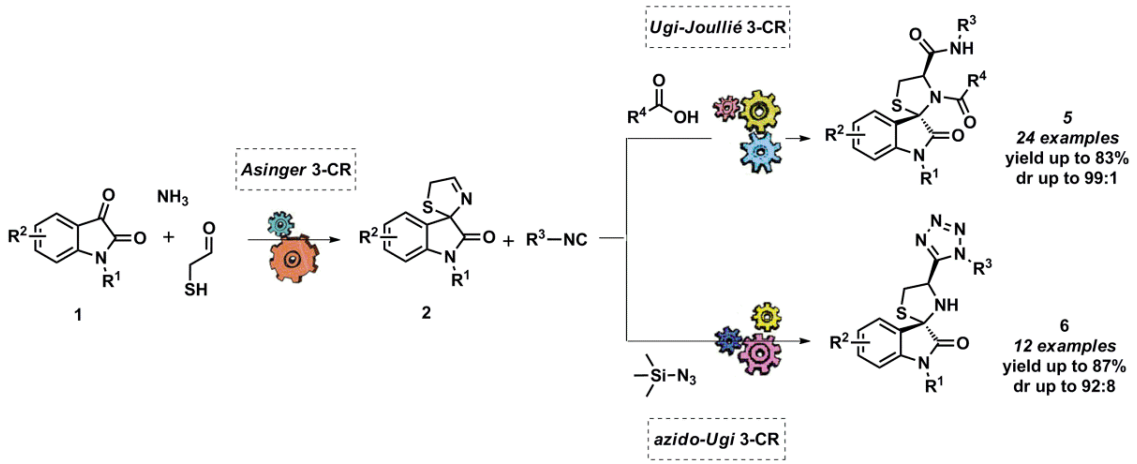
2-Oxindoles, especially 3,3-disubstituted and spiro-fused derivatives, are widely recognized as highly relevant compounds for drug discovery.

As part of our interest in multicomponent reactions (MCRs) applied to the synthesis of oxindole-based compounds,[2] we report here a novel synthetic approach towards the title compounds, based on sequential MCRs. Starting from isatin derivatives **1**, ammonia and mercaptoacetaldehyde, spirooxindole-fused 3-thiazolines **2** were easily obtained by means of the underutilized Asinger reaction.[3,4] Intermediates **2** were then subjected to a Joullié-Ugi reaction, which afforded products **5** in high yields. Compounds **2** also underwent an azido-Ugi reaction, affording products **6.** Both MCRs proved to be highly diastereoselective and displayed a broad substrate scope, allowing to quickly generate a diverse library of compounds **5** and **6**, for which R^1-R^4 substituents could be varied extensively.

The therapeutic potential of selected compounds is currently under evaluation by means of high throughput screening from Biopharma (Merck group).



Scheme: Sequential multicomponent approach for the synthesis of Densely Functionalised Spirooxindole-fused Thiazolidines.

References:

1. Tice, C. M. *Expert Opinion on Drug Discovery* **2016**, *11*, 831.
2. Rainoldi, G.; Faltracco, M.; Lo Presti, L.; Silvani, A.; Lesma, G. *Chem. Commun.* **2016**, *52*, 11575. Rainoldi, G.; Sacchetti, A.; Silvani, A.; Lesma, G. *Org. Biomol. Chem.* **2016**, *14*, 7768. Stucchi, M.; Lesma, G.; Meneghetti, F.; Rainoldi, G.; Sacchetti, A.; Silvani, A. *J. Org. Chem.* **2016**, *81*, 1877.
3. Asinger F. *Angew. Chem.*, **1956**, *68*, 377.
4. Rainoldi, G.; Begnini, F.; Silvani, A.; Lesma, G. *Synlett* **2016**, *27*, 2831.

Stereoselective Synthesis of Chiral Spirooxindole-Based 4-Methyleneazetidines via Formal [2+2] Annulation Reaction

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The strained four-membered ring system of azetidines occurs as a structural motif in several natural products and pharmaceutical agents with different biological activities.[1]

Our long-standing interest in the asymmetric synthesis of 3,3-disubstituted oxindoles derivatives, combined with the growing interest in hybrid drugs as therapeutic agents, inspired us to connect the two pharmacologically relevant moieties in a synthetically challenging spiro arrangement.

Since Shi's pioneer work,[2] examples of [2+2] annulations involving allenoates were reported, both on electron-deficient aldimines and ketimines.[3] As a continuation of our previous work,[4] reporting the first highly diastereoselective entry into chiral spirooxindole-based 4-methyleneazetidines, and considering the advantages of catalytic methods, we now demonstrate the suitability of bifunctional cinchona-based organocatalysts to promote the [2+2] annulation, leading to enantiomerically enriched derivatives. Alongside, efforts aimed to establish these compounds as possible lead compounds for drug discovery programs are currently underway.

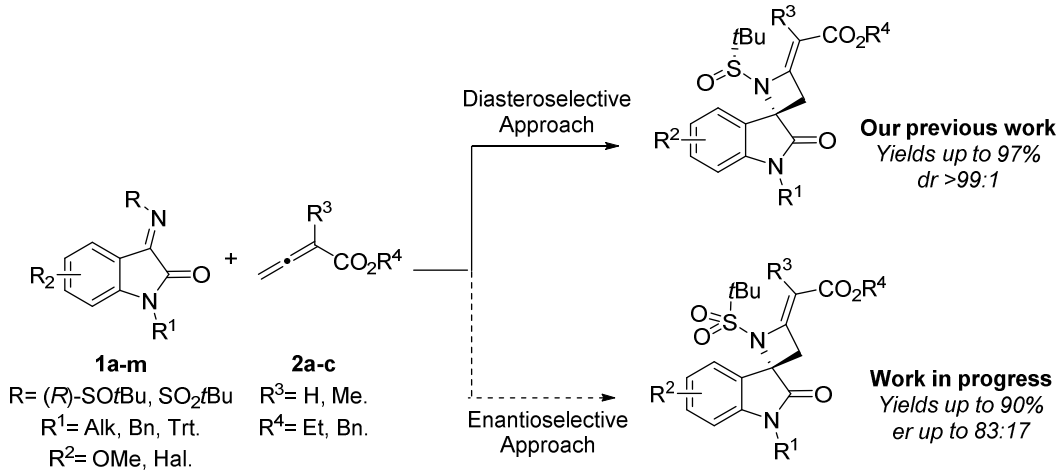

Figure: Proposed stereoselective approaches for the formal [2+2] annulation reaction.

References:

1. A. Brandi, S. Cicchi, F. M. Cordero, *Chem. Rev.* **2008**, *108*, 3988-4035.
2. G. L. Zhao, J. W. Huang, M. Shi, *Org. Lett.* **2003**, *5*, 4737-4739.
3. (*a*) L. J. Yang, S. Li, S. Wang, J. Nie, J. A. Ma, *J. Org. Chem*. **2014**, *79*, 3547-3558. (*b*) J. B. Denis, G. Masson, P. Retailleau, J. Zhu, *Angew. Chem. Int. Ed.* **2011**, *50*, 5356-5360.
4. G. Rainoldi, M. Faltracco, L. Lo Presti, A. Silvani, G. Lesma *Chem. Commun.* **2016**, *52*, 11575-11578.

Lilly Open Innovation Drug Discovery Program (OIDD): For Scientists, By Scientists

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The Lilly Open Innovation Drug Discovery program (OIDD) was created to engage external investigators in a hypothesis-driven approach to early drug discovery. Program participants have the opportunity to contribute to the discovery of novel therapeutics that will improve patients' lives, and benefit by having access to cutting-edge research tools and data that can help them advance their own scientific work. The OIDD program is directed to investigators in academic/research institutions and small biotechs. Many of them encountered barriers to evaluate the therapeutic potential of their compounds and the OIDD platform was designed to minimize obstacles by offering:

- In-kind access to a panel of proprietary biological assays in the areas of Diabetes, Oncology, Pain, Neurodegeneration and Immunology, plus certain neglected and tropical diseases in collaboration with global leaders in the area,
- A variety of *in silico* tools to prioritize molecules with desirable drug-like properties,
- Opportunity to prepare compounds remotely in our Automated Synthesis Lab (ASL),
- Opportunity to have chemical samples selected for purchase through an algorithm applied to the molecular descriptor profile.

Affiliation is established at the institution level via a universal agreement that protects participant's intellectual contributions. Once the agreement is signed, investigators at the affiliated institution may create a user account that manage chemical structure selection, sample transfers, and biological data in a secure manner. The OIDD program is supported by a secure web-based interface that protects the confidentiality of proprietary information such as chemical structures. All Lilly-generated data is owned by the participating investigator and/or institution, and results are used to initiate collaboration discussions based on promising results and mutual interest of both parties. Otherwise, the investigator is free to publish and/or use the biological results in grant proposals.

This poster will describe the scientific rationale behind OIDD, the business model, operational details and metrics illustrating the performance of the program. Detailed information can be found online (https://openinnovation.lilly.com/dd/). The website provides details about the process, our offerings, sample logistics, biological screening and user account management. Our universal agreement is also available online. If you have questions, please feel free to contact openinnovation@lilly.com

Iridium(I) Catalyzed C(sp^2)-H Activation and Intramolecular Hydroarylation and Hydroalkenylation of Alkenes and Alkynes

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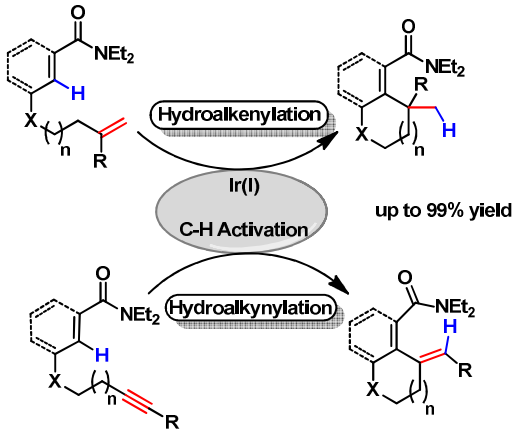
C-H bond activation is an active field of research because it enables the access to very challenging scaffolds without need of substrate pre-activation using shorter and atom economical protocols. Low valence transition metals (Rh(I), Ru(0), Co(0), Ni(0), Pd (0), etc.) are widely used to perform catalyzed C-H functionalizations assisted by heteroatom containing directing groups.[1]

The intermolecular Ir(I) catalyzed hydroalkenylation and hydroalkynylation is well known using different directing groups and scaffolds, however the intramolecular version is not yet explored.[2]

Herein is presented a cationic Ir(I) catalyzed C(sp^2)-H activation-hydroalkenylation or hydroalkynylation process yielding a new series of cyclic scaffolds including the enantioselective formation of quaternary centers.[3]



Scheme 1: Ir(I) catalyzed C(sp^2)-H activation followed by intramolecular hydroakenylation or hydroalkynylation.

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References:

1.a) M. Gulías, J. L. Mascareñas, *Angewandte Chemie International Edition* **2016**, 55, 11000-11019; b) Z. Dong, Z. Ren, S. J. Thompson, Y. Xu, G. Dong, *Chemical Reviews* **2017**.

2.a) S. Pan, N. Ryu, T. Shibata, *J Am Chem Soc* **2012,** 134, 17474-17477; b) S. Pan, T. Shibata, ACS Catalysis **2013**, 3, 704-712; c) G. E. Crisenza, N. G. McCreanor, J. F. Bower, *J Am Chem Soc* **2014**, 136, 10258-10261; d) T. Kang, Y. Kim, D. Lee, Z. Wang, S. Chang, *J Am Chem Soc* **2014**, 136, 4141-4144.

3. D. F. Fernandez, M. Gulías, J. L. Mascareñas, F. López, *Angewandte Chemie International Edition*, **2017**, Accepted.

Toward New Catalysts – CycloAminoAryloCarbenes (CAArCs) as Ligands for Transition Metal Complexes

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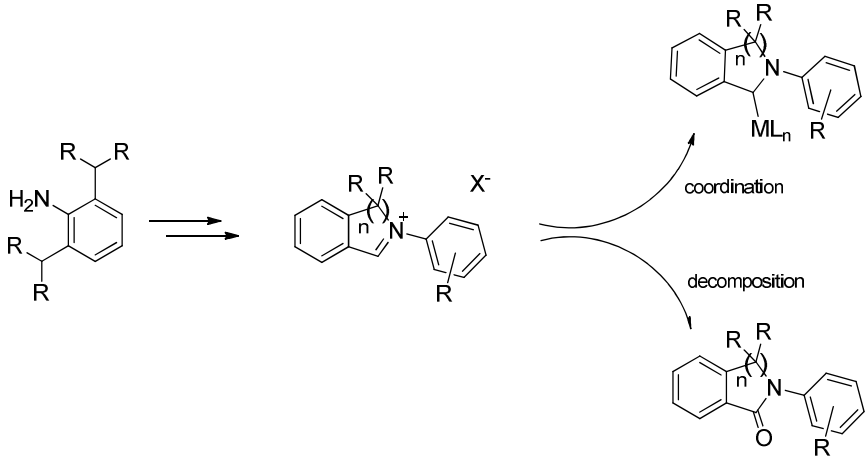
N-Heterocyclic carbenes (NHCs), owing to their valuable properties, have become versitile ligands in organometallic catalysis[1]. Since their first application in transition-metal catalysis[2], unprecedented advances have been made in designing active NHC-bearing metal catalyts.[3] Recent work of prof. Bertrand group introduced a new family of carbenes called **C**ycloAminoAryloCarbnes (CAArCs)[4] with interesting stereo-electronic properties. In comparison to the widely studied classic Arduengo carbenes, this kind of ligand has not attained much attention in the field of organometallic chemistry and catalysis.

In this communication we shall present the synthesis of new ligands and their application in coordination chemistry of transition metals **(Scheme 1)**. We will introduce our new protocol of synthesis of isoquinoline carbene precursors as well as studies of their reactivity. In addition, the application of known precursors of CAARCs in the organometallic chemistry will be conferred.



Scheme or Figure 1: Synthesis and reactivity of **C**ycloAminorAryloCarbnes (CAArCs) ligands.

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References:

1. *N-Heterocyclic Carbenes: Effective Tools for Organometallic Synthesis* (Ed.: S. P. Nolan), Wiley-VCH, Weinheim, **2014**
2. W. A. Herrmann, M. Elison, J. Fischer, C. Kocher, G. R. J. Artus, Angew. Chem. Int. Ed. Engl. 1995, *34*, 2371–2374; Angew. Chem. **1995**, *107,*2602–2605.
3 *N-Heterocyclic Carbenes In Transition Metal Catalysis And Organocatalysis*, (Ed.: C. Cazin), Springer, Dordrecht, 2011.
4 B. Rao, H. Tang, X. Zeng, L. Liu, M. Melaimi, G. Bertrand, *Angewandte Chemie International Edition* **2015,** *54*, 14915-14919.

A Comparative Study of the Preparation Method of CuMgAl Mixed Oxides on the Catalytic Activity of SCR of NO with Ammonia

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Selective catalytic reduction (SCR) of NO with ammonia ([NO] = [NH_3] = 1000 ppm) has been studied over both hydrotalcite-based CuMgAl mixed oxide catalysts prepared by co-precipitation method and Cu/MgAl prepared by impregnation of copper in MgAl mixed oxides. The solids were characterized by X-ray diffraction (XRD), Energy-dispersive_X-ray_spectroscopy (EDX) (table 1) and N_2 physisorption (BET).
The results of the catalytic test revealed that the main product is N_2 (scheme 1).
Copper-free samples MgAl (1:1) and MgAl (2:1) don't present any activity toward SCR of NO. CuAl sample presents low catalytic activity.The influence of impregnation of the transition metal on the catalytic performance has been investigated. When copper species are impregnated on MgA l (1:1) a better NO conversion is obtained nearly 40% at 543 K with a volume space velocity of 60000 h^{-1} (figure 1).

Table 1: EDX results

atomic%	Mg	Al	Cu
Cu0.25Mg0.5Al0.25	43.65	30.09	26.25
Cu/MgAl (2:1)	17.84	8.56	73.60
Cu/MgAl (1:1)	7.02	9.43	83.56
CuAl	_	10.86	89.14

Scheme1: $NO + NH_3 + \frac{1}{4} O_2 \rightarrow N_2 + \frac{3}{2} H_2O$

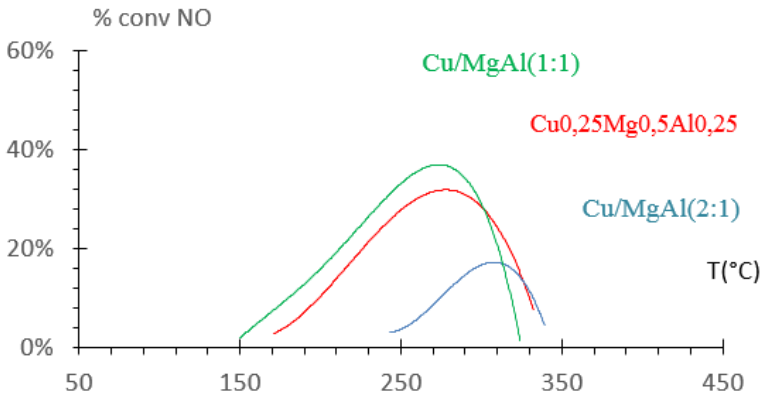

Figure 1

Acknowledgements: We thank l'Institut Français for financial support

Heterolytic Cleavage of H_2 by Molybdenum Diphosphine Complexes Bearing Pendant Amines: Thermodynamic and Kinetic Study

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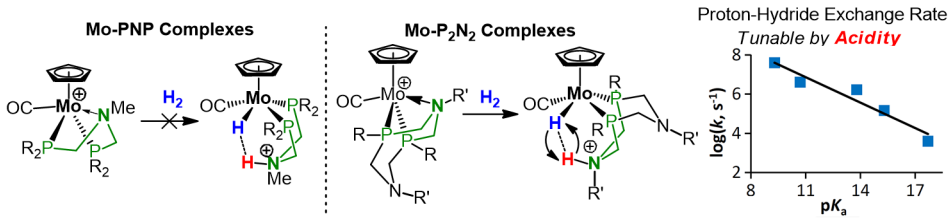
The utilization of H_2 has been of intense interest, particularly in the context of H_2 produced by renewable solar energy.[1] Heterolytic cleavage of the H-H bond into a proton and hydride is a critical process in the catalytic hydrogenation of ketones,[2] the oxidation of hydrogen by hydrogenases in nature[3] and by synthetic molecular catalysts.[4] Understanding the fundamental thermodynamics and kinetics of heterolytic H-H bond cleavage, and controlling the transfer of the proton and hydride, are critically important for the design of new catalysts. We have developed a series of bifunctional [CpMo(CO)(κ^3-diphosphine)]$^+$ complexes that feature the amine bound to the metal for heterolytic cleavage of H_2 into a proton and a hydride, akin to Frustrated Lewis Pairs.[5] Both P_2N_2 (1,5-diaza-3,7-diphosphacyclooctane) and PNP ($R_2PCH_2NR'CH_2PR_2$) ligands were studied, and the resulting Mo complexes showed different reactions with H_2. CpMo(CO)(κ^3-PNP)$^+$ complexes are stable and unreactive toward H_2 addition due to flexibility of PNP ligand skeleton and strong Mo-N coordination. However, CpMo(CO)(κ^3-P_2N_2)$^+$ readily reacts with H_2. The H-H bond cleavage is enabled by the basic amine in the second coordination sphere. The products of heterolytic cleavage of H_2, Mo hydride complexes bearing protonated amines, [CpMo(*H*)(CO)(P_2N_2*H*)]$^+$, were characterized by spectroscopic studies and by X-ray crystallography. Variable temperature ^{1}H, ^{15}N and 2-D ^{1}H-^{1}H ROESY NMR spectra indicated rapid exchange of the proton and hydride. The rate can be controlled, spanning four orders of magnitude at 25 °C, from 2.1 × 10^3 s^{-1} to ≥10^7 s^{-1}. The pK_a values determined in acetonitrile range from 9.3 to 17.7, and show a linear correlation with the logarithm of the exchange rates. This correlation likely results from the exchange process involving key intermediates that differ by an intramolecular proton transfer. The exchange dynamics are controlled by the relative acidity of the [CpMo(*H*)(CO)(P_2N_2*H*)]$^+$ and [CpMo(*H*$_2$)(CO)(P_2N_2)]$^+$ isomers, providing a design principle for controlling heterolytic cleavage of H_2.



Scheme 1: Heterolytic Cleavage of H_2 by Mo Complexes

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References:

1. a) Kubas, G. J. *Chem. Rev.* **2007,** *107*, 4152; b) Morris, R. H. *Chem. Rev.* **2016,** *116*, 8588.
2. a) Noyori, R. *Angew. Chem., Int. Ed.* **2002,** *41*, 2008; b) Morris, R. H. *Acc. Chem. Res.* **2015**, *48*, 1494.
3. Vincent, K. A.; Parkin, A.; Armstrong, F. A. *Chem. Rev.* **2007,** *107*, 4366.
4. a) Bullock, R. M.; Helm, M. L. *Acc. Chem. Res.* **2015,** *48*, 2017; b) Camara, J. M.; Rauchfuss, T. B. *Nat. Chem.* **2012,** *4*, 26.
5. a) Zhang, S.; Bullock, R. M. *Inorg. Chem.* **2015,** *54*, 6397-6409; b) Zhang, S.; Appel, A. M.; Bullock, R. M. *J. Am. Chem. Soc.* **2017,** *139,* 7376−7387.

Biocatalytic Synthesis of 1,2-Naphtoquinones Derivatives Mediated by Cota-laccase

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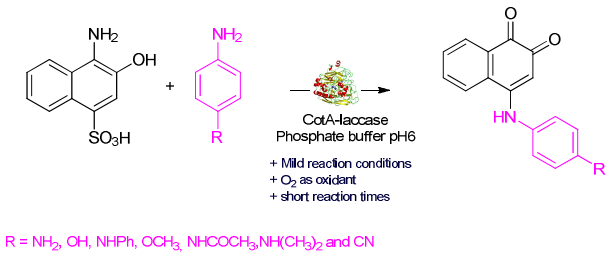
Catalysis is one of the cornerstones of our present economy and society and the formation of value-added products is many times directly dependent on catalytic technologies. Nowadays, there is a growing need for development of green strategies involving clean organic reactions, which do not use harmful organic solvents and toxic reagents. Amongst the many options available for a synthetic organic chemist, biocatalysis has emerged as one approach with an excellent potential. Enzyme-catalyzed reactions offer a number of advantages compared to the traditional chemistry-catalyzed reactions and biocatalytic methods impart a "greener" character to the synthesis. Laccases (EC 1.10.3.2, *p*-diphenol:dioxygen oxidoreductases) are multicopper oxidoreductive enzymes which have proven to be versatile and highly/efficient biocatalyst for the synthesis of different value-added chemicals and pharmaceuticals.[1]

A large number of 1,2-naphthoquinones derivatives have been reported to show antitumor activities by inhibit on of multiple enzymes.[2] In addition to their anticancer properties, the naphthoquinone framework has significance in the development of new substances with promising biological activities in other diseases like neurodegenerative and viral diseases.[3] The formation of naphthoquinone frameworks is quit-well documented and reported methods include various approaches using organic solvents and different chemical oxidants.[4] In this context it is still a challenge to explore alternative and more sustainable synthetic routes for these compounds. As a part of our going research program for exploring the catalytic properties of CotA-laccase, a bacterial laccase isolated from the Bacillus *subtilis*, we describe in the present communication a practical and simple oxidative CotA-laccase mediated eco-friendly method to obtain 1,2-naphthoquinones derivatives using mild aqueous conditions and O_2 as oxidant (**Scheme 1**). All compounds were isolated in good yields and fully characterized by FTIR, NMR and ESI techniques.



Scheme 1: Synthetic route for 1,2-naphthoquinones derivatives catalysed by CotA-laccase

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (Projects PTDC/BBB-EBB/0122/2014, IUD/QUI/00100/2013 and REM2013) and the IST-UTL NMR Network for facilities.

References:

1. Mogharabia M and Faramarzia M. A. *Adv. Synth. Catal*. **2014**, 356, 897.
2. Wu L. *RSC Adv*. **2015**, 5, 24960.
3. Moura K. C. G., Carneiro P.F., Pinto, M.C. *et al*. *Bioorg. Med. Chem.* ***2012***, 20, 6482.
4. Ferreira V. F., Baptista S., Silca F. C. *Org. Biomol. Chem.* **2010**, 8, 4793.

Synthesis of Alpha-Glucosidases and Cholinesterases Inhibitors

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The design, synthesis, inhibition and toxicity assays, as well as docking studies (including homology modelling) for *S.cerevisae*'s and Rat (intestinal) α-glucosidases were performed for analogues of deoxinojirimicin (DNJ) and 1,4-dideoxy-1,4-imino-D-arabitol (DAB-1). These studies rendered sensitive information about both ligands and enzymes' structural features and have been reported[1-4].

An interesting structural relation was noted between phtalimide and indolinone derivatives[5], the latter being both acetylcholinesterase and butyrylcholinesterase inhibitors, therefore of strong clinical interest, leading to indolone analogue synthesis, inhibition assays, STD-NMR and docking studies, already reported[6-10]. Our current developments, with emphasis on the synthetic strategies, will be shown here.

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References:

1. V.H. Lillelund, H.H. Jensen, X. Liang, M. Bols, *Chem. Rev.* **2002**, 102, 515. b) M. Sugiyama, Z. Hong, P-H. Liang, S.M. Dean, L.J. Whalen, W.A. Greenberg, C-H. Wong, *J. Amer. Chem.* **2007**, 129, 14813-17 and references cited therein. 2. M.E.C. Caines, S.M. Hancock, C.A. Tarling, T.M. Wrodnigg, R.V. Stick, A.E. Stütz, A. Vasella, S.G. Withers, N.C.J. Strynadka, *Angew. Chem.* **2007**, *46*, 4474-76.
3. L.R. Guerreiro, EP Carreiro, L. Fernandes, T.A.F. Cardote, R.Moreira, A.T. Caldeira, R.M. Guedes, A.J. Burke, *Bioorg. Med.Chem.* **2013**, *21*, 1911-1917 and references cited therein.
4. E. P. Carreiro, P. Louro, G. Adriano, R. A. Guedes, N. Vannuchi, A. R. Costa, C. M.M. Antunes, R. C. Guedes, A.J. Burke, *Bioorg. Chem.* **2014,** *54*, 81-88
5. N. S. H. N. Moorthy, M. J. Ramos, P. A. Fernandes, *J. Chemolab.* **2011**, *109* 101-112.
6. Vine, K. C., Lake, J. M., Ronson, M., Pyne, S. G., Bremner, B. Bioorg. Med. Chem, **2007**, 15, 931-938
7. Ellman, G.; Courtney, K.; Andres, V.; Featherstone, R.; Biochemical Pharmacology, **1961**. 7, p. 88.
8. Bacalhau, P. ; Joan, A.S.; Marques, C. ; Peixoto, D. ; Burke, A.J. ; Caldeira, A. ; Martins, M.R. Neurodegener Dis.. **2015**, 15(suppl 1) 741. 9. Yvain Nicolet, Oksana Lockridge, Patrick Masson, Juan C. Fontecilla-Camps and Florian Nachon *J. Biol. Chem*. **2003** Vol. 278, No. 42, Issue of October 17, pp. 41141–41147
10. Jane Totobenazara, Patrícia Bacalhau, Amor A. San Juan, Carolina S. Marques, Luís Fernandes, Albertino Goth, A. Teresa Caldeira, M. Rosário Martins, Anthony J. Burke *ChemistrySelect,* **2016***, 1,* 3580–3588.

Antioxidant Activity of Carvone and Derivatives against Superoxide Ion

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Natural compounds are crucial in organic chemistry not only for their biological activities but to be chiral starting materials for the synthesis of other interesting drugs. Our group has been involved in the use of different natural product as sclareol or ent-halimic acid for the synthesis of biological active compounds. Recently we have being interested in carvone to made building blocks for organic synthesis.[1], see figure 1, as is one of the most used for drugs or building blocks synthesis [2]. As several diseases are associated with oxidative stress caused by free radicals [5] we decide to test (R)-carvone **1** and the chloro-derivative **8**. As several diseases are associated with oxidative stress caused by free radicals [3] we decide to test (R)-carvone **1** and the chloro-derivative **8**. The first because is a very available natural compound and the second because is obtained with the better yield in our reactions.

A new lactone has been achieved by oxidation of (R)-carvone using aluminum trichloride as catalyst and hydrogen peroxide as oxidant. Increasing the oxidant amount, time reaction and temperature influence the results in carvone oxidation. The study on the antioxidant activity of compounds 1 and 8 using vascular superoxide production assay shows that (R)-carvone 1 has the most powerful effect on the $\cdot O_2^-$ scavenging activity.

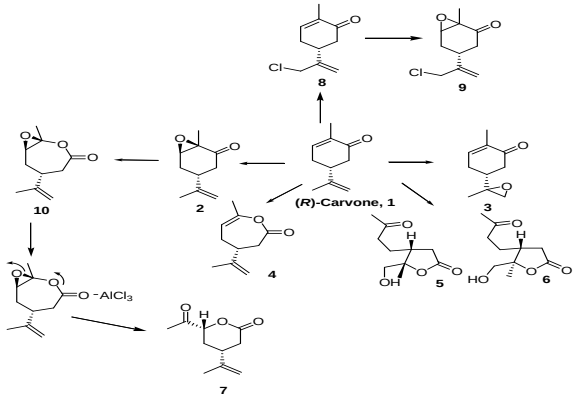

Figure 1: Some building blocks obtained from carvone

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References:

[1] Rodilla, JM, Neves PP, Pombal S, Rives V, Trujillano R, Diez D. (2016) Hydrotalcite catalysis for the synthesis of new chiral building blocks. Natural Product Research, 26, 486-492.

[2] (a) Ghosh AK, Xi K, (2009) Total synthesis of (-)-platensimycin, a novel antibacterial agent. Journal Organic Chemistry, 74, 1163-1170; (b) Valeev RF, Selezneva N K, Starikova ZA, Pankrat'ev EY, Miftakho MS. (2010) Chiral building blocks from R-(–)-carvone: N-bromosuccinimide-mediated addition – sceletal rearrangement of (–)-cis-carveol. Mendeleev Communications, 20, 77–79; (c) Hagiwara H. (2013) Carvone as a versatile chiral building block for total syntheses of heterocyclic sesquiterpenoids. Natural Product Communications, 7, 935-948.

[3] Tahir I, Khan MR, Shah NA Aftab M, (2016) Evaluation of phytochemicals, antioxidant activity and amelioration of pulmonary fibrosis with Phyllanthus emblica leaves. BMC Complementary and Alternative Medicine, 16, 268-284.

Engineered MAO-N for the Enantioselective Synthesis of Bioactive Tetrahydroisoquinolines

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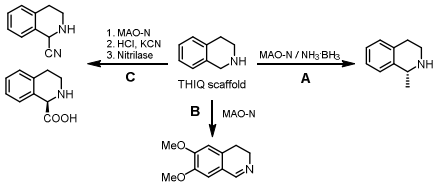
The chemical industry is under increasing pressure to change its environmental policy, shifting towards sustainable processes while maintaining product quality and production cost. The use of classical methods, particularly in asymmetric synthesis, severely limits this change by requiring a compromise between yield, purity and waste generation. Biocatalysis represents an attractive alternative to these methods, employing enzymes or whole microorganisms in the fast synthesis of complex molecules. Moreover, the confined active site in which an enzymatic reaction occurs usually leads to incomparable selectivities in water, at low temperatures and ambient pressures.

Monoamine oxidase from *Aspergillus niger* (MAO-N) catalyses the deamination of primary amines in fungi. A "toolbox" of MAO-N variants has been developed at the Manchester Institute of Biotechnology for the oxidation and deracemisation of chiral amines, exhibiting high activities towards 1,2,3,4-tetrahydroisoquinoline (THIQ). Remarkably, a MAO-N catalysed dynamic kinetic resolution procedure allows 100% yield in the conversion of racemic amine to one enantiomer, a significant improvement over classic resolution methods **(Scheme 1 – A)**.[3]

In this work, MAO-N variants were screened with different THIQs to determine the influence of the presence and position of substituents in the enzyme's activity, allowing the first model to approximately predict its substrate scope. None of the variants tested presented significant activity with compounds containing a catechol or dimethoxy group in the sixth and seventh positions, limiting its application in industrial synthesis. To solve this problem, the mutations in known variants were combined to design MAO-N D13, the first reported variant capable of oxidizing 6,7-dimethoxytetrahydroisoquinoline with great yield and complete *(S)* selectivity **(Scheme 1 – B)**.

Finally, a one-pot three-step process was developed for the novel C1 functionalization of THIQs through oxidation, cyanation and hydrolysis reactions, presenting good yields and exceptional selectivities, in water and at mild conditions **(Scheme 1 – C)**. The high selectivities and environmental advantages of this enzymatic process support a future application of this process in the chemical industry. Furthermore, this stand as proof of success in the combination of enzyme engineering, biocatalysis and chemical synthesis for the novel production of complex bioactive compounds.



Scheme 1: Biocatalysis in the synthesis of enantiopure 1,2,3,4-tetrahydroisoquinolines.

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References:

1. Ghislieri D.; Turner N. J. *Top. Catal.* **2014**, *57*, 284-300.
2. Reetz M. *JACS* **2013**, *135*, 12480-12496.
3. Ghislieri D.; Green A.; Pontini M.; Willies S.; Rowles I.; Frank A.; Grogan G.; Turner N. J. *JACS* **2013**, *135*, 10863-10869.

Vitamin B_{12} as a Drug Delivery Agent – a Chemical Point of View

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Delivery of an active compound to its site of action is one of the crucial issues in drug development. A promising strategy is to use naturally occurring compounds, such as vitamin B_{12} (cobalamin, Cbl) due to its unique ability to penetrate cells via a system of transport proteins.[1] In order for B_{12} to act as a carrier, its structure must be modified to allow selective coupling of biologically active compounds and at the same time high affinity to transport proteins must be retained. Selective and high-yielding functionalizations of B_{12} are highly desirable; however, the complexity of cobalamin's structure makes this extremely challenging. Our group has introduced new methods allowing to achieve this goal (**Figure 1: A**). Now, B_{12} can be selectively and directly attached to alkynes (via CuAAC),[2] acids (via amide bond formation)[3] or thiols (via disulfide bond formation).[4] Also reduction-free, direct alkynylation of vitamin B_{12} at cobalt center that leads to previously unknown heat and light stable acetylide cobalamins has been developed.[5] The selective orthogonal conjugation at both the Co center and 5'-OH group can also be achieved.[6] Recently, we have developed the method that involves modifications at previously unexplored *meso* position.[7] The idea of using cobalamin as a delivery vehicle is well documented in mammals and was applied to increase bioavailability of different therapeutics including proteins, anti-cancer drugs, fluorescent and radioisotope labels. However such approach has not been applied to bacteria yet. Thus, in our work we focus on creating a connection of B_{12} and PNA (peptide nucleic acid) that will be targeted at bacterial DNA or RNA (**Figure 1: B**).[8] The use of such short, modified oligonucleotides as inhibitors of bacterial translation seems a promising alternative for antibiotics, which are currently overused leading to fast development of bacterial resistance. We found that vitamin B_{12} transports antisense PNA into *E. coli* cells more efficiently than the most widely used cell-penetrating peptide (KFF)3K. Moreover, we have analyzed the structure and conformational dynamics of conjugates of Cbl with a PNA monomer and oligomer and B_{12} was found to increase the flexibility of PNA in a way that could be beneficial for its hybridization with natural nucleic acid oligomers.[9] The results of our study provide the foundation for considering vitamin B_{12} as a delivery tool for PNA oligonucleotides into bacterial cells.

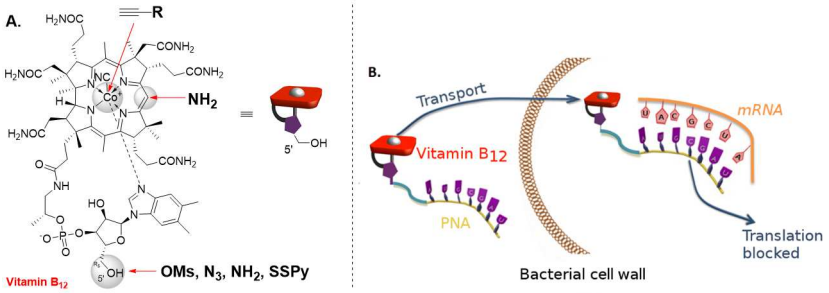

Figure 1: Sites suitable for conjugation in B_{12} (**A**). Vitamin B_{12} as a PNA transporter (**B**).

Acknowledgements: Financial support for this work was provided by the National Science Centre, grant SYMFONIA 2014/12/W/ST5/00589

References: 1. Banerjee R. *Chemistry and Biochemistry of B_{12}*, John Wiley & Sons, Inc, **1999**. 2. Chromiński M.; Gryko D. *Chem. - Eur. J.* **2013**, *19*, 5141. 3. Jackowska A.; Giedyk M.; Chromiński M.; Gryko D. *unpublished work*. 4. Wierzba A. J.; Wojciechowska M.; Trylska J.; Gryko D. *Bioconjugate Chem*. **2016**, *27*, 189. 5. Chromiński M.; Lewalska A.; Gryko D. *Chem. Commun*. **2013**, *49*, 11406. 6. Chromiński M.; Lewalska, A.; Karczewski, M.; Gryko., D. *J. Org. Chem*. **2014**, *79*, 7532. 7. Wierzba A. J.; Wincenciuk A.; Gryko D. *unpublished work* 8. Równicki M.; Wojciechowska M.; Wierzba A. J.; Czarnecki J.; Bartosik D.; Gryko D.; Trylska J. *accepted*. 9. Pieńko T.; Wierzba A. J.; Wojciechowska M.; Gryko D.; Trylska J. *J. Phys. Chem. B* **2017**, *121*, 2968.

The Photophysicochemical Properties of Pyridone Derivatives Phthalocyanines

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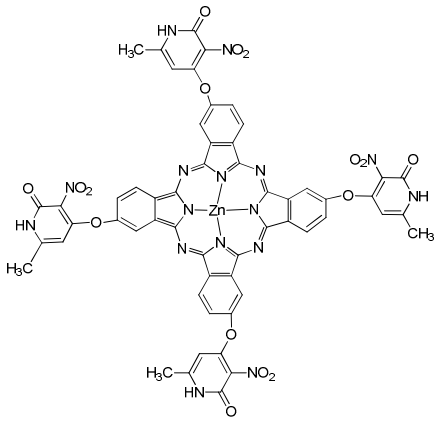
Phthalocyanines have interesting and uniq electronic and physical properties becaus of their high conjugation[1]. Recently, to improve these properties many phthalocyanines were desingned by changing metals and substituents[2,3]. In this study, starting with 4-nitrophthalonitrile and 3-hydroxy-6-methyl-2-nitro-pyridin, 4-(6-methyl-2-nitropyridin-3-yloxy) phthalonitrile was synthesized in dimethyl formamide at 60ºC for 36 h[4]. In the second step, metal-free phthalocyanine (H_2Pc), zinc phthalocyanine (ZnPc) and cobalt(II) phthalocyanines(CoPc) were prepared. The novel compounds were characterized by elemental analyses, UV/vis, ^{1}H-NMR, MALDI-MS spectroscopy and IR spectroscopy. The synthesized compounds were studied using appropriate experimental setups from the point of view of their main photophysical and photochemical characteristics for photodynamic therapy (PDT). The singlet oxygen, photodegradation, fluorescence quantum yield, triplet quantum yield and triplet life time of the complexes in DMSO were determined[5]. Zinc complex showed higher singlet oxygen quantum yield than unmetalled complex. The photobleaching stabilities of complexes were determined in dimethyl formamide. The obtained values showed that the molecules are of high stability in the solvent used.



Scheme 1: Chemical structure of ZnPc

Acknowledgements: We are thankful to The Foundation of Marmara University, The Commission of Scientific Research (BAPKO) (Project No: FEN-A-101013-0397). This work was supported by the Department of Science and Technology (DST) and National Research Foundation (NRF), South Africa through DST/NRF South African Research Chairs Initiative for Professor of Medicinal Chemistry and Nanotechnology as well as Rhodes University and Yildiz Technical University.

References:

1. Leznoff_, C. C.; Lever, A. B. P. Phthalocyanines: Properties and Applications; VCH: New York, NY, USA, 1993. Thomas
2. A. L., Pthalocyanine Research and Application, CRC Press, Florida, 1990.
3. Dennis K. P. Ng.,Jianzhuang J., *Chemical Society Rewiews*, **1997**, 26, 433.
4. Mızrak B., Ağar M., Altındal A., Abdurrahmanoglu S., , *Journal of Porphyrins and Phthalocyanines,* **2016,** 20, 1457.
5. Oluwole D.O., Prinsloo, E. and Nyokong T., Polyhedron, **2016** 434.

Synthesis of *P*-Stereogenic Analogues of Isoindolin-1-ones

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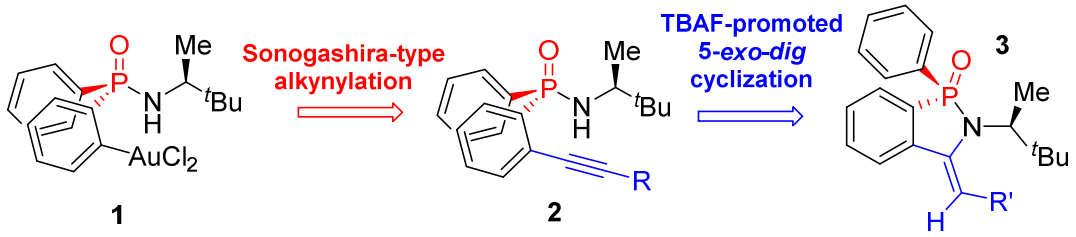
The isoindolin-1-one motif is a core structure of numerous natural and synthetic products that show a wide range of biological activities.[1] On the other hand, the widespread presence of organophosphorus compounds in biological systems and their potential as pharmaceuticals, make them the focus of great interest.[2] Since there is a remarkable similarity in reactivity and bioactivity between carbon species and their phosphorus counterparts, the phosphorus analogues of isoindolin-1-ones become desirable targets. This type of compounds brings an additional advantage, the possibility of synthesizing *P*-stereogenic enantiopure heterocycles since the planar carbonyl group is replaced by a tetrahedral P=O linkage.

As part of our ongoing research on the synthesis, reactivity and biological properties of Au(III) complexes,[3] we have recently developed an efficient method for the synthesis of *P*-stereogenic (O^C)-cyclometalated gold(III) complexes **1** and their Sonogashira-type alkynylation to afford the corresponding *ortho*-alkynylphosphinic amides **2**.

We describe herein an efficient methodology for the synthesis of *P*-stereogenic 1,2-benzoazaphosphole 2-oxides **3**, analogues of the important isoindolin-1-one core in which the carbon atom of the C=O group has been replaced by a *P*-chirogenic moiety. The synthesis is based on the *5-exo-dig* cyclization of the *ortho*-alkynyl derivatives **2** promoted by TBAF. The reaction proceeds with high yield and with the exclusive formation of the five-membered heterocycles. The diastereoselectivities of the exocyclic carbon-carbon double-bond ranged from modest to high and proved to be dependent on the substituents present in the alkyne.



Scheme 1: Synthesis of *P*-stereogenic analogues of isoindolin-1-ones

Acknowledgements: We thank the MINECO and FEDER program for financial support (projects CTQ2011-27705 and CTQ2014-57157-P).

References:

1. a) Breytenbach, J. C.; van Dyk, S.; van den Heever, I.; Allin, S. M.; Hodkinson, C. C.; Northfield, C. J.; Page, M. I. . *Bioorg. Med. Chem. Lett*. **2000**, *10*, 1629. b) Speck, K.; Magauer, T. *Beilstein J. Org. Chem.* **2013**, *9*, 2048.
2. a) Westheimer, F. H. *Science* **1987**, *235*, 1173. b) Seto, H.; Kuzuyama, T. *Nat. Prod. Rep*. **1999**, *16*, 589.
3. a) Oña-Burgos, P.; Fernández, I.; Roces, L.; Torre-Fernández, L.; 931 García-Granda, S.; López-Ortiz, F. *Organometallics* **2009**, *28*, 1739. b) Belmonte-Sánchez, E.; Iglesias, M. J.; El Hajjouji, H.; Roces, L.; García-Granda, S.; Villuendas, P.; Urriolabeitia, E. P.; López-Ortiz F. *Organometallics* **2017**, *36*, 1962.

NHC-ligands for Silver-free Gold(III) Catalysis

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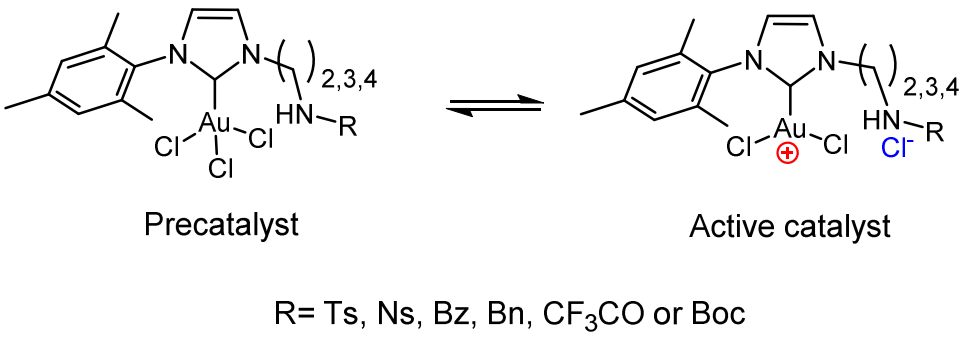
We have recently developed a concept in which a functionalized "arm" of Au(III) N-heterocyclic carbene (NHC) complex generates catalytic activity without the need to change coordinative chloride counter ion(s) to non-coordinative ones.[1] Essentially, this allows us to carry out catalytic reactions without silver additives. Previously, we demonstrated the proof-of-principle with pyridine functionalized NHC "arms" of Au(III) complexes with Hashmi phenol synthesis and cyclization of *o*-alkylanilines. In the presumed mechanism the pyridine arm replaced coordinative counter ion releasing a free coordination site for activated substrates i.e. π-systems to be activated for nucleophilic attacks. In this work, we have studied and developed the concept further and generated a new set of functional groups (R) in NHC "arms" that shows varying group dependent catalytic activity in test reactions including A3-reaction, lactonization and hydration of alkynes (**Scheme 1**).[2] Reaction conditions, kinetics and presumed reaction mechanism have been studied in specific reactions.



Scheme 1: NHC-Au(III) complexes for silver-free gold catalysis

Acknowledgements: We thank the University of Helsinki for financial support.

References:

1. M. Muuronen, J. E. Perea-Buceta, M. Nieger, M. Patzschke, and J. Helaja, *Organometallics* **2012**, *31*, 4320-4330

2. O. Seppänen, M. Nieger, and J. Helaja, *Unpublished results*

Immobilization of Cinchonidine-9-picolinamide Organocatalyst on a Polystyrene Support: Heterogeneous Ketimine Hydrosilylations

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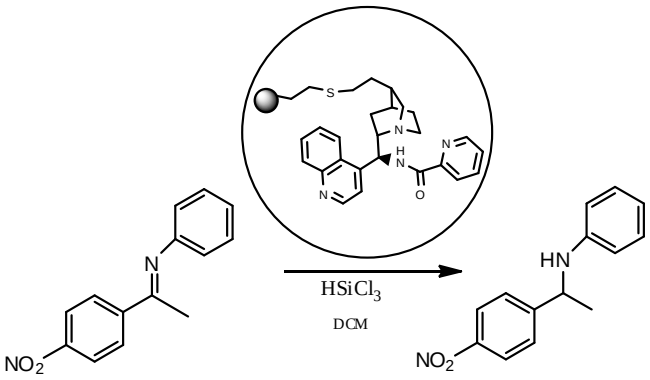
Heterogeneous catalysts are distinguished from homogeneous catalysts by the different phases present during reaction. Homogeneous catalysts are present in the same phase as the reactants and products, usually liquid, whilst heterogeneous catalysts are present in a different phase, usually the solid phase. The main advantage of using heterogeneous catalysts is the relative ease of catalyst separation from the product stream that aids in the creation of continuous chemical processes.[1]

The aim of this work was the immobilization of the well-known cinchonidine-9-picolinamide organocatalyst on a polymeric support (polystyrene resin) and the evaluation of its efficiency in the heterogeneous hydrosilylation reaction (Scheme 1). These results will be compared with the results obtained for other types of immobilized cinchonidine-9-picolinamide organocatalysts using SiO_2, MCM-41 and Iron oxide nanoparticle supports.[2] We found that the polymer immobilized organocatalyst was more stable, and more robust than the other types of immobilized cinchonidine-9-picolinamide organocatalysts, generally giving better results. These results will be discussed in this communication.



Scheme 1: Benchmark heterogeneous catalytic ketimine hydrosilylation.

Acknowledgements: We are grateful also for funding from FCT via the Strategic Projects UID/QUI/0619/2016 (contributed to CQE-UE). We are grateful to project LADECA (ALENT-07-0262-FEDER-001878) for financing the acquisition of the Bruker Avance III NMR spectrometer.

References

1. White, M. (1990). *Heterogeneous catalysis*. 1st ed. Englewood Cliffs, N.J.: Prentice Hall.

2. a) Barrulas, P. (2014). *Síntese e Aplicação de Novos Organocatalisadores de Alcalóides de Cinchona em Catálise Assimétrica*. Doutor. Universidade de Évora; b) Barulas P.C.; Genoni A.; Benaglia M.; Burke A.J. *Eur. J. Org. Chem.* **2014**, 7339-7342; c) Novel Picolinamide-Cinchona Organocatalysts and derivatives, P.C. Barrulas, A.J. Burke, WO2015052656.

Synthesis of α-Amido Ketones from 1,2-Azido Acetates

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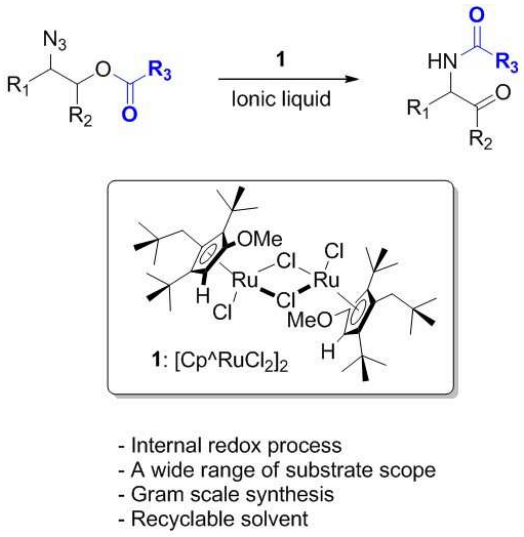
α-Amido ketones have been evaluated as biologically relevant molecules and important intermediates in organic sythesis. They are valuable substrates in oranic transformations, including the Robinson–Gabriel reaction to oxazoles and thiazoles, the Norrish–Yang photocyclization to 2-aminocyclobutanols, the epoxy-annulation reaction to epoxide-fused heterocycles and the reaction with ammonium acetate (or primary amines) to imidazoles. Due to the importance of their synthetic application, various approaches to form α-amido ketones have been developed. However, these methods frequently suffer from difficulties in preparing substrates, harsh reaction conditions, and the requirement of stoichiometric oxidants or additives. Herein we demonstrate an efficient transformation of esters of 1,2-azido alcohols that gives access to a wide scope of α-amido ketones. A broad scope of α-amido ketones are synthesized by internal redox process thereby oxidants and reductants are not necessary. A gram scale reaction was demonstrated in nonflammable ionic liquid to diminish safety concerns associated with the use of organic azides as substrates.



Scheme 1: Synthesis of α-amido ketones.

References:

1. Kim, Y.; Pak, H. K.; Rhee, Y. H.; Park, J. *Chem. Commun.* **2016**, *52*, 6549.

Synthesis of Aryl Nitrile and Anilines by the Redox Reaction of N-H Imines with Aryl Azides

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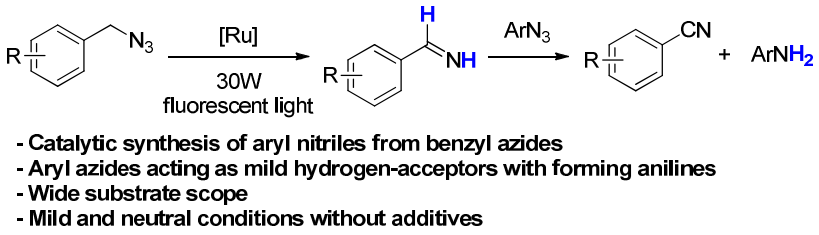
Nitriles are important class of compounds in organic synthesis as well as valuable building blocks in natural products, pharmaceuticals, agricultural chemicals and functional materials. Although there are numerous methods for the synthesis of nitriles, they suffer from several drawbacks such as the use of toxic reagents, high temperature, harsh reaction conditions and the use of strong oxidants or additives.

Herein we reports a unique and novel reaction between benzyl azides and aryl azides to synthesize nitriles and anilines, which is catalyzed with a photoactivated dirutheium complex. N-Unsubstituted imines (N-H imines) are generated first from benzyl azides, followed by the hydrogen transfer reaction between N-H imines and aryl azides. A wide range of aryl nitriles and anilines were synthesized by a unique catalytic redox reaction under neutral and mild reaction conditions without any additives.



Scheme or Figure 1: Redox reaction of N-H imines with aryl azides: Synthesis of aryl nitriles and anilines.

Acknowledgements: We thank to National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP)

References:

1. Y. Kim; Y. H. Rhee; J. Park. *Org. Biomol. Chem.* **2017**, *15*, 1636

Development of Synthetic Method for Isomerization-Free-N-Acylimines

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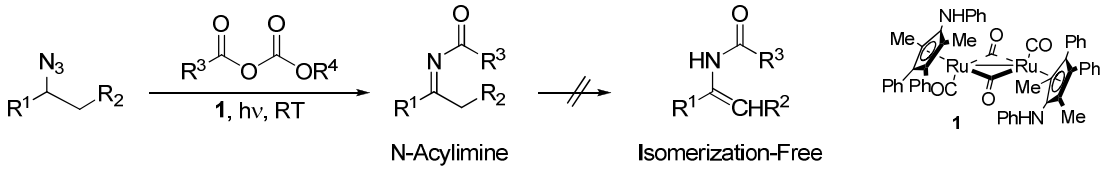
N-Acylketimines are one of the important synthetic precursors in organic and medicinal chemistry. N-Acylkeimines have electron-withdrawing acyl group to overcome the low electrophilicity of imine. Despite of their importance, the general strategy for N-acylketimines is rarely reported due to the instability of N-acylketimines. N-acylketimines are known to be too unstable to be stored and easily isomerized to corresponding enamide. Therefore, they are generally prepared in situ for the reaction with nucleophiles. We successfully synthesized various N-acylketimines including enolizable aliphatic ones from the alkyl azides in a one-pot procedure.[1] And we demonstrated the applicability of cyclic N-acylketimine in nucleophilic addition of Grignard reagent to afford acetamide with high diastereoselectivity.



Scheme or Figure 1: Synthesis of N-acylkeitmines from secondary azides and acyl alkyl carbonates..

References:

1. Kwon Y.; Rhee Y. H.; Park J. *Adv. Synth. Catal*. **2017**, *359*, 1503.

Reductive N-methylation Amines and Amino Acids using Nanoscale Co_3O_4-based Catalysts

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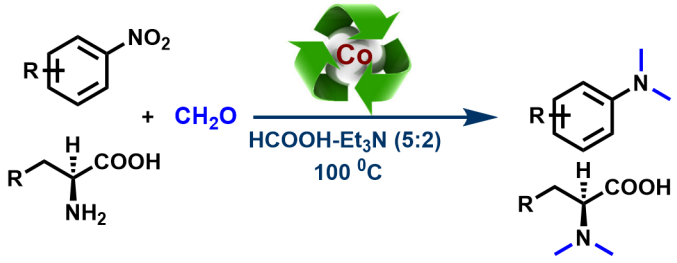
N-Methylated amines are special kind of amines, which play an important role in regulating chemical and the biological life science molecules.[2-3] As an example, the top selling drugs such as olanzapine, oxycodone, Imatinib, and venlafaxine contain N-methyl amino groups, which play a significant role in their activities. In nature, N-methylation of biomolecules, such as amino acids, peptides and DNA plays a vital role in epigenetic changes in gene expression for cellular phenotypes. In general, this class of compounds is synthesized via reductive amination reactions using high pressure of molecular hydrogen. On the other hand in laboratory and drug discovery, activated methyl compounds such as methyl iodide, dimethyl sulfate are employed, which are known to be toxic and generate significant amounts of waste. In ordered to avoid the activated methyl compounds, the development of convenient methodologies for the synthesis of N-methyl amines in laboratory scale is highly desired. Herein, we report the synthesis of functionalized and structurally diverse N-methylamines directly from nitroarenes and aqueous formaldehyde and formic acid. [1] The key to success for this synthesis is the use of cobalt based nanocatalysts, which have been prepared by the pyrolysis of Co-phenanthroline complexes on carbon. Interestingly, N-methylation of amino acids and biological amines has been performed.



Scheme or Figure 1: Reductive methylation of nitroarenes to N-methylamines.

Acknowledgements: The Federal Ministry of Education and Research (BMBF) and the State of Mecklenburg-Vorpommern are gratefully acknowledged for their general support. Thankful to the analytical staff of the Leibniz-Institute for Catalysis, Rostock for their excellent service.

References:

1. a) R. V. Jagadeesh, A. -E. Surkus, H. Junge, M. -M. Pohl, J. Radnik, J. Rabeah, H. Huan, V. Schünemann, A. Brückner, M. Beller, Science 342, 1073-1076 (2013). b) R.V. Jagadeesh, H. Junge, M. Beller, Nature Commun. 5, 4123 (2014)..

2. K. Natte, H. Neumann, M. Beller and R. V. Jagadeesh, Angew. Chem., Int. Ed., 2017, 56, 2–13.

3. Chatterjee, J., Rechenmacher, F. & Kessler, H. N-Methylation of peptides and proteins: An important element for modulating biological functions. Angew. Chem. Int. Ed., 52, 254-269 (2003).

Graphitic Shell Encapsulated Nanoscale Cobalt-catalyzed Reductive Amination Reactions for the Synthesis of Advanced Amines

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Amines represent momentous class of chemicals and this motif presented in natural and life science molecules. These essential chemicals, serve as key building blocks and central intermediates for value-added chemicals, pharmaceutical and materials[1]. Therefore the synthesis and functionalization of amines continues to be an important mission. For the advanced synthesis of this class of vital chemicals, the development of suitable catalysts, especially based on earth abundant metals are highly desired. Particularly, nanomaterials-based heterogeneous catalysts are mostly preferable for the advancement of sustainable and cost-efficient synthesis of amines[2]. In this respect in recent years our group has developed innovative Fe-and Co-based materials by the pyrolysis of organometallic complexes and carbon for sustainable redox reactions[3]. Based on this novel procedure, we prepared graphitic shell encapsulated cobalt-based nanocatalysts by the pyrolysis of amine or carboxylic acid-ligated cobalt complexes on heterogeneous support. Interestingly, these cobalt-based nano catalysts exhibit excellent selectivity and reactivity for the reductive aminations. Applying these catalysts, starting from easily accessible carbonyl compounds and nitroarenes, structurally diverse and functionalized amines have been synthesized under industrial viable conditions. This green methodology has been demonstrated for the alkylation of biomolecules and also for the preparation of existing life science molecules. Notably this catalyst is highly stable and recyclable, which enables the selective reductive aminations for a synthesis of different kinds of interesting amines with >140 examples.

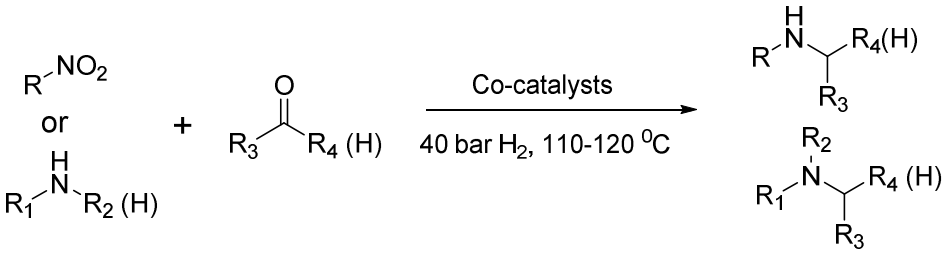

Figure 1: Sustainable reductive amination processes using novel cobalt-catalysts.

Acknowledgements: We gratefully acknowledge the support of Federal Ministry of Education and Research (BMBF), the State of Mecklenburg-Vorpommern and European Research Council. We thank the analytical staff of the Leibniz-Institute for Catalysis, Rostock for their excellent service.

References:

1. S. A. Lawrence, Amines: Synthesis, Properties and Applications (Cambridge University Press, 2004).
2. P. Munnik, P. E. de Jong, K. P. de Jong, Chem. Rev. 115, 6687-6718 (2015).
3. a) R. V. Jagadeesh, A. -E. Surkus, H. Junge, M. -M. Pohl, J. Radnik, J. Rabeah, H. Huan, V. Schünemann, A. Brückner, M. Beller, Science 342, 1073-1076 (2013). b) R.V. Jagadeesh, H. Junge, M. Beller, Nature Commun. 5, 4123 (2014).

Copper-Porphyrin-MOFs as Oxidative Heterogeneous Catalysts

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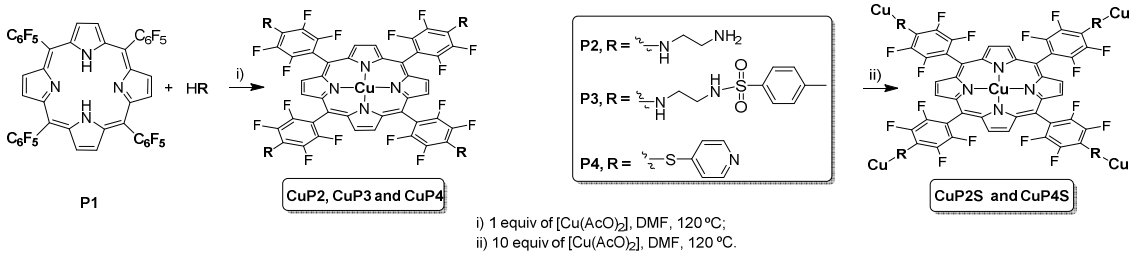
The search for heterogeneous catalysts represents an important challenge for a sustainable development. A fundamental pillar of green chemistry is catalysis, generally resulting in significant gains in terms of overall efficiency of a chemical reaction. Metalloporphyrins and analogues have already proved their selectivity and efficiency as catalysts, namely for oxidative reactions. The insertion of diverse metal salts into the core, such as Fe, Mn, or Cu, can modulate the catalytic activity associated with the structure of the macrocycle.[1] In recent years, many research groups, including ours, have focused their attention on the development of synthetic and functional models of biological systems based on copper. Following our interest on this subject, we describe here the synthesis and characterization of the copper porphyrins obtained by structural modification of 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin (**P1**) with the nucleophiles: ethylenediamine (**P2**), *N*-tosylethylenediamine (**P3**) and 4-mercaptopyridine (**P4**) (**Scheme 1**).[2,3] The tetra-substituted free-base porphyrins **P2** and **P4**, after metallation with Cu(II) (10 equiv.), afforded a new class of copper-porphyrin-based MOFs allowing its use as heterogeneous catalysts. **CuP3** and **CuP4S** were further isolated and studied in the solid state, by using single-crystal X-ray diffraction studies. The catalytic activity of these copper complexes was investigated in the oxidation of catechol under "homogeneous" (**CuP2**, **CuP3** and **CuP4**) and heterogeneous (**CuP2S** and **CuP4S**) conditions, using dioxygen or hydrogen peroxide as oxidant. The copper porphyrins prepared were able to efficiently mimic the activity of catecholase. The results show that the catalysts' performance depends on the structure of the porphyrin. Additionally, it was possible to reuse the copper-porphyrin-based MOFs for at least three cycles.



Scheme 1: Schematic representation of the metalloporphyrins prepared in this work.

Acknowledgements: The research leading to these results has received funding from QREN, FEDER and COMPETE founds for QOPNA (FCT UID/QUI/00062/2013), CICECO (FCT UID/CTM/50011/2013)) and CQE (FCT UID/QUI/0100/2013) research units, to CNPq, University of Aveiro and UFPR. K.A.D.F. Castro also thanks CNPq for the pos-doctoral scholarship granted (Process: 201107/2014-7). FCT is also gratefully acknowledged for the Ph.D. grant No. SFRH/BD/84231/2012 (for R.F. Mendes).

References:

1. Castro, K.A.D.F.; Simões, M.M.Q.; Neves, M.G.P.M.S.; Cavaleiro, J.A.S.; Ribeiro, R.R.; Wypych, F.; Nakagaki, S. *Appl. Catal. A* **2015,** *503*, 9.
2. Castro, K.A.D.F.; Rodrigues, J.M.M.; Mendes, R.F.; Neves, M.G.P.M.S.; Simões, M.M.Q.; Cavaleiro, J.A.S.; Paz, F.A.A.; Tomé, J.P.C.; Nakagaki, S. *J. Catal.* **2016,** *344*, 303.
3. Castro, K.; Figueira, F.; Mendes, R.; Cavaleiro, J.; Neves, M.; Simões, M., Paz, F.A.; Nakagaki, S.; Tomé, J.P.C. *ChemCatChem* **2017**, doi:10.1002/cctc.201700484.

Transition Metal-catalyzed Dehydroperoxidation of Alkyl Hydroperoxides

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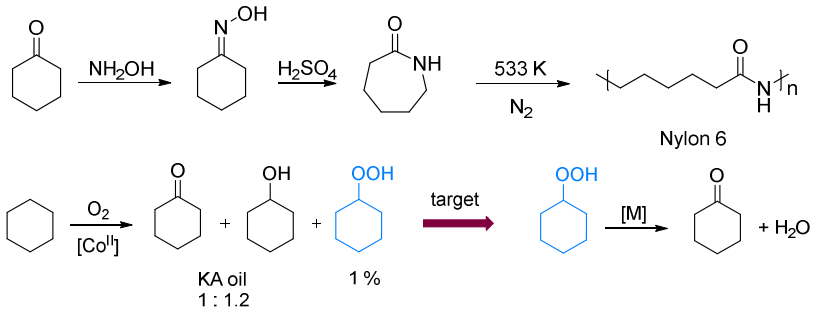
Nylon 6 is one of the most widely-used nylon and it is produced on a large industrial scale (~ 4 million t/a). This important polymer has a wide range of applications, for example in the textile industry in the manufacture of yarn or as thin plastic film for packaging purposes. On the industrial scale, Nylon 6 is produced *via* the ring-opening polymerization of ε-caprolactam at high temperatures. The required starting material for the synthesis of ε-caprolactam is cyclohexanone that is formed starting from cyclohexane in an oxidation process. In detail: in the first step, cyclohexane is oxidized to cyclohexyl hydroperoxide in a radical chain reaction, using dioxygen O_2 at elevated temperatures. The formed hydroperoxide decomposes subsequently to a ~ 1:1 mixture of cyclohexanone and cyclohexanol. In further steps, cyclohexanone reacts with hydroxylamine in a condensation reaction to the corresponding cyclohexane oxime and *via* an acid catalyzed Beckmann rearrangement, the desired ε-caprolactam is formed (**Scheme 1, top**).[1] In order to minimize the number of process steps in the production of ε-caprolactam, a selective decomposition of the hydroperoxide solely to the ketone and one equivalent water would be a very attractive target (**Scheme 1, below**).



Scheme 1: Top: Industrial process for the production of Nylon 6, starting from cyclohexanone; below: production of cyclohexanone.

Therefore, different transition metal complexes were investigated and identified as very promising homogeneous catalysts, as they form alkylperoxo complexes, which by intramolecular hydrogen transfer, release the corresponding alkyl ketone together with one equivalent of water. One approach focuses on mono- and binuclear vanadium(V) complexes with different dipic-based or Schiff base ligands and their reactivity towards the decomposition of alkyl hydroperoxides were investigated. For the decomposition of the cyclohexyl hydroperoxide, a mechanism *via* a vanadium(V) alkylperoxo complex was proposed. This reactive intermediate was characterized by X-ray diffraction and the proposed mechanism was further investigated by comprehensive DFT calculations.[2]

Acknowledgements: CaRLa is being co-financed by the Ruprecht-Karls-University of Heidelberg and BASF SE, Ludwigshafen.

References:

1. a) Hermolin, J.; *US 4465861*, **1984**. b) Pugi, K.; *US 3530185*, **1970**. c) Kuessner, A.; Herrmann, G.; *US 3917708*, **1975**. d) Druliner, J. D.; Ittel, S. D.; Krusic, P. J.; Tolman, C. A.; *US 4326084*, **1982**. e) Musser, M. T.; Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH, Weinheim, **2000**.
2. Schmidt, A.-C.; Hermsen, M.; Rominger, F.; Dehn, R.; Teles, J. H.; Schäfer, A.; Trapp, O.; Schaub, T.; *Inorg. Chem.* **2017**, *56(3)*, 1319-1332.

Computational Study of the Metal Catalyzed Decomposition of Alkyl Hydroperoxides to Ketones

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Several vanadium(V)dipicolinato complexes were identified as promising candidates for the decomposition of hydroperoxides to corresponding ketones and water. As hydroperoxide decomposition is currently the main industrial route to cyclohexanone, but also inevitably forms the corresponding alcohol, we set out to explain the formation of ketone in a radical-free mechanism that has so far not been reported. The insight gained will be of interest for development of ketone-selective decomposition catalysts. This poster will focus on the computational investigation of different possible mechanisms and the identification of an intramolecular hydrogen transfer to the metal catalyst that is key to the observed reactivity.[1]

Acknowledgements: CaRLa (Catalysis Research Laboratory) is cofinanced by the Ruprecht-Karls-Universität Heidelberg (Heidelberg University) and BASF SE.

References:

1. Schmidt. A.-C.; Hermsen M.; Rominger F.; Dehn F.; Teles J. H.; Schäfer A.; Trapp O.; Schaub T. *Inorg. Chem.* **2017**, *56* (3), 1319.

D-Penicillamine and L-Cysteine Based 2-Arylthiazolidine Ligands in the Enantioselective Alkylation of Benzaldehyde: Structure-Enantioselectivity Relationship.

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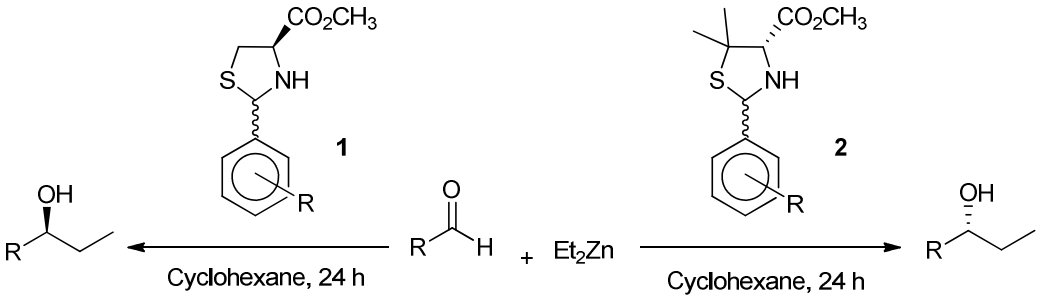
Chiral secondary alcohols, compounds with vast application in fine chemistry, pharmaceuticals, perfumes, herbicides and pesticides, can be obtained with high enantiomeric purity, using adequate chiral ligands, through catalytic alkylation reactions with diethylzinc. Several types of ligands have been used in this process, namely diamines, their derivatives, diols and amino alcohols, among others.[1,2]

In our studies, we synthesized a library of 2-phenylthiazolidines derived from D-penicillamine and L-cysteine, with different substituents on the aromatic ring. The synthetic procedure that initially led to the thiazolidines was reviewed, and a new and greener strategy was developed.

The efficiency of the synthesized compounds as chiral ligands in the enantioselective alkylation of benzaldehyde was evaluated (**Scheme 1**). Products with *ee* up to 90% were obtained. Futhermore, the opposite chiral configuration of the two natural sources allowed us to obtain both (*R*) and (*S*)-1-phenylpropan-1-ol with high *ee*.[3] Synthetic and catalytic results, as well as the influence of ligand structure on the *ee*, will be disclosed in this communication.



Scheme 1: Enantioselective alkylations using chiral thiazolidines **1** and **2**.

Acknowledgements: CQC is supported by FCT, Portuguese Agency for Scientific Research, through the project Nº 007630 UID/QUI/00313/2013, co-funded by COMPETE2020-UE. N.C.T.T. acknowledge FCT for PhD grant PD/BD/128496/2017. The authors also thank the UC-NMR facility for NMR spectroscopic data (www.nmrccc.uc.pt).

References:

1. L. Pu, H. B. Yu, *Chem. Rev*. **2001**, *101*, 757.
2. G. Lin, Y. Li, A. S. C. Chan, *Principles and Applications of Asymmetric Synthesis*, John Wiley & Sons, Inc., New York, **2001**.
3. Serra, M. E. S.; Costa, D.; Murtinho, D.; Tavares, N. C. T.; Pinho e Melo, T. M. V. D. *Tetrahedron,* **2016**, *72*, 5923.

Transfer Hydrogenation using Fe-NHC Based Catalysts

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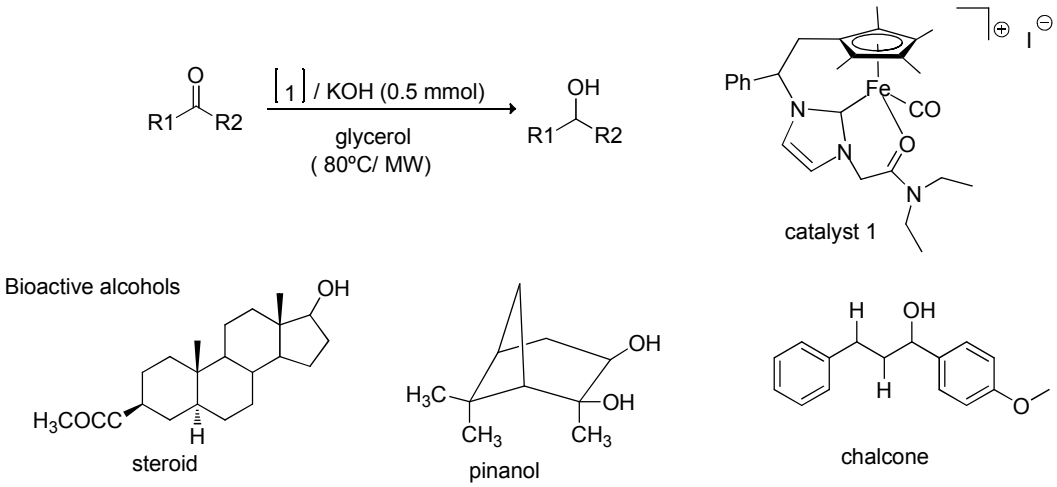
Metal-catalysed transfer hydrogenation (TH) is a powerful method for the reduction of carbonyl groups. The operational simplicity of this approach, avoiding the use of highly flammable molecular hydrogen has made TH an elegant tool for hydrogenation of unsaturated molecules. In the last few years, we have been involved in the development of iron N-heterocyclic carbene (NHC) complexes for their application in the reduction of functional groups through transfer hydrogenation and hydrosilylation processes [1 - 3]. Herein, we present our latest results on a new family of iron complexes bearing functionalized NHCs and their application in the catalytic transfer hydrogenation of ketones (**Scheme 1**) under 80ºC/isopropanol and under microwave (MW) irradiation/glycerol. The use of MW heating has a tremendous impact in shortening reaction times. Notable, catalyst **1** allowed the synthesis of interesting bioactive alcohols in high yields.



Scheme 1: Transfer hydrogenation with Fe-NHC catalyst and bioactive alcohols obtained by TH.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support through project UID/QUI/00100/2013 and CQC (PEst-OE/QUI/UI0313/2014), grant fellowship SFRH/BD/52373/2013 (R.L), and B. R. thanks for IF/00346/2013.

References:

1. Warratz, S., Postigo, L., Royo, B., *Organometallics*, **2013**, *32*, 893.
2. Cardoso, J. M. S., Royo, B, *Chem. Commun*. **2012**, *48*, 4944.
3. Krisnha Mohan, V. V., Cardoso, J. M. S., Peris, E., Royo, B, *Organometallics* **2010**, *29*, 2777.

Folded Biomimetic Oligomers as Asymmetric Catalysts for Michael Addition in Water

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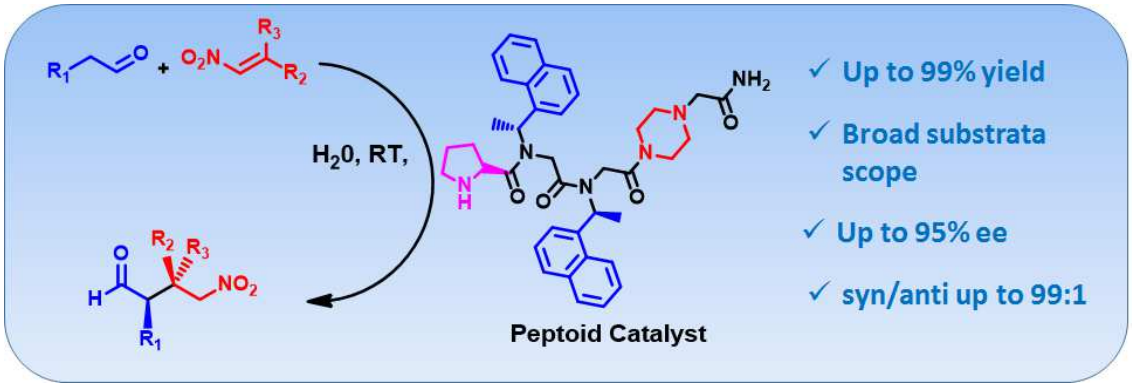
Many naturally occurring biopolymers (i.e., proteins, RNA, DNA) owe their unique properties to their well-defined three-dimensional structures.[1] These attributes have inspired the design and synthesis of folded architectures with functions ranging from molecular recognition to asymmetric catalysis.[2] Among these are synthetic peptoids,[3] which can display conformational ordering at short chain lengths. Moreover the inherent modularity of peptoids permits various chemical transformations simply by introducing different types of catalytic centers. Potentially, catalytic activity and selectivity can be adjusted and optimized systematically by simply altering the placement of catalytic sites and chiral recognition sites on the oligomeric scaffold. Peptoids, however, have only been explored as platforms for asymmetric catalysis in one reported example.[4:]This report describes a library of synthetic helical ‘‘peptoid’’ oligomers that enable enantioselective transformations at an embedded catalytic center, as illustrated by asymmetric michael addition of aldehydes to nitroalkenes. We have discovered that the enantioselectivity of the catalytic peptoids depends on the handedness of the asymmetric environment derived from the helical scaffold, and the degree of conformational ordering of the peptoid scaffold.



Acknowledgements: D.C.M thanks the PBC foundations for his postdoctoral fellowship.

References:

1. Breslow R. *Biochemistry*, **2011**, *50*, 10422.

2. a) Zhongand C.; Shi, X. *Eur. J. Org. Chem.,* **2010**, 2999. b) Shao Z.; Zhang, H. *Chem. Soc. Rev.,* **2009**, *38,* 2745.

3. Jing S.; Zuckermann, R.N. *ACS Nano, **2013**, 7* 4715–4732.

4. Maayan, G.; Ward, M. D.; Kirshenbaum, K.*Proc. Natl. Acad. Sci. U.S.A. **2009**, 106,* 13679

A Metallopeptoid as an Efficient Catalyst for the Aerobic Oxidative Synthesis of Imines from Alcohols and Amines

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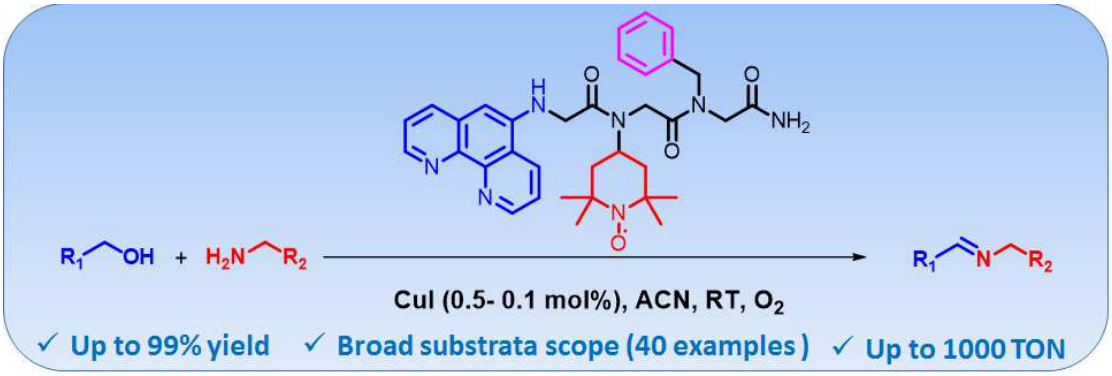
Enzymatic catalysis is largely based on cooperativity between a metal center and functional organic molecules located at its surrounding folds. This concept has inspired the design of a unique metallopeptoid catalyst incorporating phenanthroline-copper and TEMPO, and one non-catalytic group (benzyl group) that performs in the oxidation of various benzylic, allylic and aliphatic primary alcohols with TON of up to 16 times higher than a mixture of the two catalytic groups or the peptoid dimer that is lacking the non-catalytic group.[1] Here we will present our recent have results with this catalyst in the oxidative synthesis of benzylic, aryl, heteroaryl, allylic and aliphatic primary imines from alcohols and amines with a TON of up to 20 times higher than a mixture of the two catalytic**.**



Acknowledgements:. D.C.M thanks PBC foundations for his postdoctoral fellowship.

References:

1. Prathap, J. K.; Maayan G. *Chem. Commun*. **2015***, 51*, 11096.

Dynamic Kinetic Resolution of Diarylmethanols with a Highly Active Lipoprotein Lipase Preparation

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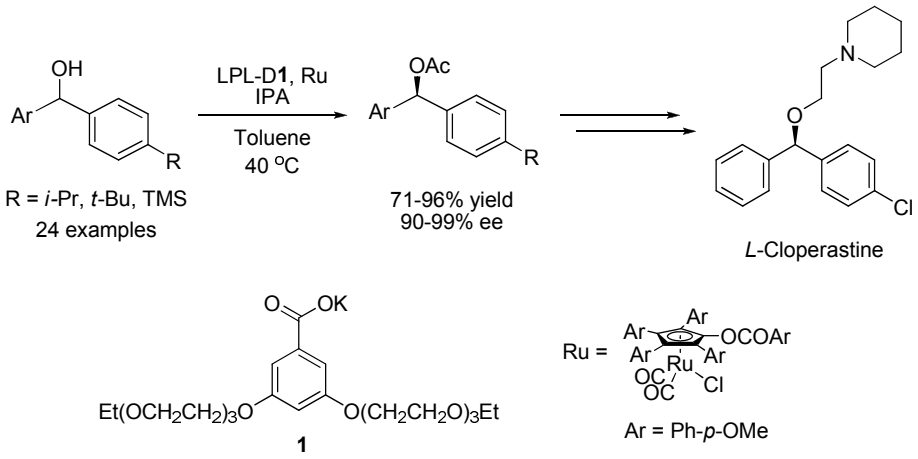
Recently, we reported a practical method using an ionic-surfactant (**1**) as the coating material for improving the activity of lipoprotein lipase (LPL). The activated LPL displayed a dramatically-enhanced activity than its native counterpart and accepted sterically-demanding secondary alcohols. As an application of activated LPL, we explored the dynamic kinetic resolution (DKR) of 24 diarylmethanols and the synthesis of *L*-cloperastine, an antitussive drug (**Scheme 1**).[1] In most cases, the DKRs provided satisfactory yields (71-96%) and high enantiopurities (90-99% ee). *L*-Cloperastine was synthesized successfully via DKR. In the meeting, we will present the results from these studies with detailed experimental procedures.



Scheme 1: Dynamic Kinetic Resolution of Diarylmethanols.

Acknowledgement: We thank the National Research Foundation of Korea (project numbers, 2012R1A1A2006595 and 2012-007235) for financial support.

References:

1. Lee, J.; Oh, Y.; Choi, Y. K.; Choi, E.; Kim, K.; Park, J.; Kim, M.-J. *ACS Catal.* **2015**, *5*, 683.

Activation of Lipoprotein Lipase as the Catalyst for Dynamic Kinetic Resolution

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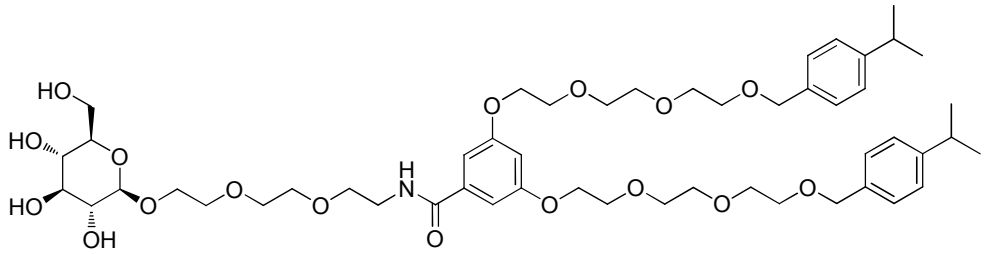
Enzymes are useful as the catalysts for organic synthesis because of their excellent enantioselectivities. However, enzyme catalysis in organic solvent often suffers from low activity of enzyme. Thus, it is important to develop a useful method to enhance the activity of enzyme in organic solvent. In this work, we developed a new glucose-headed surfactant (GHS) for enhancing the activity of lipoprotein lipase (LPL). This surfactant enhanced the activity of LPL by more than 10^5-fold in both toluene and *t*-butyl methyl ether. In the meeting, we will present the synthesis of GHS, the preparation of GHS-activated LPL, and the results from the dynamic kinetic resolution of secondary alcohols with GHS-activated LPL.[1]



Glucose-headed surfactant

Acknowledgements: This work was supported by the National Research Foundation of Korea (2015R1D1A1A01059851).

References:

1. Oh, Y.; Choi, Y. K.; Yun, I.; Lee, E.; Kim, K.; Kim, M.-J. *J. Mol. Catal. Enzym.* **2016**, *134.* 148

Cerium Oxide (IV) Hollow Nanospheres and their Performance in the Adsorption of 4-Nitrophenol

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4-nitrophenol (4-NP) is frequently present in many industrial wastewater effluents and may cause numerous damages in human's health. The adsorption of 4-NP is considered as a cleaning technique. Recently, high 4-NP adsorption capacity of some inorganic oxide hollow nanospheres, based on alumina or iron oxide had been found [1, 2]. Nevertheless, till now the adsorption of 4-NP on hollow Cerium Oxide (IV) nanospheres (@CeO_2) has not been reported. This work presents a facile synthesis route of @CeO_2 with different structural properties and its performance in the adsorption of 4-NP from aqueous solutions. @CeO_2 were synthesized via hydrothermal method as reported by Jian Qi et al. [3]. Modification of hydrothermal treatment heating profile permitted to obtain a narrow nanospheres size distribution. Cerium oxide (IV) nanospheres with a tunable structure were successfully synthesized via a variation of the Urea and $Ce(NO_3)_3$*$6H_2O$ (U/Ce) weight ratio. Ceria average domain size, pore size and specific surface area present a clear dependence on the U/Ce ratio. The @CeO_2 maximum adsorption capacity (q_{max}) is noticeably higher than that reported for both @Al_2O_3 and @Fe_2O_3.

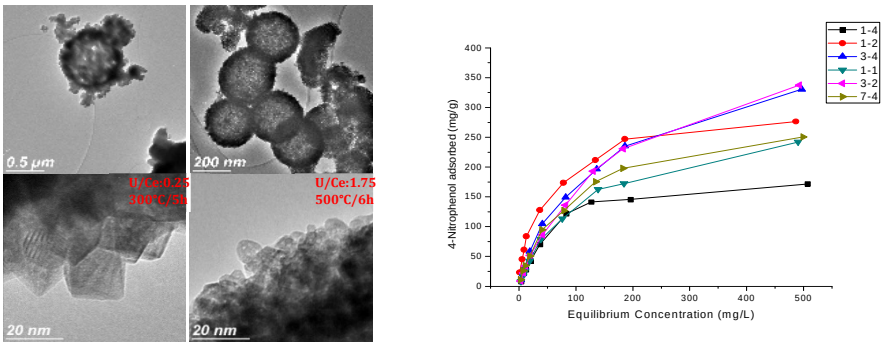

Figure 1: TEM Images of @CeO_2 nanospheres prepared at different Urea/Ce ratio and calcination temperatur (left) and Adsorption Isotherm for 4-NP on @CeO_2 prepared with different U/Ce ratios (■ 0.25, ● 0.5, ▲0.75, ▼1.0, ◄ 1.5 y ►1.75) and calcined at 400°C (right).

Acknowledgements: The authors thank to E. Flores, P. Casillas, F. Ruiz, J. Mendoza and J. Peralta for their kind technical support in this work. This research project was partially supported by CONACyT (Mexico) and PAPIIT-UNAM (Mexico) through grants 179619, 203117, respectively.

References:

1. Jiabin Zhou, Zhong Zhang, Bei Cheng, Jiaguo Yu. Chem. Eng. J., 211–212 153–160, (2012).
2. Liangmiao Zhang, Wencong Lu, Rongrong Cui, Shanshan Shen. Mater. Res. Bul., 45, 429-436, (2010).
Jian Qi, Kun Zhao, Guodong Li, Yan Gao, Huijun Zhao, Ranbo Yu and Zhiyong Tang. Nanoscale, 6, 4072-4077 (2014)

Synthesis of Au NPs encapsulated in Cerium Hydroxide (III) or Iron Oxyhydroxide (III) and their Performance in the reduction of 4-Nitrophenol

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At the moment, the gold nanoparticles (AuNPs) are one of the most studied NPs of Nobel metals in catalysis. In 1997, Haruta et al. demonstrated that the catalytic activity of the AuNPs is deeply linked to their average size [1]. Nevertheless, AuNPs are highly unstable due to their high specific surface energy. As a consequence of this, AuNPs tend to coalescence and, as a result, to lose their catalytic properties [1]. There are different methods to stabilize metallic NPs. A favorable and efficient way to increase their stability consists in NPs encapsulation into permeable inorganic oxide shells [2]. The aim of the present work is to study the encapsulation of AuNPs into thin shells of Cerium Hydroxide (III) ($Au@Ce(OH)_3$) or Iron oxyhydroxide (Au@Fe(OOH) as well as to compare the catalytic performance of the free AuNPs with the $Au@Ce(OH)_3$ and Au@Fe(OOH) in the reduction of 4-nitrophenol to 4-aminophenol. AuNPs were synthesized using the Turkevich Method. Then, AuNPs were encapsulated via hydrolysis of cerium (III) or iron (III) chlorides in the presence of Urea. Both, AuNPs Synthesis and AuNPs encapsulation were monitored by UV-Vis in situ spectroscopy. Encapsulation of AuNPs into cerium or iron hydroxide shell led to the noticeable enhancement of their stability and affected the mechanism of the 4-nitrophenol reduction to 4-aminophenol.

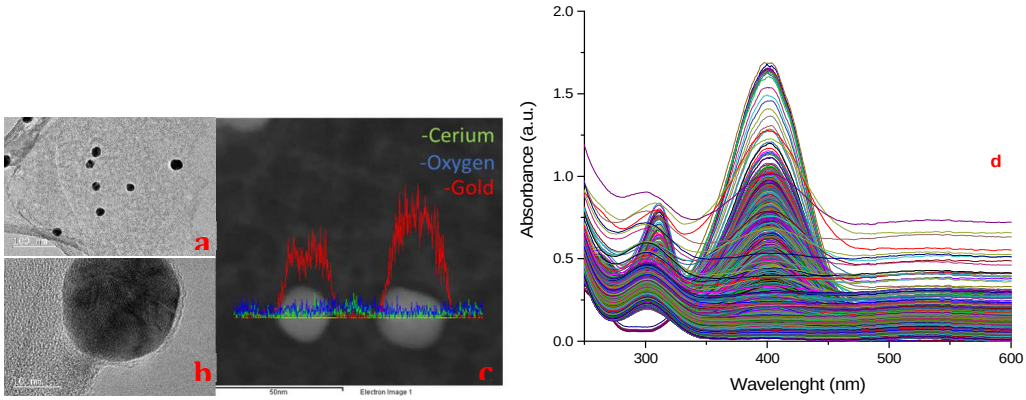

Figure 1: TEM Image (a), HR-TEM micrography (b), Chemical Mapping (c) and 4-Nitrophenol Reduction Spectra (d) for AuNPs encapsulated into $Ce(OH)_3$.

Acknowledgements: The authors thank to E. Flores, P. Casillas, F. Ruiz, J. Mendoza and J. Peralta for their kind technical support in this work. This research project was partially supported by CONACyT (Mexico) and PAPIIT-UNAM (Mexico) through grants 179619, 203117, respectively.

References:

1. Haruta M. (1997) Catalysis Today, 153-166.
2. E. Smolentseva, V. Gurin, & V. Petranovskii. (2012). Self-assembly of size-selected clusters and nanoparticles of Cu, Ag and Au in mordenite matrix. Revista Mexicana de Ingeniería Química, 11(3), 469–474. Du, J.,
3. Qi, J., Wang, D., & Tang, Z. (2012). Facile synthesis of Au@TiO2 core-shell hollow spheres for dye-sensitized solar cells with remarkably improved efficiency. Energy & Environmental Science, 5(5), 6914–6918.

Synthesis And Biological Activity of 2-Substituted Vinylidene-1,1-Bisphosphonates Against *Plasmodium falciparum* and *Trypanosoma brucei*

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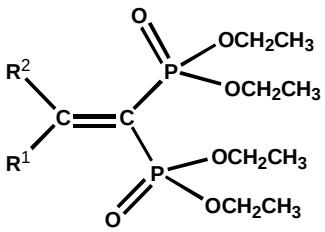
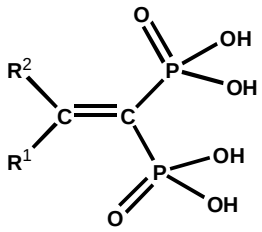
Malaria and African trypanosomiasis are diseases caused by protozoan parasites of the genera *Plasmodium* and *Trypanosoma* respectively.[1] Malaria affects about 500 million people per year causing about 2 – 3 million deaths whilst trypanosomiasis affects about 20 million individuals each year.[2] Due to lack of vaccines and constant emergence of drug-resistant strains, it is necessary to develop improved drugs candidates. In this work, a series 2-substituted vinylidene-1,1-bisphosphonate esters and their acids were synthesized and tested for activity against *Plasmodium falciparum* and *Trypanosoma brucei.* For each compound, 50% inhibitory concentration (IC_{50}) and % parasite viability in treated wells were calculated relative to untreated controls for both *P. falciparum* and *T. brucei*. Chloroquine and pentamidine were used as positive control drug standards for activity against *P. falciparum* and *T. brucei* respectively. Some of the compounds reduced % parasite viability to as low as 24.3% for *P. falciparum* and down to 0.602% for *T. brucei.* The best IC_{50} obtained for activity against *T. brucei* was 0.0345 µmol/ml.



Bisphosphonate esters

R^1, R^2 = H, Aryl, Alkyl



Bisphosphonic acids

Figure 1: General structures of vinylidenebisphosphonate esters and acids.

Acknowledgements: This research project was supported by the South African Medical Research Council (MRC) with funds from National Treasury under its Economic Competitiveness and Support Package, and Rhodes University Sandisa Imbewu.

References:

1. Cox F.E.G. *Parasites & Vectors* **2010**, 3, 1
2. Delhaes L.; Abessolo H.; Biot C.; Berry L.; Belcourt P.; Maciejewski L.; Brocard J.; Camus D.; Dive D. *Patasitol Res* **2001**, 87, 239

Synthesis of Substituted 1,2-Epoxy Ethyl*gem*bisphosphonate Esters Using a Green and Facile Method

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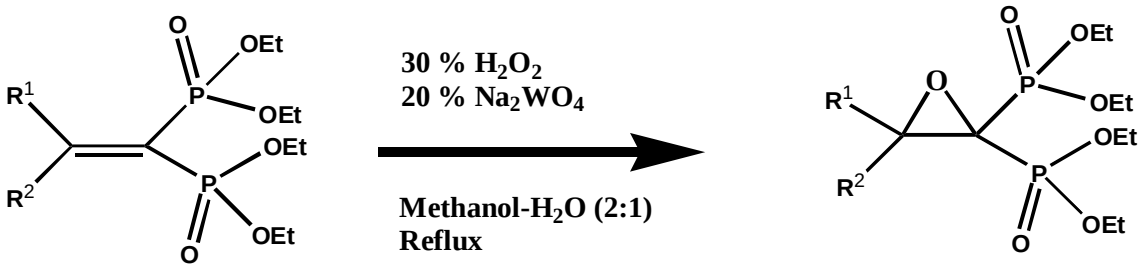
Bisphosphonates containing the epoxy group on the alpha carbon are very important because they can be used as intermediates to synthesize a wide range of compounds including new bisphosphonate drug leads.[1,2] In this work we wish to report a simple and environmentally friendly protocol for synthesis of substituted 1,2-epoxy ethyl*gem*bisphosphonate esters by tungstate-catalyzed oxidation of substituted vinylidene-1,1-bisphosphonate esters with hydrogen peroxide in a methanol-water (2:1) solvent system. The catalyst was easily recycled and reused without any significant loss of activity. This method provided the epoxides in good to excellent yields.



R^1, R^2 = Aryl, alkyl, hydrogen

Scheme 1: Epoxidation using hydrogen peroxide and sodium tungstate in methanol-water (2: 1).

Acknowledgements: We thank the South African National Research Foundation and University of Johannesburg for financial support.

References:

1. Nash R.P.; McNamara D.E.; Ballentine W.K.; Matson S.W.; Redinbo R.M. *Biochem. Biophys. Res. Commun.* **2012,** 424, 697.
2. Saikia L.; Satyarthi J.K.; Srinivas D.; Ratnasamy P. *J. Catal.* **2007**,252,148.

Stainless Steel Foam as Catalyst for Bleed Air Contamination

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Aerotoxicity is becoming an increasing concern as it is thought to cause sickness in passengers and flight crew members. The main cause of the sickness is believed to be due to the toxic contaminants present in the jet engine oil, which enter the cabin through bleed air. Modern aircrafts supply a combination of recirculated cabin air and compressed air drawn from the compressor of the jet engine (bleed air), instead of fresh atmospheric air. As the air passes through the engine, it can be contaminated with engine or jet oil.[1] Catalyst filters could be a way to overcome the issue of contaminants entering the cabin. However, to date these systems have not been implemented in the aircrafts. Monolith-base catalysts are preferred for these systems, compared to powder catalysts. When a monolith-base catalyst is used, a thin layer of catalyst is placed on a solid porous support, such as ceramic or metallic foam.

In this work, a series of stainless steel foams (SS 314 and 316) have been prepared to be evaluated as catalysts for the breakdown of some of the known toxic contaminants in the bleed air of aircrafts, i.e. tricresyl phosphate (TCP), toluene and cresol. During the catalytic process, these toxic contaminants will break down into less toxic components, such as CO_2 and H_2O(v). The raw SS foam was modified via two different pre-treatments, i.e. oxidation in static air and impregnation via dip coating. The oxidation under static air aims to achieve a uniform layer of metal oxide on the surface of the SS foam, which will be the active specie for the decomposition of the target contaminants.[2] For this pre-treatment, the influence of the oxidation temperature and the duration of the oxidation process were evaluated. In the case of the impregnation pre-treatment, the oxide layer is incorporated by impregnation onto the surface of the raw or pre-oxidised SS foam. The influence of the substrate (raw or pre-oxidised foam), nature of the solution and concentration of the metal precursor were the experimental parameters studied in this case. The surface morphology of the foams was investigated using FEG-SEM and EDX analysis. The results show that the oxidised SS 314 and SS 316 foams had optimal properties to be used as a substrate for the impregnation pre-treatment. From the dip coating studies, it was concluded that the foams (raw or pre-oxidised) impregnated in metal nitrate ethanol base solution (with surfactant) are also a promising catalyst according to the metal loading achieved and their textural properties. In the next step, these materials will be tested in a lab-scale rig to evaluate their catalytic activity towards the degradation of TCP, toluene and cresol and the degraded gas products would be analysed using GC-MS.

Acknowledgements: We would like to thank EPSRC for funding

References:

1.C. Winder and J.C. Balouet, *Environ. Res.*, 2002, 89, 146–164

2.J. P. Bortolozzi, E. D. Banús, V. G. Milt, L. B. Gutierrez and M. A. Ulla, *Appl. Surf. Sci.*, 2010, **257**, 495–502.

Acetalization of Glycerol with Butanal over Heteropolyacids Supported on Silica

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The glycerol is a by-product of biodiesel production. For every 9 kg of biodiesel produced, about 1 kg of a crude glycerol is formed. In order to develop new uses for glycerol different catalytic processes, including oxidation, reforming, hydrogenolysis, etherification and esterification, acetalisation reactions, have been used in the transformation of glycerol.[1] Another catalytic process to valorisation of glycerol is the condensation of glycerol with butanal, which provides a branched oxygen-containing compound and could be used as an additive in the biodiesel formulation, improving the cold properties and lowering the viscosity.[2]

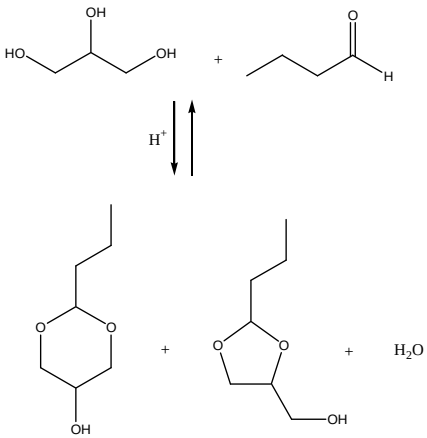

Fig1. Scheme of acid-catalyzed acetalization of glycerol with butanal

Traditionally, the acetalisation of glycerol with butanal is carried out over mineral acids, as catalysts (Fig. 1). However, the effluent disposal leads to environmental problems and economical inconveniences. These problems can be overcome by the use of heterogeneous catalysts. However, only Amberlyst-15 resin[2], MoO_3 supported on silica[3] and zeolites[4] were used as heterogeneous catalysts in acetalisation of glycerol with butanal. Heteropolyacids (HPAs) are typical strong Brönsted acids, which catalyse a wide range of reactions. The major disadvantages of HPAs as catalysts are low surface area (1-10 m^2/g), separation problem from reaction mixtures and solubility. In order to increase the specific area of the heteropolyacids, a variety of supports have been used as support to immobilize HPAs[5]. In this work we studied the synthesis of bio-additives to fuel by acetalisation of glycerol with butanal over different heteropolyacids supported on silica.

References:

1. Zhou C. H.; Zhao H.; Tong D.S.; Wu L.; Yu W. *Catal. Rev.: Sci. and Eng.* **2013**, *55*, 369.

2. Silva P.H.R., Gonçalves V.L.C., *Mota* C.J.A. *Bioresource Technol.* **2010**, *101*, 6225.

3. Umbarkar S.B.; Kotbagi T.V.; Biradar A.V.; Pasrichab R.; Chanale J; Dongare M.K.; Mamede A.-S.; Lancelot C.; Payen E. *J. Mol.Catal. A:Chem.* **2009,** *310,*150.

4. Serafim H.; Fonseca I.M.; Ramos A.M.; Vital J.; Castanheiro J.E. *Chem. Eng. J.* **2011**, *178,* 291.

5. Kozhevnikov I.V. *Chem. Rev*. **1998,** *98,* 171.

Understanding Enantioselectivity in Indium-Catalyzed Reactions

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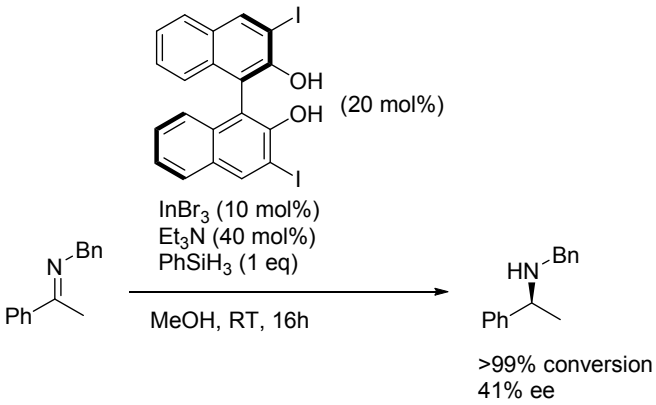
Indium has received increasing attention within the past decades as a catalyst for organic reactions, due to a number of favorable properties including low toxicity, diverse functional group tolerance and chemoselectivity. Furthermore, many indium(III) salts have proven to exhibit stability towards oxygen and water. Indium(III) salts are mild but effective Lewis acids and catalyse a variety of different reactions.[1] Enantioselectivity induced with indium(III) salts and BINOL ligands have been reported for allylation of ketones[2] and alkynylation of aldehydes.[3] However, not much is know about the mechanisms of these enantioselective indium-mediated reactions. The range of indium-catalyzed reactions include imine reduction and preliminary investigations have found the electronic effects of the 3,3'-substituents of the BINOL ligand to be crucial for inducing asymmetry in hydrosilane-mediated reduction of an imine. Furthermore, the choice of solvent is of utmost importance and only in polar protic solvents has this reaction showed promising enantioselectivity. Much work is yet to be performed to develop a highly enantioselective ligand for the developed system, which so far has yielded up to 41% enantiomeric excess (**Scheme 1**). Further experimental investigations will be accompanied by computational work to gain mechanistic insight in order to understand how the chiral ligands interact with the indium metal center, why the electronic effect of the ligands are of utmost importance, and how solvent affects the enantioselectivity. By understanding the mechanism of action herein, we will apply this knowlegde to develop appropiate ligands for achieving enantioselectivity in other indium-catalysed reactions including spiroiminolactonisations.



Scheme 1: Hydrosilane-mediated reduction of an imine with indium(III)bromide and (R)-(+)-3,3'-diiodo-1,1-bi-2-naphthol.

Acknowledgements: We thank the EPSRC and Cambridge Trust for financial support.

References:

1. a) Cintas, P. *Synlett* **1995**, *11*, 1087. b) Frost, C. G.; Hartley, J. P. *Mini-Rev. Org. Chem.* **2004**, *1*, 1.
2. Teo, Y.-C.; Goh, J.-D.; Loh, T. P. *Org. Lett.* **2005**, *7*, 2743.
3. Takita, R.; Yakura, K.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 13760.

Atmospheric Oxidation of 1,3-Dithianes and Acyclic Dithioacetals Anions

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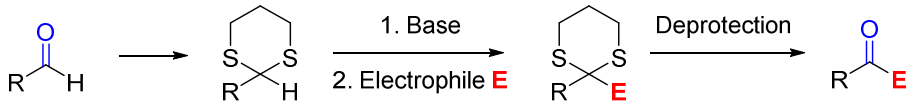
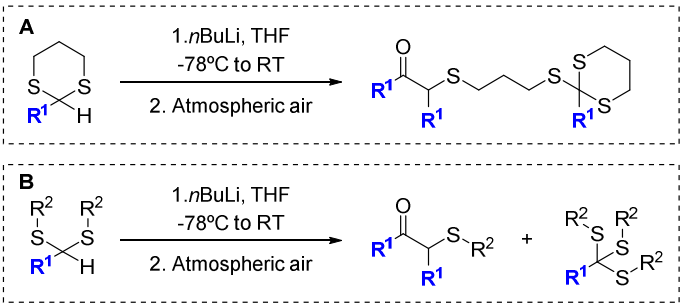
Since the discovery of the Umpolung character of 1,3-dithianes in 1969[1], this moeity has been used extensively to mask and alter the reactivity of aldehydes. The formation of a dithioacetal from a starting aldehyde originates a weakly acidic proton, α to the sulfur atoms, which is prone to depronation *via* a strong base, usually *n*-BuLi. The resulting lithiated dithiane is a strong nucleophile, able to attack various electrophiles such as alkyl halides, carbonyls, Michael acceptors, and others[2] (**Scheme 1**). In a later stage, the deprotection of the dithiane group regenerates the now substituted carbonyl. This sequence of reactions are usually high-yielding and have been used constantly in total synthesis[2].



Scheme 1: Umpolung reactivity of 1,3-dithianes.

Although the reactivity of dithianes is nowadays quite well established, some unexpected reactions still ocur[3]. In fact, our group has found that, in the absence of a suitable electrophile, and upon exposure to atmospheric air, the lithiated dithiane undergoes a remarkably fast (within seconds) oxidation with atmospheric oxygen. This oxidation gives rise to a molecule consisting of three unities of the original dithiane (**Scheme 2, A**), isolated generally in good yields (up to 74%). This reaction also occurs in acyclic dithiacetals, originating an α-keto thioether and a thioortoester (**Scheme 2, B**). In this work we report the optimization of this atypical reaction, its scope, and propose a mechanism for the oxidative cascade reaction, based on experimental and theoretical work. The valorization of the obtained products is also currently being explored.



Scheme 2: Atmospheric air oxidation of 1,3-dithianes (**A**) and acyclic dithioacetals (**B**), and resulting products.

Acknowledgements: Fundação para a Ciência e Tecnologia (SFRH/BD/120119/2016) and Academy of Finland (Decision 310334) are thanked for financial support.

References:

1. Seebach D. *Synthesis* **1969**, 17.
2. Gröebel B.-T.; Seebach D. *Synthesis* **1977**, 357. b) Yus, M.; Nájera, C.; Foubelo, F. *Tetrahedron* **2003**, *59*, 6147.
3. a) Argade, N. P.; Hazra, B. G. Joshi P. L. *Synth. Commun.* **1996**, *26*, 2797. b) Valiulin, R. A.; Kottani, R., Kutateladze, A. G. J. Org. Chem., **2006**, *71*, 5047.

Towards the Total Synthesis of the Cystobactamids

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Cystobactamids are a group of nonribosomal peptides which were isolated in small amounts (<100 µg/L) from *Cystobacter sp.*[1] Müller *et al.* reported the isolation and structure elucidation of cystobactamids **919-1**, **919-2** and **507**, as well as the identification and annotation of their biosynthetic gene cluster. They are strong antibacterial agents that inhibit several clinically relevant Gram-negative and Gram-positive bacteria such as *Acinetobacter baumannii* (minimum inhibitory concentration, MIC = 7.4 to >59 µg/mL), *Enterococcus faecalis* (MIC = 0.1-7.4 µg/mL), *Staphylococcus aureus* (MIC = 0.1-32.5 µg/mL), *Streptococcus pneumoniae* (MIC = 0.1-14.7 µg/mL) as well as *E. coli* (MIC = 0.9-29.4 µg/mL).

Further studies of Müller *et al.* showed the even more promising cystobactamid **861-2** (Figure 1). Progress towards the synthesis of cystobactamid **861-2** and other cystobactamids will be presented.

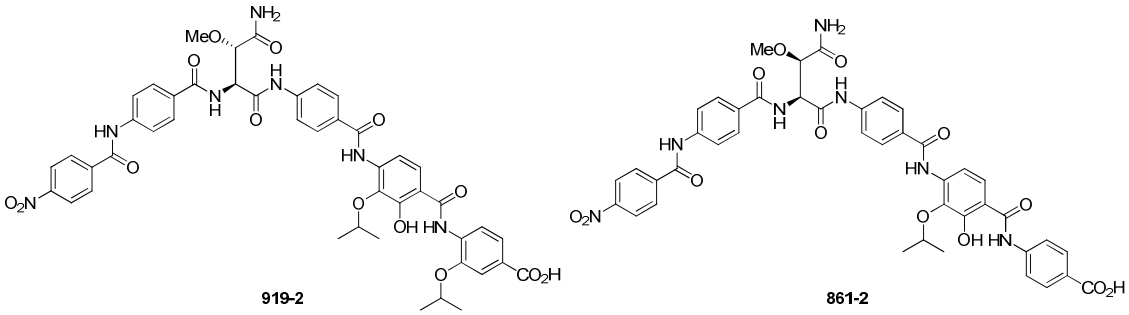

Figure 1: Structure of Cystobactamid 861-2 and 919-2.

References:

1. S. Baumann, J. Herrmann, R. Raju, H. Steinmetz, K. I. Mohr, S. Hüttel, K. Harmrolfs, M. Stadler, R. Müller, *Angew. Chem. Int. Ed.* **2014**, *53*, 14605 – 14609.

The Effect of Water on the Aromatic Claisen Rearrangement under High Pressure and High Temperature Conditions under Flow Conditions

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The application of water in organic synthesis bears several advantages such as cost issues, safety and environmental concerns. There is an increasing interest to use water in industrial processes.[1] Water displays unique reactivity patterns such as acceleration of reaction rates of organic reactions.[2] The suspension of conventional organic solvents in water under high temperature and high pressure conditions removes the phase boundary. The usage of inductive heating can overcome problems like low solubility and it allows very rapid heating.[3] Pressure stable reactors can inductively be heated and used for rapid phase transfer reactions with high mass transfer.

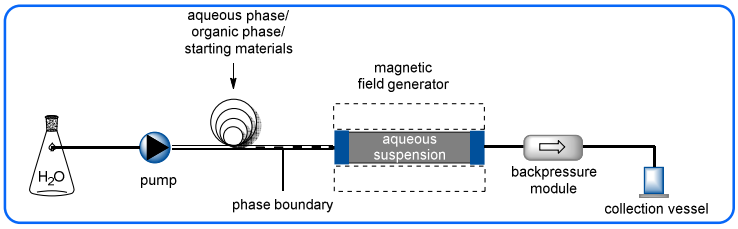

Figure 2: Inductively heated used flow system.

First experiments have shown that water could have an impact of organic reactions.[4]
The aromatic Claisen rearrangement offers a useful synthetic way for the synthesis of building blocks, biologically active compounds and natural products. In the synthesis of the marine sesquiterpene (-)-aplysin and antihypertensive reagent (*S*,*R*,*R*,*R*)-nebivolol the aromatic *ortho* Claisen rearrangement was used as a key step.[5]
With a resistant and reliable system in hand the allylation as well as the following Claisen rearrangement of allyl phenyl ether derivatives with electron-withdrawing groups (with water as reaction media) were investigated under flow conditions. The fluorine derivative with the strongest electron-withdrawing groups shows under flow condition in water an excellent yield (89%), which could not reached under the same conditions in dry toluene (~24%). For comparison the experiments are also done under batch conditions. In all cases no full conversation (max. 54%) was detected after 4h treatment by microwave radiation.

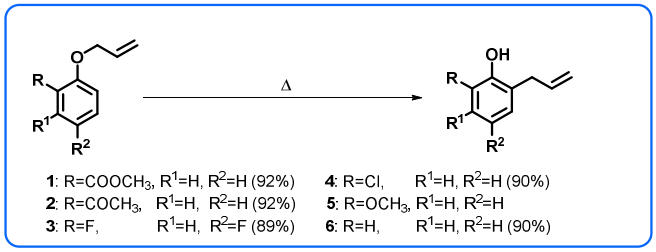

Figure 3: Synthesized derivatives in water under flow conditions.

References:

1. a) F. M. Kerton, R. Marriott, *Alternative Solvents for Green Chemistry* RSC, Croydon, **2013**; b) U. M. Lindstrom, *Chem. Rev.* **2002**, *102*, 2751; c) P.A. Grieco, *Organic Synthesis in Water*, Blackie, London, **1998**. 2. S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2005**, *44*, 3275. 3. a) J.Hartwig, S. Ceylan, L. Kupracz, L. Coutable, A. Kirschning, *Angew. Chem. Int. Ed.* **2013**, *52*, 9813-9817; b) J. Hartwig, L. Kupracz, A. Kirschning, *Chem. Lett.* **2012**, *41*, 562-570; c) P. E. Savage, S. Gopalan, T. I. Mizan, C. J. Martino, E. E. Brock, *AIChE* **1995**, *41*, 1723. 4. J. Hartwig, A. Kirschning, *Chem. Eur. J.* **2016**, *22*, 3044-3052. 5. A. M. Martin Castro, *Chem. Rev.* **2004**, *104*, 2939.

Enzymatic Stereoselective Alcoholysis of *rac*-Lactide.

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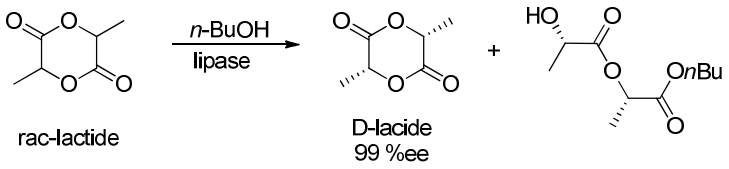
The biodegradable polymers based on lactic acids with steadily increasing applications deserve more effective methods for the manufacturing of both enantiomers of this important α-hydroxyacid. Since a couple of years, there is a large need for chirally pure (*R*,*R*)-lactide especially as a monomer for PDLA or as a co-monomer for polymerization with L-lactide since stereo block copolymers show some special material properties in comparison to homochiral PLLA. Currently poly-L-lactic acid (PLLA) is dominating the market. Whilst L-lactic acid is readily available via fermentation of biomass in large quantities, the production of D-lactic acid is rather difficult and expensive.

(*R*,*R*)-Lactide is produced traditionally from (*R*)-lactic acid by the same procedure as (*S*,*S*)-lactide. Besides numerous biochemical methods there are also some chemical approaches for the production of enantiopure (*R*)-lactic acid with excellent stereoselectivities >99%ee.[1] Nevertheless (*R*)-lactic acid remains expensive starting material up to now. It should be also noted that production of enantiopure lactides via thermal tin-catalyzed cyclisation of corresponding oligolactic acids has certain drawback. The epimerisation of stereocenter takes place under these conditions that leads to the formation of *meso*-compound and even significant decrease of enantiopurity.[2] More advantageous seems to be the use of *rac*-lactide as a starting material. Since this compound is readily available in bulk and to the fair price. *rac*-Lactide is also available via base or frustrated Lewis pair mediated racemisation of corresponding *meso*-lactide.[3]
The preparation of the enantiomerically pure (*R,R*)-lactide (>99 %ee) on the gram scale by alcoholysis of rac-lactide in the presence of immobilized lipase was developed.[4] The synthesis of enantiopure lactide by this method is advantageous over traditional preparation via thermal tin-catalysed cyclisation of corresponding oligolactic acids, since the reaction temperature are much lower. That results that no meso-lactide is formed. The alcoholysis of rac-lactide with n-BuOH was studied in the presence of various enzymes in different solvent systems **(Scheme 1).**



Scheme 1. Alcoholysis of *rac*-lactide with *n*-BuOH.

References:

1. Shuklov, I. A., Dubrovina N. V., Kühlein K., Börner A. *Adv. Synth. Cat.* **2016**, 3910**.**
2. a) Shuklov, I. A., Dubrovina N. V., Kühlein K., Börner A. *Tetrahedron Lett.* **2011**, *52*, 1027; b) Zhu J.-B. ,Chen ., E. Y.-X. *J. Am. Chem. Soc.* **2015**, *137*, 12506.
3. Noda M., Okuyama H. *Chem. Pharm. Bull*. **1999**, *47*, 467.
4. Shuklov I. A., Shuklov A.D., Dubrovina N.V., Kühlein K., Börner A. *Pure Appl. Chem.* **2017***,* submitted*.*

Towards the Synthesis of Unnatural Biomolecules via Novel Asymmetric Conjugate Additions

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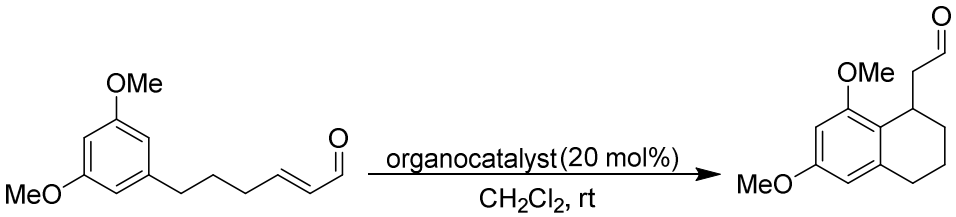
The resorcinol system is present in a variety of natural products known to have therapeutic effects against diseases including Alzheimer's and Huntingdon's disease.[1] The structural motif is particularly prevalent in cannabinoid systems which are found in the cannabis plant. The medicinal utility of these systems has led to the development of multiple cannabinoid-derived medications such as Nabilone and Sativex.[2] For these reasons, the design of an enantioselective method for the construction of resorcinol derivatives holds importance for the synthesis of bioactive natural products and medicines.

The Friedel-Crafts alkylation is one of the most useful methods for the generation of a new carbon-carbon bond and has been exploited across industry and academia.[3] During the last decade or so, organocatalysts have been used to promote this transformation in an enantioselective fashion; however successful examples are typically limited to pyrroles, indoles and furans.[4] This creates a need to develop novel asymmetric Friedel-Crafts reactions of electron-rich arenes and in particular examples including resorcinol derivatives.

An enantioselective intramolecular Friedel-Crafts cyclisation reaction of a resorcinol derived α,β-unsaturated aldehyde has been developed promoted by organocatalysis (Scheme 1). The method affords access to chiral synthetically useful analogues of cannabinoid systems.



Scheme 1 Enantioselective intramolecular Friedel-Crafts reaction

Acknowledgements: We thank the Biotechnology and Biological Sciences Research Council for financial support

References:

1. O. Aizpurua-Olaizola, U. Soydaner, E. Öztürk, D. Schibano, Y. Simsir, P. Navarro, N. Etxebarria and A. Usobiaga, *J. Nat. Prod.*, 2016, **79**, 324–331
2. G. a Thakur, R. Tichkule, S. Bajaj and A. Makriyannis, *Expert Opin. Ther. Pat.*, 2009, **19**, 1647–1673.
3. M. Bandini, A. Melloni and A. Umani-Ronchi, *Angew. Chemie Int. Ed.*, 2004, **43**, 550–556.
4. L. Hong, L. Wang, W. Sun, K. Wong and R. Wang, *J. Org. Chem.*, 2009, **74**, 6881–6884.

Vancomycin/D-Ala-D-Ala Interaction: a New Strategy to Obtain Artificial Imine Reductases

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Dalbapeptides, such as vancomycin, teicoplanin, ristocetin, are known for their strong antibacterial activity due to their interaction with D-Ala-D-Ala dimer in the terminal chain of bacterial cell wall peptidoglycan. This interaction has a low dissociation constant (K_D = ~10^{-17} M),[1]and for this reason could represent an innovative alternative to the classical biotin/(strept)avidin second sphere coordination system and to artificial metallo-enzymes.[2] In this system, indeed, the source of chirality stems from the presence of the aminoacidic chain, but also from the atropoisomerism induced by the restricted rotation around the aryl-aryl bonds present in dalbapeptides, a substantial feature of their structure.[3] In particular, our attention was focused on the synthesis of hybrid metal catalysts with various functionalized ligands bearing the dimer D-Ala-D-Ala at the *N*-terminal position. (Figure 1) The so obtained metallo-enzymes have been employed in the stereoselective reduction of the salsolidine precursor, a cyclic imine used as standard substrate under ATH reaction conditions.

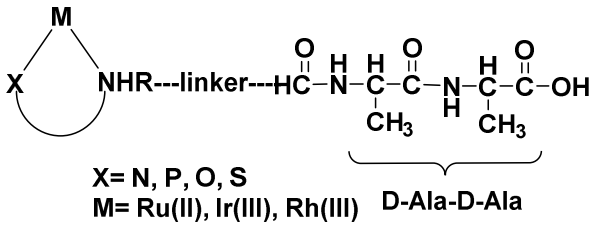

Figure 1: Structure of hybrid catalysts bearing the dimer D-Ala-D-Ala

References:

1. J. Rao, J. Lahiri, L. Isaacs, R. M. Weis, G. M. Whitesides, *Science* **1998**, *280*, 708-711.
2. M. Pellizzoni, G. Facchetti, R. Gandolfi, M. Fusè, A. Contini, I. Rimoldi, *ChemCatChem* **2016**, *8*, 1665-1670.
3. M. Cheng, Z. M. Ziora, K. A. Hansford, M. A. Blaskovich, M. S. Butler, M. A. Cooper, *Org. Biomol. Chem.* **2014**, *12*, 2568-2575.

Dynamic Kinetic Resolution of Calchones by Chemo- and Bio-Catalytic Approach

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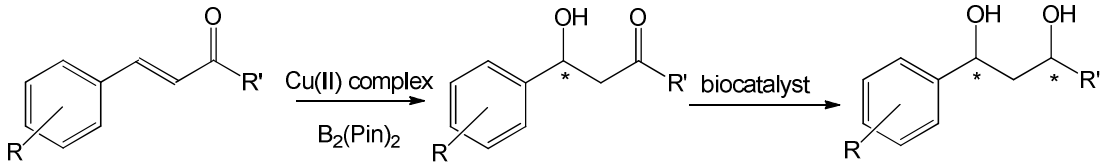
Asymmetric transition-metal catalysts and enzymes have emerged as the most effective synthetic stereoselective tools for the preparation of many chiral compounds. The possibility to exploit different catalytic approaches for enantio- and diasteroselective catalysis has been one of the most challenging topics in chemical synthesis, especially when the control of multiple stereogenic centers is involved.[1] Combining transition-metal homogeneous catalysis with the use of enzymes in a cascade reaction applied to the reduction of differently substituted α,β-unsaturated carbonyl compounds [2], a keto-alcohol and a diol have been obtained by dynamic kinetic resolution (DKR). To enhance catalytic performances, Cu(II) complexes [3] bearing tripodal ligands based on cycloalkyl-fused pyridines have been successfully employed in the asymmetric catalytic boron conjugate-addition leading to the keto-alcohol in an enantiomerically enriched form. A subsequent step involving the use of whole cells *Rhodotorula rubra* MIM147[4] allowed the reduction of the *S*-keto-alcohol substrate to the corresponding diol in high e.e. (97% *SS*), leaving the unreacted *R*-keto-alcohol in 98% e.e..



Scheme 1: Dynamic kinetic resolution (DKR) of calchones.

References:

1. R. Millet, A. M. Träff, M. L. Petrus, J.-E. Bäckvall, *J. Am. Chem. Soc.* **2010**, *132*, 15182-15184.
2. L. Zhu, T. Kitanosono, P. Xu, S. Kobayashi, *Chem. Commun.* **2015**, *51*, 11685-11688.
3. D. Zerla, G. Facchetti, M. Fuse, M. Pellizzoni, C. Castellano, E. Cesarotti, R. Gandolfi, I. Rimoldi, *Tetrahedron: Asymmetry* **2014**, *25*, 1031-1037.
4. I. Rimoldi, G. Facchetti, D. Nava, M. L. Contente, R. Gandolfi, *Tetrahedron: Asymmetry* **2016**, *27*, 389-396.

A Novel Organocatalytic Synthesis of ɣ-Amino Acid Precursors

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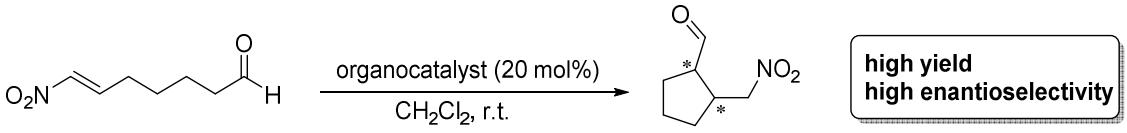
Unnatural γ-amino acids are interesting tools for drug discovery. They can treat neurological disorders, such as epilepsy, anxiety and neurological pain.[1] These systems also have very interesting synthetic potential as monomeric building blocks of peptidomimetic foldamers which may regulate several biological functions through the modulation of protein-protein interactions (e.g. anti-Alzheimer properties).[2]

Due to the biological importance of these compounds, this project focuses on the synthesis of enantiopure cyclic γ-amino acids via a novel intramolecular Michael addition assisted by organocatalysis.

Asymmetric organocatalysis has become one of the major categories in asymmetric synthesis. It is a proficient method for accelerating the rate of the reactions using exclusively organic molecules and to obtain selectively single enantiomers, which are essential for biological purposes.[3]

A variety of organocatalysts have been tested to optimize a fascinating 5-exo-trig cyclisation developed in order to achieve the targeted 5-membered ring in high enantioselectivity (**Scheme 1**). Enamine catalyzed processes present high yields and high rate of the reaction, however combining enamine catalysis with H-bond directing activation has given the best results in terms of enantioselectivity. As a result, an intramolecular synthesis of cyclic ɣ-amino acid precursors has been established, and a method which provides high enantioselectivity has been successfully developed.



Scheme 1: 5-exo-trig intramolecular cyclisation assisted by organocatalysis.

Acknowledgements: We thank King's College London and the University of Reading for financial support.

References:

1. a) Silverman, R. B.; Andruszkiewicz, R.; Nanavati, S. M.; Taylor, C. P.; Vartanian, M. G., *J. Med. Chem.* **1991,** *34* (7), 2295-2298; b)Tassone, D. M.; Boyce, E.; Guyer, J.; Nuzum, D., *Clin. Ther.* **2007,** *29* (1), 26-48.

2. a) Gellman, S. H. *Acc. Chem. Res.*, **1998**, *31*, 173–180 b) Pelay-Gimeno, M. *et al. Angew. Chem. Int. Ed.* **2015**, *54*, 8896 – 8927 c) Mándity, I. M. ; Fülöp, F. *Expert Opin. Drug Discov.* **2015**, *10*, 1163-1177.

3. a) Dalko, P. I.; Moisan, L. *Angew. Chem. Int. Ed.* **2004**, *43*, 5138-5175; b) Giacalone, F.; Gruttadauria, M.; Agrigento, P.; Noto, R. ***Chem. Soc. Rev.*, 2012**, ***41***, 2406-2447**.**

Regioselective Thiocarbonylation of Vinyl Arenes

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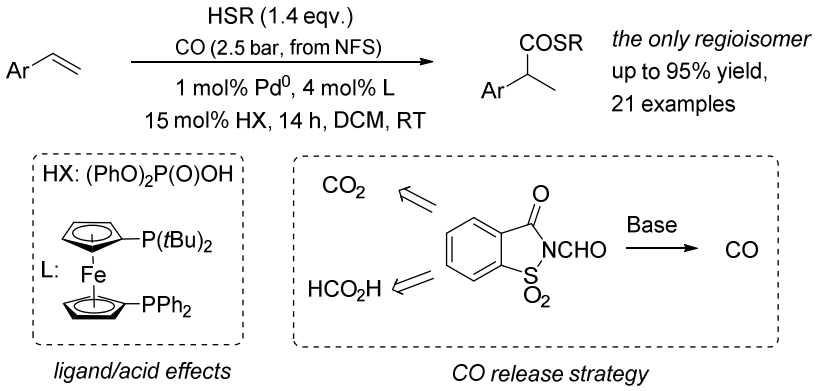
Thioesters are valuable synthetic intermediates in bioorganic chemistry and preparative organic chemistry.[1] They serve as more selective synthetic equivalents to acyl chlorides and give access to carboxylic acid derivatives, acyl alkynes and heterocycles. Moreover, they are employed as starting materials in the Pd-catalyzed Fukuyama- and Liebeskind Srogl cross-coupling reactions to give ketones.[2] Alkene thiocarbonylation presents an atom-economic route to thioesters, which are normally prepared from the corresponding carboxylic acids *via* active esters. The only available reports of hydrothioesterification of alkenes concern the transformation of allenes or vinylcyclopropanes at 100 °C with a CO pressure of 27 bar and Pd-loadings from 3-5 mol%.[3] Thus, we investigated the hydrothioesterification reaction and found a mild (2.5 bar CO pressure, RT) and regioselective catalyst system for the conversion of alkenes to thioesters by using a combination of GC-FID-enabled optimization, exploration of substrate scope as well as deuteration and competition experiments (**Scheme 1**).[4] We coupled the new catalyst system to a safe CO release strategy we recently reported, using a two-chamber system with *N*-formylsaccharin as a recyclable ex situ CO source.[5] As opposed to reported alkoxycarbonylations,[5] we could achieve highly branched-selective hydrothioesterifications of *ortho*-substituted terminal vinylarenes, which questions the contribution of η^3-benzylpalladium species to such selectivity. The possibility to select a terminal vinyl group over an internal olefin by use of the bidentate ferrocenylphosphine dppdtbpf could be employed in chemoselective transformations of compounds containing several alkene functionalities.



Scheme 1: Branched-selective thiocarbonylation of vinyl arenes to give thioesters under mild conditions.

Acknowledgements: This work was supported by the Fonds der Chemischen Industrie (Liebig fellowship, I.F. and PhD fellowship, V.H.) and the Institutional Strategy of the University of Tübingen (DFG, ZUK63).

References:

1. Cremlyn R.J., *An Introduction to Organosulfur Chemistry*, Wiley-VCH, Weinheim, **1996**. 2. a) Fukuyama T. *et al*., *Tetrahedron Lett.* **1998**, 39, 3189 b) Liebeskind L., Srogl J., *J. Am. Chem. Soc.* **2000**, 122, 11260. 3. a) Alper H. *et al., J. Org. Chem.* **1998**, 63, 2609. b) Alper H. *et al., J. Org. Chem.* **2009**, 74, 888. 4. Hirschbeck V., Gehrtz P.H., Fleischer I., *J. Am. Chem. Soc.* **2016**, 122, 11260. 5. Gehrtz P.H., Hirschbeck V., Fleischer I., *Chem. Comm.*. **2015**, 51, 12574.

Conversion of Biomass Catalyzed by Oxo-molybdenum and Oxo-rhenium Complexes

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With growing concerns about the issues of the exhaustion of fossil fuel resources and increased environmental concerns, it is quite necessary to develop and utilize renewable resources. Carbohydrates derived from biomass are one of the most abundant renewable resources and possess a great potential as raw materials to product fuels and added value chemicals.
In continuation of our work using oxo-molybdenum and oxo-rhenium complexes as catalysts for the deoxygenation of organic compounds,[1,2] in this communication we describe the efficient and selective conversion of carbohydrates into ethyl levulinate (EL), 5-ethoxymethylfurfural (EMF), 5-hydroxymethylfurfural (HMF) and levulinic acid (LA) catalyzed by oxo-molybdenum or oxo-rhenium complexes in good to excellent yields (Figure 1).[3]

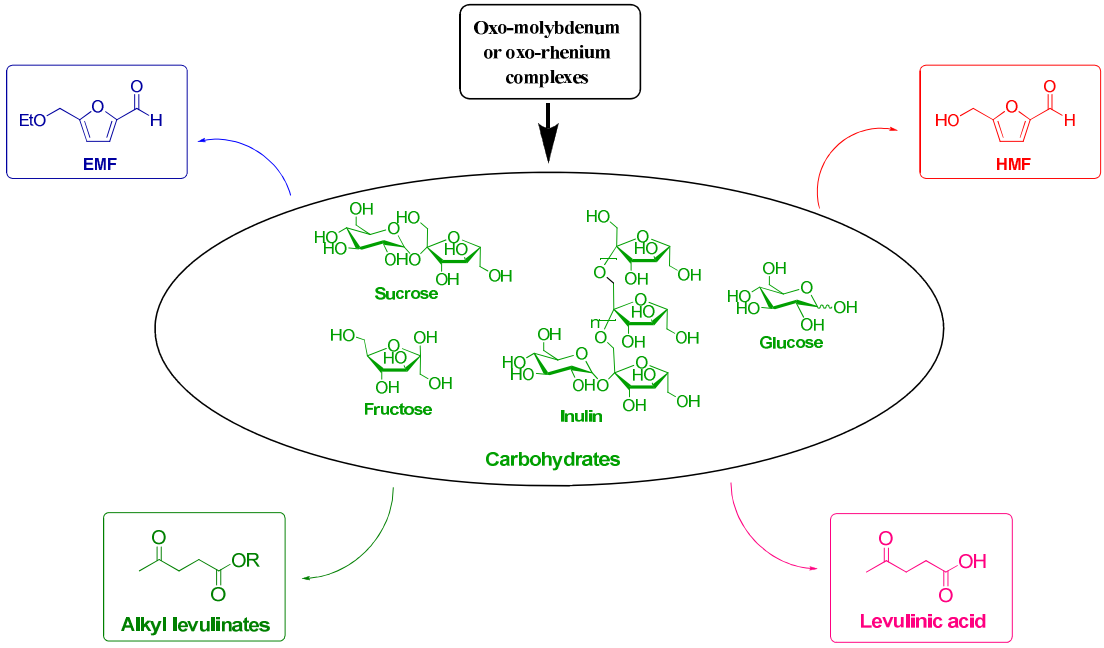

Figure 1: Conversion of carbohydrates catalyzed by oxo-molybdenum and oxo-rhenium complexes

Acknowledgements: The authors thank the project UID/QUI/00100/2013 and the Portuguese NMR Network (IST–UTL Center) for providing access to the NMR facilities. Sara Sousa and Joana Bernardo (SFRH/BD/90659/2012) thank FCT for grants and ACF (IF/00849/2012) acknowledges FCT for the "Investigador FCT" Program.

References:

1. Sousa S. C. A.; Fernandes A. C. *Coord. Chem. Rev.* **2015**, *284*, 67.
2. Bernardo, J. R.; Fernandes, A. C. *Green Chem.* **2016**, *18*, 2675.
3. Pereira, J. G.; Sousa, S. C. A.; Fernandes, A. C. *ChemistrySelect* **2017**, accepted. (DOI:10.1002/slct.201700807).

f-Block Complexes Supported by a Chelating Bis(aryloxide) Ligand: Synthesis and Reactivity with Nitrogenous Bases

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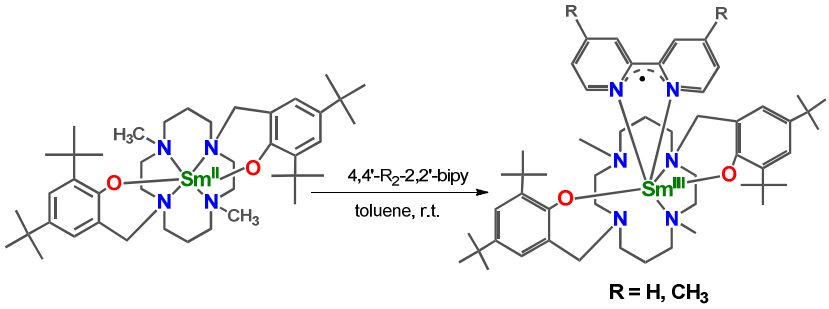
Low-valent uranium compounds have earned considerable attention because of their ability to reduce and activate small molecules and to accommodate multi-electron-transfer processes.[1] The use of Sm(II) complexes in small molecule activation is less developed, however, Sm^{2+} (Sm^{3+}/Sm^{2+}, $E_{1/2}$ = −1.55 V) is highly used as a reductive source of single electron in organic transformations, including the reduction of unsaturated chemical bonds.[2]

The new dianionic ligand {(^{tBu2}ArO)$_2$Me$_2$-cyclam}$^{2-}$, featuring two aryloxide donors and a tetraazamacrocycle, has been used to prepare the U(III) compound [U{(^{tBu2}ArO)$_2$Me$_2$-cyclam}I] and the Sm(II) compound [Sm{(^{tBu2}ArO)$_2$Me$_2$-cyclam}].[3,4] The reaction of the U(III) compound with azobenzene conducted to the four electron reduction of the N=N bond, with formation of the U(VI) bis-imido complex [U{(^{tBu2}ArO)$_2$Me$_2$-cyclam}(NPh)$_2$}], while the reaction of the Sm(II) compound conducted to the formation of a mixture of Sm(III) species, with the isolation of a few crystals of a Sm(III) compound with a reduced azobenzene ligand [Sm{(^{tBu2}ArO)$_2$Me$_2$-cyclam}(PhNN(H)Ph)}]. The compound [Sm{(^{tBu2}ArO)$_2$Me$_2$-cyclam}].is able to reduce bipyridine ligands with the formation of Sm(III) complexes with a bipyridine radical ligand (Scheme 1). The uranium compound showed no evidence of reduction of bipyridine ligands in absence of an additional reducing agent, nevertheless the reductive studies showed that both compounds can reduce pyrazine.

The results indicate the potential usefulness of the U(III) and Sm(II) compounds in electron transfer reactions, and led us to explore the reduction of other unsaturated organic substrates.



Scheme 1

Acknowledgements: We thank the Fundação para a Ciência e a Tecnolgia for financial support through the grant SFRH/BPD/101840/2014 and the projects UID/Multi/04349/2013 and RECI/QEQ-QIN/0189/2012.

References:

1. Liddle, S. T., *Angew. Chem., Int. Ed.* **2015**, *54*, 8604.
2. Szostak, M. S.; Procter, D. J. *Angew. Chem. Int. Ed.* **2012**, *51*, 9238.
3. Maria, L.; Santos, I. C.; Sousa, V. R.; Marçalo, J. *Inorg. Chem.* **2015**, *54*, 9115.
4. Maria, L.; Soares, M.; Santos, I. C.; Sousa, V. R. ; Mora, E.; Marçalo, J.; Luzyanin, K. V. *Dalton Trans.* **2016**, *45*, 3778.

Poly(methacrylate)s with POSS Moieties – Synthesis and Characterization

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Polyhedral oligosilsesquioxanes (POSS) with the empirical formula $RSiO_{1.5}$ are one of the most intriguing examples of well-defined, nanostructured moieties for the construction of high-performance, hybrid polymers. Among various types of POSS monomers, the most promising one is a cubic-octameric framework with a single polymerizable vinyl group, leading to the linear processable polymers via ionic or radical polymerization.[1]

The first POSS-based polymers described in the literature were poly(methacrylate)s obtained by the conventional free radical polymerization (FRP) of (c-C_5H_9)$_7$POSS-(CH_2)$_3$-MA and (c-C_6H_{11})$_7$POSS-(CH_2)$_3$-MA. The molecular weights of the resulted poly((c-C_5H_9)$_7$POSS-(CH_2)$_3$-MA) and copolymer (c-C_5H_9)$_7$POSS-(CH_2)$_3$-MA-co-(c-C_6H_{11})$_7$POSS(CH_2)$_3$-MA reached $M_{n,GPC}$=117,000 (M_w/M_n=1.9) and $M_{n,GPC}$=147,000 (M_w/M_n=2.55), respectively, indicating that POSS-MA monomers can be readily polymerized. Due to their unique structures and high thermal stability (up to ca. 400 °C), the interest in such systems has arisen instantly; however, all further works employing FRP (in bulk or solution) provided only low MW macromolecules.[1]

Since high MW polymers with different types of POSS moieties could strongly enhance their mechanical and thermal properties, or facilitate self-assembly of block copolymers, we decided to use POSS-methacrylates with various linkers and inert substituents bonded to silicon-oxygen cube and investigate the possibility of the formation of poly(R_7POSS-(Y)-MA)s with high polymerization degree by atom transfer radical polymerization (ATRP). In this communication, we present the results of our studies which concern both synthetic methods as well as characterization of obtained polymers.[2]

Acknowledgments: The authors acknowledge the financial support from The National Centre for Research and Development - PBS3/A1/16/2015; and Foundation for Polish Science - START Programme.

References:

1. a) Cordes D. B., Lickiss P. D., Rataboul F. *Chem. Rev.* **2010**, *110*, 2081. b) Zhang W., Müller A. H. E. *Prog. Polym. Sci.* **2013**, *38*, 1121. c) Hussain H., Shah S. M. *Polym. Int.* **2014**, *63*, 835. d) Zhang Z., Zhang P., Wang Y., Zhang W. *Polym. Chem.* **2016**, *7*, 3950. e) Ullah A., Ullah S., Khan G. S., Shah S. M., Hussain Z., Muhammad S., Siddiq M., Hussain H. *Eur. Polym. J.* **2016**, *75*, 67.
2. a) Franczyk A., Burdyńska J., He H., Hui C. M., Matyjaszewski K., Marciniec B. *ACS MacroLett.* **2014**, *3*, 799. b) Alexandris S., Franczyk A., Papamokos G., Marciniec B., Matyjaszewski K., Koynov K., Mezger M., Floudas G. *Macromolecules* **2015**, *48*, 3376.
c) Alexandris A., Franczyk A., Papamokos G., Marciniec B., Graf R., Matyjaszewski K., Koynov K., Floudas G. *Macromolecules* **2017**, *50*, 4043.

Nanometer-sized Alkenyl-silsesQuioxanes and Spherosilicates – Synthesis and Characterization

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Alkenyl-substituted polyhedral oligomeric silsesquioxanes and spherosilicates are among the most intriguing examples of well-defined, nanostructured building blocks for the synthesis of novel, high-performance, hybrid materials.[1] They are characterized by a unique, three-dimensional structure which is based on inorganic core surrounded by organic functional groups. Additionally, the presence of unsaturated double bonds in the structure makes them highly reactive in a number of commonly used in organic synthesis reactions such as addition processes, Suzuki, Heck or Sonogashira reactions etc. Mentioned transformations can lead to the formation of derivatives with conjugated π-bonds, often used as components for the preparation of organic or polymer light-emitting diodes (OLED, PLED). It has been established that the attachment of silsesquioxane as a pendant group onto conjugated polymers provides materials with improved color stabilities, higher brightness, and improved quantum efficiencies, compared with parent polymers that do not bear silsesquioxane groups.[2]

In the communication, we report our studies on the hydrosilylation of a wide spectrum of terminal and internal alkynes with alkyl, aryl as well as heteroatom-containing substituents with monofunctional silsesquioxane ($(HSiMe_2O)(i\text{-}Bu)_7Si_8O_{12}$) and octafunctional spherosilicate ($(HSiMe_2O)_8Si_8O_{12}$). By the developed method, a series of new alkenyl-silsesquioxanes and spherosilicates were obtained in high yields and fully characterized. Moreover, detailed research on the optimization of the reaction conditions concerning uses of homogeneous catalysts as well as conventional organic solvents and compressed or supercritical CO_2 will be also discussed.

Acknowledgments: The authors acknowledge the financial support from The National Centre for Research and Development - PBS3/A1/16/2015 and Lider Programme No. LIDER/26/p527/L-5/13/NCBR/2014.

References:

1. a) Li G., Wang L., Ni H., Pittman Jr. C. U. *J. Inorg. Organomet. Polym.* **2001**, *11*, 123. b) Cordes D. B., Lickiss P. D., Rataboul F. *Chem. Rev.* **2010**, *110*, 2081.
2. Chan K. L., Sonar P., Sellinger A. *J. Mater. Chem.* **2009**, *19*, 9103.

Aerobic Oxidation of Lignin Model Compound Catalyzed by a $VO(acac)_2$/triazole System

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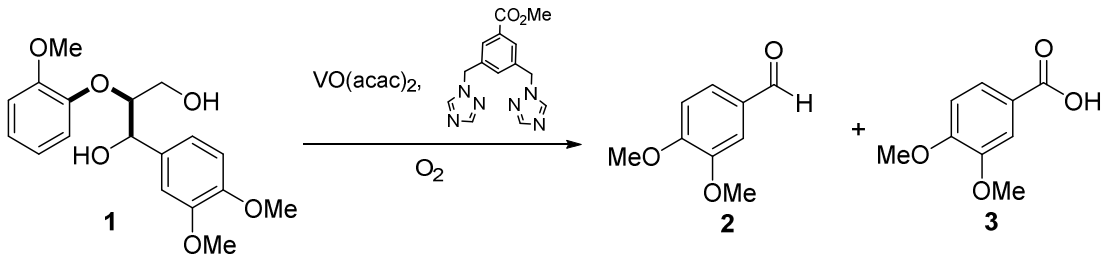
In a world aware of environmental issues, finding renewable sources of energy and chemicals has become a priority. The use of biomass for that purpose is an obvious and attractive option. Lignin is one of the most abundant components of biomass and, therefore, the development of methods for its transformation into valuable aromatic chemicals has attracted broad attention in recent years.[1] Lignin is a natural aromatic polymer produced by random polymerization of oxyphenylpropane units by C-O-C bond linkages. A methodology for breaking the ether bonds of its structure would constitute a good way of depolymerizing. Among other strategies for achieving this goal, the oxidative cleavage of lignin or model compounds has emerged as a promising strategy.[2]

Recently, we have found that very low amounts of vanadyl acetylacetonate and a triazole based pincer type ligand system catalyses aerobic oxidative debenzylation of ethers in green media.[3] We dediced to evaluate this catalytic system in the aerobic oxidative cleavage of lignin. Since lignin is a structurally complex polymer we prepared 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol **1** (Scheme 1), a model that contains the β-O-4 linkage present in the natural polymer, in order to use it as substrate in oxidative cleavage assays. In this communication, we wish to report our preliminary results on this matter.



Scheme 1: Aerobic oxidative cleavage of lignin model catalyzed by a vanadyl acetylacetonate/bis-triazolyl ligand system.

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References:

1. See for example: a) Calvo-Flores, F. G.; Dobado, J. A. *ChemSusChem*, **2010**, *3*, 1227. b) Bozell, J. J. *Top. Curr. Chem.*, **2014**, *353*, 229. c) Xu, C. P.; Arancon, R. A ; Labidi, J.; Luque, R. *Chem. Soc. Rev.*, **2014**, *43*, 7485. d) Li, C. Z.;. Zhao, X. C; Wang, A. Q.; Huber, G. W.; Zhang, T. *Chem. Rev*. **2015**, *115*, 11559.
2. a) Zakzeski, J.; Bruijnincx, P. C. A.; Jongerius, A. L.; Weckhuysen, B. M.. *Chem. Rev*. **2010**, *110*, 3552. b) Deuss, P. J.; Barta, K.; de Vries, J. G. *Catal. Sci. Technol*. **2014**, *4*, 1174. c) Rinaldi, R.; Jastrzebski, R.; Clough, M. T.; Ralph, J.; Kennema, M.; Bruijnincx, P. C. A.; Weckhuysen, B. M. *Angew. Chem., Int. Ed*. **2016**, *55*, 8164. d) Kärkäs, M. D.; Matsuura, B. S.; Monos, T. M.; Magallanes, G.; Stephenson, C. R. *Org. Biomol. Chem*. **2016**, *14*, 1853.
3. Urgoitia, G.; SanMartin, R.; Herrero, M.T.; Dominguez, E. *Adv. Synth. Catal*. **2016**, *358*, 3307.

Amine Exchange Reactions for the Synthesis of *N*-substituted 4-Quinolones

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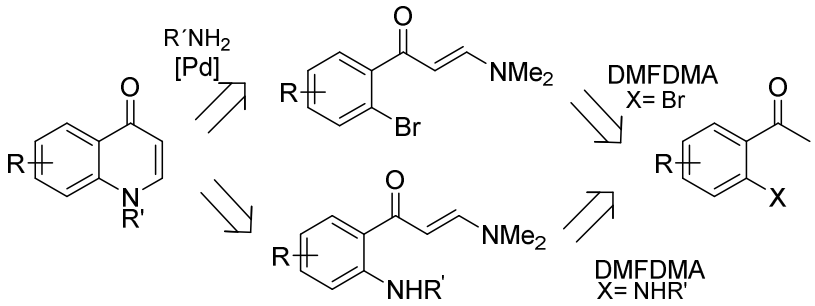
The quinolinone moiety is present in many natural products as well as in synthetic compounds with diverse pharmacological properties.[1] Traditional methods to synthesize quinolinone skeleton such as Gould–Jacobs reaction or Conrad-Limpach synthesis need harsh reaction conditions to effect final cyclization and show poor regioselectivity.[2] In recent years, synthetic methods based on amine exchange of enaminoketones have allowed much milder reaction conditions and better regioselectivities.[4] The reaction of enaminoketones with amines results, through an amine exchange reaction, in the formation of new enaminoketones that may, if they are suitably functionalized, undergo a cyclization reaction.

Taking advantage of our previous experience in this subject[3] we designed two simple synthetic routes for the access to *N*-aryl and *N*-benzylsubstituted 4-quinolones, potential precursors of more complex polyheterocyclic systems (Scheme 1). In both pathways, enaminoketones were key intermediates. The two routes differed, however, in the strategy to carry out the *C-N* bond formation leading to the quinolinone core. Herein, we report the most remarkable results obtained.



Scheme 1: Designed pathways to synthesize 4-quinolones FROM 1-aril-3-dimetilamino-2-propen-1-ones

Acknowledgements: We thank Basque Government (IT-774-13), the Spanish Ministry of Economy and Competitiveness (CTQ2013-46970-P) and the University of the Basque Country (UFI QOSYC 11/12) for financial support. G.U thanks the Basque Government for a postdoctoral scholarship. Finally, technical and human support provided by SGIker of UPV/EHU is gratefully acknowledged.

References:

1. a) Okamoto, N. ; Takeda, K.; Ishikura, M.; Yanada, *J. Org. Chem.* **2011**, *76*, 9139. b) Dhar, T. G. M.; Watterson, S. H.; Chen, P.; Shen, Z.; Gu, H. H. Norris, D.; et al. J .*Bioorg. Med. Chem. Lett.*, **2003**, *13*, 547.
2. See, for example: a) Bunce, R.; Nammalwar, B. *Org. Prep. Proced. Int.* **2010**, *42*, 557. b) G. Hiltensperger, N. G. Jones, S. Niedermeier, A. Stich, M. Kaiser, J. Jung, et al. *J. Med. Chem.* **2012,** *55,* 2538. c) Joule, J. A.; Mills, K. Het. Chem. **2000**, 133.
3. a) Hernández, S.; Moreno, I.; SanMartin, R.; Herrero, M.T.; Domínguez, E. *Org. Biomol. Chem.* **2011,** *9,* 2251. b) Hernández, S.; Moreno, I.; SanMartin, R.; Gómez, G.; Herrero, M.T.; Domínguez, E. *J. Org. Chem.* **2010,** *75,* 434.
4. Wang, F.; Jin, L.; Kong, L.; Li, X. *Org. Lett.* **2017**, *19*, 1812.

Application of an Enzymatic Extract Obtained from *Brassica rapa* L. as Catalyst in Transformation of Aromatic Compounds

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Peroxidases are heme-containing oxidoreductases that have the ability to catalyze the oxidation of organic and inorganic electron donor substrates through a reaction with hydrogen peroxide or organic hydroperoxides.[1] These enzymes have great interest because of their potential applications in the clinical, biochemical, biotechnological, and industrial fields, in the synthesis of useful compounds (*e.g.*, various aromatic chemicals) and especially in bioremediation.[1] The only source of commercial production of peroxidase is the horseradish root (*Armoracia rusticana* P.Gaertn., B.Mey. & Scherb.), however, other cultivated species can also provide peroxidases with similar or better substrate specificities, stability, yield, and economic feasibility.[2] In this work, turnip roots (*Brassica rapa* L.) were chosen as source of peroxidase because they are inexpensive, easily available and the preparation of a peroxidase-rich enzymatic extract is a simple and cheap process, with no prejudice to enzyme activity. The study aimed to the determine optimal working conditions (pH, temperature, stability, resistance to organic solvents) of the enzymatic extract from turnip roots and, subsequently, to apply the extract to the transformation of structurally variated aromatic compounds, namely, phenols and acetophenones, which has never been tested with peroxidase before. The results showed that the turnip peroxidase extract exhibits better activity at pH 4.5 (**Figure 1A**) and at 35º, maintaining stability during 48 h. The extract also maintains considerable stability using DMSO/water (20%) as solvent. The extract also showed the ability to catalyze the quick guaiacol transformation (**Figure 1B, C D**), a well known reaction,[3] used here as control to verify the extract activity when simple phenols are used. The transformations of other substrates were evaluated in terms of yield and products obtained, with the latter being purified by chromatographic methods and structurally characterized by spectroscopic techniques.

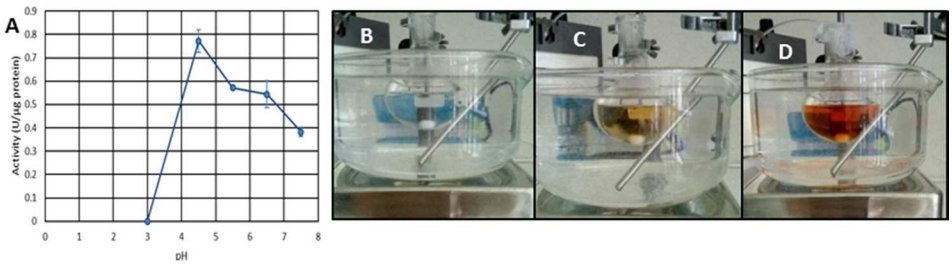

Figure 1: Turnip peroxidase extract as biocatalyst tool: Curve of enzymatic optimal pH conditions (**A**); Development of a reaction using guaiacol catalyzed by the extract at 0 minutes(**B**); 5 min (**C**)**;** 10 min (**D**).

Acknowledgements: This work was financed by Portuguese National Funds, through FCT – Fundação para a Ciência e a Tecnologia, the European Union, QREN, FEDER, COMPETE, by funding the Organic Chemistry Research Unit (QOPNA) (project PEst-C/QUI/UI00062/2013; FCOMP-01-0124-FEDER-037296) and the cE3c centre (project UID/BIA/00329/2013).

References:

1. a) Bansal N.; Kanwar S.S. *Scientific World J*. **2013**, *2013*, 714639. b) Hamid M.; Rehman K. *Food Chem*. **2009**, *115*, 1177.
2. Pandey V.P.; Awasthi M.; Singh S.; Tiwari S.; Dwivedi U.N. *Biochem Anal Biochem*. **2017**, *6*, 308.
3. a) Doerge D.R.; Divi R.L.; Churchwell M.I. *Anal. Biochem*. **1997**, *250*, b) Huixian Z.; Taylor K.E. *Chemosphere*. **1994**, *28*,1807.

Polyhydroxy Chalcones and Flavanones: Synthesis and Evaluation of Their Potential as Antioxidant and Anticholinesterasic Agents

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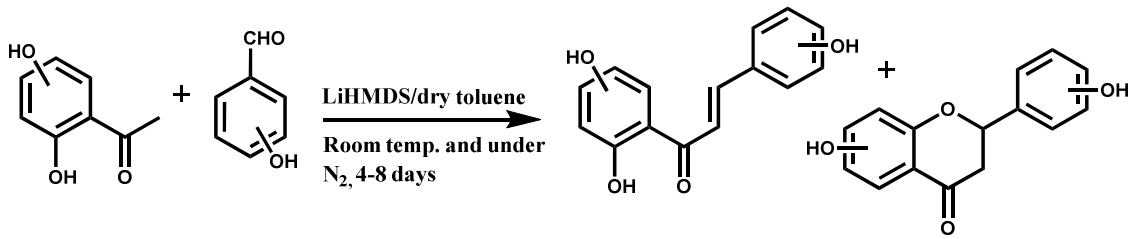
Chalcones are one of the most important classes of natural products across the plant kingdom, belonging to the flavonoids family.[1] They have a wide range of pharmaceutical and industrial applications and are key precursors in the other flavonoids biosynthesis as well as in the synthesis of many biologically valuable heterocyclic compounds. Owing to the above stated reasons, the synthesis of chalcones and chalcone based functionalized derivatives had remained primary objectives and so, a number of procedures have been reported for their synthesis, although they are mostly different approaches of an aldol condensation.[2] The synthesis of polyhydroxylated chalcones involve hydroxyl groups protection and cleavage steps consequently the procedures are more expensive. Thus a search for new or improved routes towards the synthesis of polyhydroxychalcones is still a challenge.

On the other hand, acetylcholinesterase (AChE) inhibitors are a class of drugs used in clinic therapy to treat the Alzheimer's disease (AD) symptoms while antioxidants have also an important role in the control of degenerative and aging effects and they are tangled with AD.

In this work, we report for the first time the one-pot synthesis of polyhydroxychalcones using lithium bis(trimethylsilyl)amide (LiHMDS) as base (**Scheme 1**), as well as the compounds characterization by spectroscopic methods (1D and 2D NMR and MS). The radical scavenging activity and AChE inhibitory activities of the pure compounds were assayed by well-known methods.[3] The results showed that the 2',4',4-trihydroxychalcone radical scavenging activity is similar to the one observed with quercetin, a member of the flavonoid family with industrial application as antioxidant. Moreover, chalcones have superior radical scavenging activity than the corresponding flavanones. Some structure/activity relationships will also be discussed. Concerning the anticholinesterasic activity it seems that flavanones are more active than chalcones, maybe due to their affinity with the enzyme active site.



Scheme 1: Proposed one-pot synthesis of polyhydroxychalcones using LiHMDS as base.

Acknowledgements: : This work was financed by Portuguese National Funds, through FCT – Fundação para a Ciência e a Tecnologia, the European Union, QREN, FEDER, COMPETE, by funding the Organic Chemistry Research Unit (QOPNA) (project PEst-C/QUI/UI00062/2013; FCOMP-01-0124-FEDER-037296) and the cE3c centre (project UID/BIA/00329/2013).

References:

1. Ferreyra M.L.F.; Rius S.P.; Casati P. *Front Plant Sci*. **2012**; 3, 222.
2. Bukhari S.N.A.; Jasamai M.; Jantan I.; Ahmad W. *Mini Rev. Org. Chem*. **2013**, *10*, 73.
3. Barreto M.C.; Arruda M.; Rego E.; Gouveia V.; Medeiros, J.; Rainha, N. *In*: Barreto M.C.; Simões, N. (eds.) (**2012**). pp. 65-81.

Visible Light-promoted Activation of Unactivated C(sp^3)–H Bonds and its Selective Trifluoromethylthiolation

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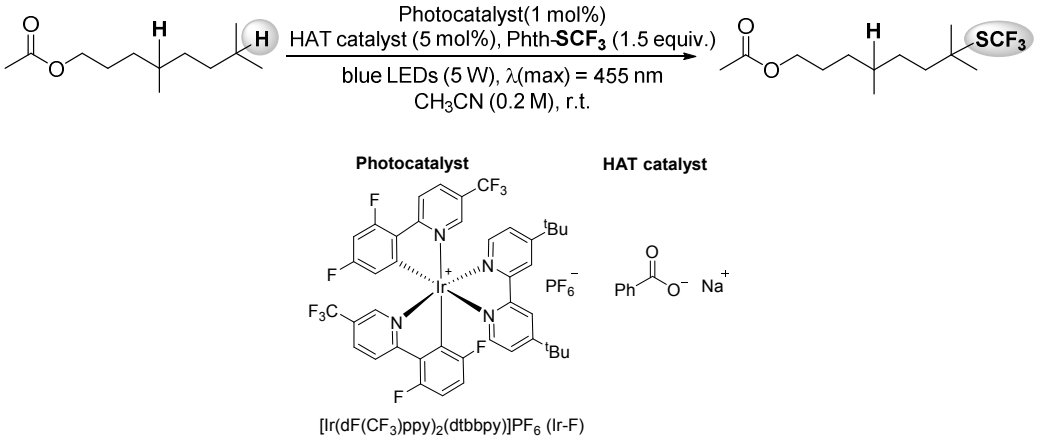
Selective functionalization of ubiquitous C(sp^3)–H bonds using visible light energy is a highly challenging yet desirable goal in organic synthesis. Developments of such processes rely both on rational design and serendipitous discoveries from innovative tools such as screening technologies. Applying a mechanism based screening strategy,[1] we have recently reported photoredox-mediated hydrogen atom transfer (**HAT**) catalysis for the selective activation of otherwise unactivated C(sp^3)–H bonds, followed by its trifluoromethylthiolation,(**Scheme 1)** which has high potential as a late stage functionalization tool. The generality of this method is exhibited through incorporation of the trifluoromethylthio group in a large number of C(sp^3)–H bonds with high selectivity without the need for excess of valuable substrates. [2]



Scheme 1: Selective trifluoromethylthiolation of unactivated C(sp^3)–H bonds

Acknowledgements: We thank the Deutsche Forschungsgemeinschaft (Leibniz Award and SFB 858) and the Humboldt Foundation (B.M.) for generous financial support.

References:

1. Hopkinson, M. N.; Gómez-Suárez, A.; Teders, M.; Sahoo, B.; Glorius, F. *Angew. Chem. Int. Ed.* **2016**, *55*, 4361.

2. Mukherjee, S.; Maji, B.; Tlahuext-Aca, A.; Glorius, F. *J. Am. Chem. Soc.*, **2016**, *138*, *50*, 16200.

Synthesis of a Novel Macrocyclic Compound

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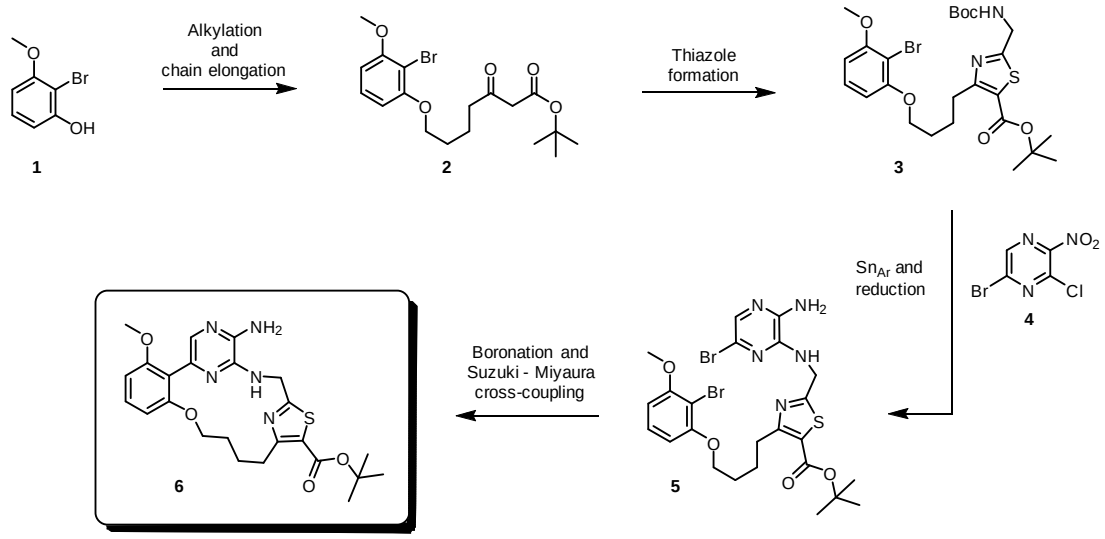
The rising resistance of microbes, particularly Gram-negative (G-) bacteria, to commonly used antimicrobials is a serious threat to human health with possibly grave consequences[1]. To combat the increasing problem various strategies are used. These include synthesis of new compounds and improvement of the efficacy of already known drugs.

We report herein the synthesis of the macrocyclic compound **6** (**Scheme 1**). This work was made within the European consortium ENABLE[2] that stems from the IMI's New Drugs for Bad Bugs (ND4BB) initiative.

The synthesis was carried out starting from phenol **1**, which after alkylation and chain elongation afforded ketoester **2**. Subsequent halogenation, thioamide alkylation and cyclization provided access to aminomethylthiazole **3**. Aminopyrazine moiety was introduced in nucleophilic aromatic substitution of chloropyrazine **4** followed by reduction of nitro group. The macrocyclization was achieved by palladium catalyzed boronation of pyrazyl bromide **5** and intramolecular Suzuki-Miyaura cross coupling which proved to be challenging because of the known unstable nature of pyrazyl boronates[3] and sterically hindered aryl bromide.



Scheme 1: Synthesis of the macrocyclic compound **6**.

References:

1. WHO web page. http://www.who.int/mediacentre/factsheets/fs194/en/ (accessed May 20, 2017).
2. ENABLE web page. https://ww.imi.europa.eu/content/enable (accessed July 19. 2017).
2. Lloyd-Jones, G. C.; Cox, P. A.; Leach, A. G.; Campbell, A. D. *J. Am. Chem. Soc.* **2016**, *138*, 9145.

An Attempt to Access 5-Methyldibenzodiazepines: Further Extension of the Buchwald-Hartwig C-N Coupling Method?

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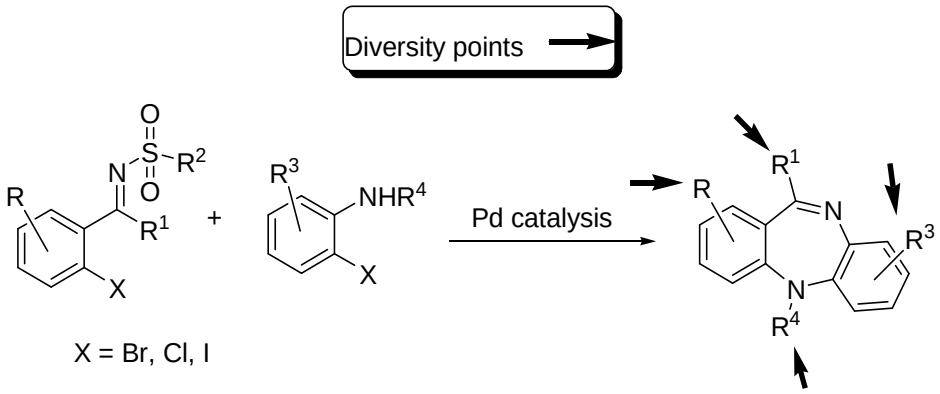
Dibenzodiazepines (DBDAs) are a potent class of pharmaceutical drugs used to treat a variety of mental illness.[1] We developed a new synthetic method for the synthesis of a family of DBDAs employing a one-pot Pd-catalyzed C-N coupling of o-bromoaldimine with o-bromoaniline cyclization which was recently reported.[1,2,3] In this work, our aim was to extend this methodology for the preparation of 5-methyl-DBDAs (**Scheme 1**). A variety of different reactions have been screened, the results of which will be discussed in this preliminary communication.



Scheme 1: Outline of reactions

Acknowledgements: We thank ERASMUS Mundus (EMMAEast 14) program for the support to Xaiza Aniban and the Fundação para a Ciência e a Tecnologia (FCT) through grant UID/QUI/0619/2016 (contributed to CQE-UE) for supporting this work.

References:

1. Peixoto, D.; Locati, A.; Marques, C.S.; Goth, A.; Ramalho, J.P.P.; Burke, A.J. *RSC Adv.* **2015**, 5 (121), 99990-99999.
2. Marques, C.S.; Peixoto, D.; Burke, A.J. *RSC Adv.* **2015**, 5 (26), 20108-20114.
3. Peixoto, D.; Burke, A.J.; WO2016/207790, **22 June 2015.**

Synthesis of 4′-Alkoxy-4-(ω-Cinnamoylalkoxy)azobenzenes and their Thermal Properties

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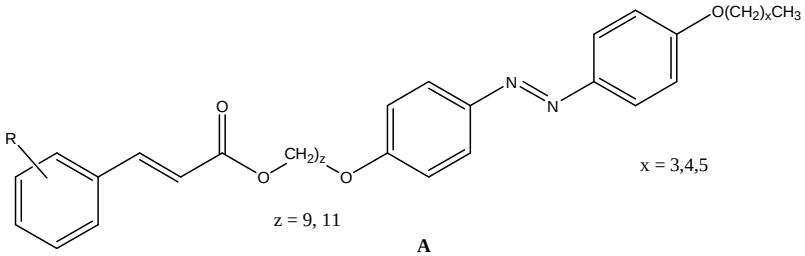
Substituted azobenzenes continue to elicit interest as liquid crystalline materials.[1] In search of new thermotropic, photoswitchable materials, we prepared a number of 4′-alkoxy-4-(ω-cinnamoylalkoxy)azobenzenes (A, Scheme 1). The procedure included *O*-alkylation of 4-nitrophenol, followed by reduction of the nitro group (H_2, Pd/C), diazotization of the aniline with ω-hydroxyalkoxybenzene, and a modified Appel-type esterification ($BrCCl_3$, PPh_3).[2] X-ray single crystal structures of two intermediate compounds in the synthetic sequence were determined. The thermal behavior of the target molecules was investigated.



A

R = 4-OMe, 3,4-di-MeO, 4-Br, H

Scheme 1. Generic structure of the 4′-alkoxy-4-(ω-cinnamoylalkoxy)azobenzenes (**A**).

Acknowledgements: We thank the UAEU for UPAR grant 270s04 and for a SURE-PLUS 2017 grant.

References:

1. a) Pajak J.; Rospenk M.; Galewski Z.; Sobczyk L. *J. Mol. Struct.* **2004**, *700*, 191. b) Das P.; Biswas A. N.; Choudhury A.; Bandyopadhyay P.; Haldar S.; Mandal P. K.; Lipreti S. *Liq. Cryst.* **2008**, *35*, 541.
2. AlAzani M.; al-Sulaibi M.; al Soom N.; Al Jasem Y.; Bugenhagen B.; al Hindawi B.; Thiemann T. *C. R. Chim.* **2016**, *19*, 921.

Frist-row-transition-metal EDTA Functionalized Magnetic Nanocatalysts for Oxidative Mild Reactions

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Selective oxidation reactions play a pivotal role in the current chemical industry. Oxidation is the second largest process after polymerization and contributes *ca.* 30% of total production in the chemical industry.[1,2] However, the indiscriminate use of harsh and corrosive chemicals, waste generation and energy consumption constitutes a real threat to sustainability. In order to overcome this limitations and envisaging the development of more sustainable catalytic methods it was prepared by co-precipitation method[3,4] a series of late-first-row-transition-metal combined with ethylenediamine tetraacetic acid (EDTA) at the surface of ferrite magnetic nanoparticles (MNPs) to apply in oxidative reactions (**Figure 1**). Those EDTA functionalized MNPs with general formula Fe_3O_4@EDTA-M^{2+} [M= Mn^{2+} (**1**), Fe^{2+} (**2**), Co^{2+} (**3**), Ni^{2+} (**4**), Cu^{2+} (**5**) or Zn^{2+} (**6**)] catalyzed the microwave-assisted oxidation of alkanes and alcohols to the corresponding oxygenated products in a solvent-free medium. The versatility of the magnetically recovered and reused nanocatalysts **1-6** were extended to ε-caprolactone production through Baeyer-Villiger cyclohexanone aerobic oxidation.

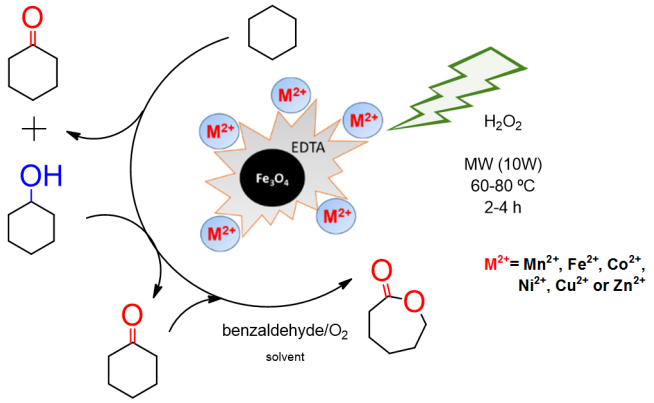

Figure 1: Solvent-free microwave-assisted catalytic oxidation reactions using reusable Fe_3O_4@EDTA-M^{2+} [M= Mn^{2+} (**1**), Fe^{2+} (**2**), Co^{2+} (**3**), Ni^{2+} (**4**), Cu^{2+} (**5**) or Zn^{2+} (**6**)] MNPs.

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References:

1 J.J.H.B. Sattler, J.Ruiz-Martinez, E. Santillan-Jimenez, B.M. Weckhuysen, Chem. Rev. ***2014****, 114, 10613.*
2 Z. Guo, B. Liu, Q. Zhang, W. Deng, Y. Wang, Y. Yang, Chem. Soc. Rev., ***2014****, 43, 3480*
3 K. Azizi, M. Karimi, F. Nikbakht, A. Heydari, Appl. Catal. A., ***2014****, 482, 336.*
4 K. Azizi, M. Karimi, A. Heydari, Tetrahedron Lett., ***2015****, 56, 812.*

EDTA@Cu(II) Functionalizated Supermagnetic Reusable Nanocatalysts Towards Solvent-free MW-assisted Direct Knoevenagel Condensation from Benzyl Alcohol

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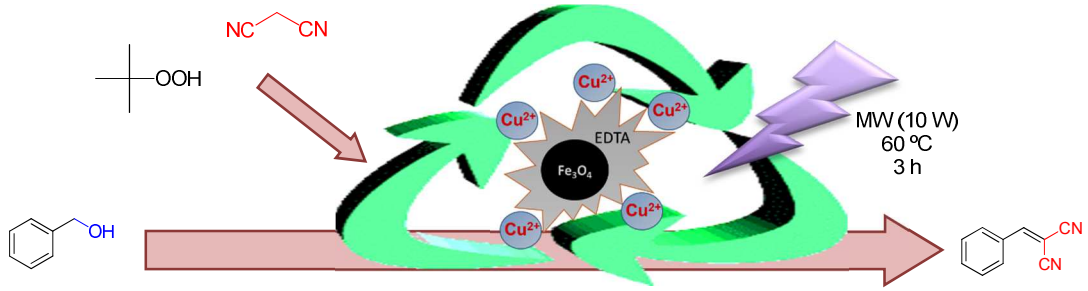
Knoevenagel condensation[1] is a widely used reaction in research and industry and has been of importance for several pharmaceutical products. Generally this reaction is catalyzed by organo-bases, such as pyridine or piperidine. But using these homogeneous-based catalysts often leads to time consuming work-up procedures. Additionally, undesired side-reactions such as oligomerizations can occur, high temperatures are necessary, and catalyst recovery is difficult.[2]

So in order to avoid complex neutralization procedures and obtain cleaner products we design an heterogeneous Knoevenagel catalyst of easy preparation and manipulation that can be reused without any regeneration procedure. For this purpose superparamagnetic Fe_3O_4@EDTA–Cu(II) nanoparticles were readily prepared by a co-precipitation method[3] and characterized by FTIR spectroscopy, powder XRD, SEM, EDS, VSM and TGA. Afterwards it were identified as an effective nanocatalysts for the tandem transformation of benzyl alcohol and malononitrile into the corresponding α,β-unsaturated ketone (conjugated enone) with *tert*-butyl hydroperoxide (TBHP) as an oxidant in a solvent-free medium heated by microwave (10 W) irradiation (**Scheme 1**). After completion of the reaction, the catalyst can be removed from the reaction vessel by assistance of an external magnet and reused at least five times without significant loss of its activity. This catalytic system affords a practical route from green chemistry perspective due the absence of organic solvents, low power heating mode, use of a recyclable cheap catalyst, presence of oxidant that forms non-hazardous by-products and starts from a cheaper substrate (alcohol instead of aldehyde).



Scheme 1: Solvent-free microwave-assisted catalytic tandem Knoevenagel condensation reaction of benzyl alcohol with malononitrile using reusable Fe_3O_4@EDTA-Cu(II).

Acknowledgements: Support for this work was provided by FCT, Portugal (UID/QUI/00100/2013 and PTDC/QEQ-ERQ/1648/2014). N.M.R.M acknowledges financial support from FCT CATSUS PhD (SFRH/BD/52371/2013). The authors are thankful to Prof. Vitor Amaral for the VSM measurements at CICECO – Aveiro.

References:

1. Knoevenagel E. *Ber. Dtsch. Chem. Ges.* **1898**, *31*, 2596.
2. Tietze LF, Beifuss U. in *Comprehensive Organic Synthesis*, (Eds: B. M. T. Fleming, BMT). Pergamon, Oxford, **1991**, pp. 341–394
3. Azizi K, Karimi M, Nikbakht F, Heydari A. *App. Cat. A: Gen.* **2014**, *482*, 336–343.

One-pot Synthesis of Substituted Alkylhydazines from Protected Carbonyl Compounds

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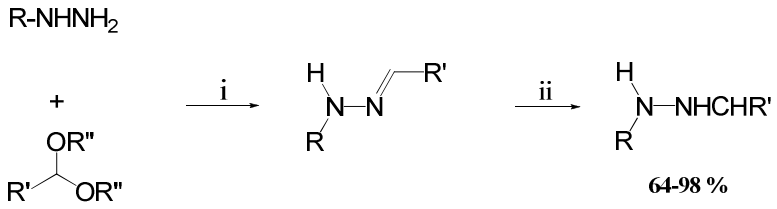
Preparation of aza-peptides, where at least one amino acid is replaced by alkylcarbazic acid residue, reguires a set of protected alkylhydrazines corresponding to natural amino acids. These compounds can be prepared by direct or reductive alkylation of protected hydrazines. (1; 2) Unfortunately, the presence of an electronegative group destabilizes aldehydes or ketones and requires protection/deprotection steps of the carbonyl group that complicated application of the latter synthetic path. To overcome these problems we developed a convenient one-pot synthesis of aza-methionine precursors from (2-methylthio)ethanal dimethyl acetal. (3) Encouraged by these results, this synthesis method was extended for use of different acetals and ketals with various substituents (**Scheme 1**). (4)



R = Fmoc; Cbz., R' = $-CH_2SCH_3$; $-(CH_2)_2CN$; $-(CH_2)_2Cl$; $-CH_2OBn$; $-CH_2NHCH_3$; $-CH_2NH_2$; $-CH_2NHCbz$; $-CH_3$; $-CH_2NHBz$; $-CH_2NHBoc$; $-CH{=}CH_2$; $-(CH_3)_2$; $-(CH_2)_5-$., R" = $-CH_3$; $-CH_2CH_3$.

i) TFA, EtOH - H_2O, Δ ii) 1. $NaBH_3CN$, AcOH, EtOH-H_2O, Δ.

Scheme 1: One-pot synthesis of protected alkylhydrazines from acetals and ketals.

As a result of this study we found that the proposed one-pot procedure works perfectly in combination with compounds having sulphide, ether-, nitrile-, carbamate and amide functional groups or branched and cyclic alkyl groups in substituent R'. However, several limitations were also revealed. Firstly, in the case of halogenated acetals their alkylation and decomposition was observed in the reaction mixture. Secondly, the presence of unprotected amino groups rapidly removed Fmoc-group, and in the case of Z-$NHNH_2$ the condensation reaction did not proceed even with 1.1 eq. of TFA. Thirdly, Boc-group was found to be unstable under the conditions of the condensation step. Finally, we found that primary aliphatic hydrazones tend to decompose during reduction in ethanolic media and tetrahydrofuran was found to be more suitable solvent for this reaction.

In summary, we developed a convenient and effective procedure for preparation of various protected alkylhydrazines.

References:

1. a) Mastitski, A.; Kisseljova, K.; Järv, J. *Proc. Estonian Acad. Sci.*, **2014,** 63, 438. b) Mastitski, A.; Haljasorg, T.; Kipper, K.; Järv, J. *Proc. Estonian Acad. Sci.*, **2015,** 64, 168.
2. Boeglin, D., Lubell, W. D. *J. Comb. Chem.*, 2005, 7, 864.
3. Mastitski, A.; Järv, J. *Org. Prep. Proced. Int.*, **2014**, 46, 559.
4. Mastitski, A., Niinepuu, S., Haljasorg, T., Järv, J. *Org. Prep. Proced. Int.*, **2015**, 47, 490.

Synthesis of P-Chiral Phosphine Ligands Containing Carbohydrate Unit

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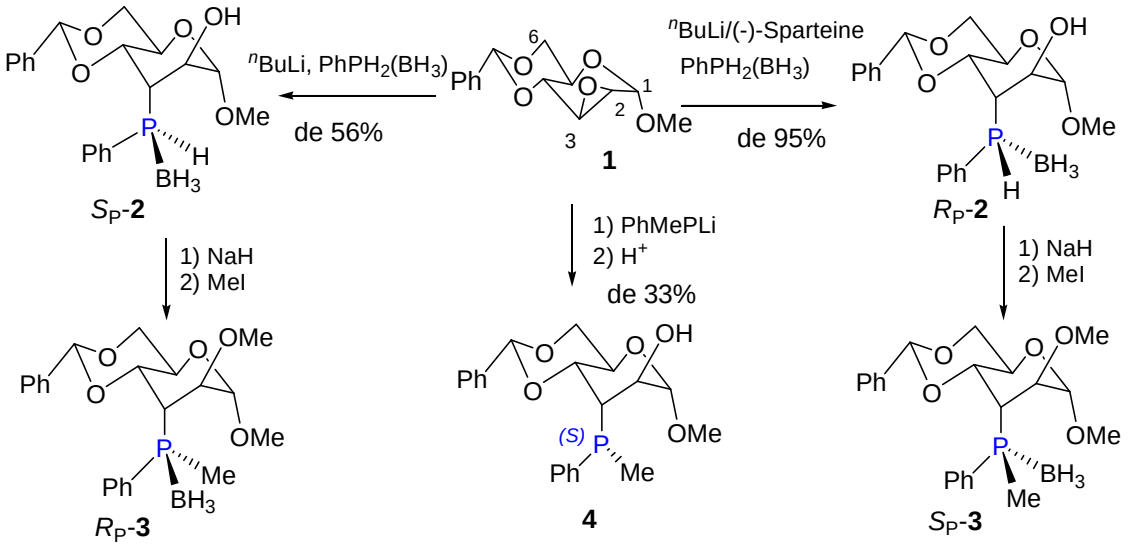
Optically active phosphine ligands have occupied an important status in metal-catalyzed asymmetric transformations, and numerous phouphines have been degined and prepared for the development of effective catalysts.[1] Although the invention of the P-chiral ligand 1,2-ethanediylbis[(2-methoxyphenyl)phenylphosphine] (dopamp) by Knowles and co-workers opened up the field of asymmetric catalysis,[2] and many P-chiral diphosphine ligands, such as BisP*, MiniPhos, TangPhos, DiSquarePhos, and QuinoxP*, exhibit almost perpect enantioinduction in some asymmetric catalysis, the total number of P-chiral phosphines is much less than other chiral types of ones, largely as the result of the synthetic difficulties.[3] Here, we introduce a new strategy to prepare new P-chiral phosphine ligands in light of carbohydrate unit (**Scheme 1**).



Scheme 1. Synthesis of P-Chiral Phosphine Ligands.

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References:

1. Tang W.; Zhang X. *Chem. Rev.* **2003**, *103*, 3029.
2. Vine B. D.; Knowles W. S.; Sabacky M. J.; Bachman G. L.; Weinkauff D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946.
3. Chen W.; McCormack, P. J.; Mohammed K.; Mbafor W.; Roberts S. M.; Whittal J. *Angew. Chem. Int. Ed.* **2007**, *46*, 4141.

When Gold Meets Isothioureas: Synthesis and Catalytic Activity of Au(I)- and Au(III)-Isothiourea Complexes

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Isothioureas (ITUs) are widely recognised as Lewis base organocatalysts,[1] but their applications as ligands for metal complexes has not been detailed yet. Herein we report the unprecedented synthesis of chiral Au(I) and Au(III) complexes bearing ITU ligands. This work shows the suitability of enantiopure HyperBTM,[2] and BTM,[3] as well as achiral DHPB,[4] for this purpose, with synthesis and full characterisation of the resulting complexes undertaken (Figure 1).[5] Air-, moisture-, and bench stable cationic (**1**), and neutral (**2**, **3**) chiral complexes were obtained in high to excellent yields by using easily available and accessible precursors. The synthesis of cationic species **1** was explored, and a series of complexes with different auxiliary ligands (NHC, PR_3) and counterions (NTf_2, BF_4) were obtained. Through a silver-free route, by starting from cationic precursors ([Au(IPr)(NTf_2)], [Au(IPr)($NCCH_3$)][BF_4]), either from neutral [Au(Cl)(L)] (L = IPr, PPh_3) species, **1** could be obtained in high to excellent yields. Pleasingly, the synthesis of Au(I) neutral species (**2**) resulted from reaction between [Au(Cl)(SMe_2)] and the corresponding chiral/or racemic ITU. The corresponding Au(III) species (**3**), could be easily accessed from **2** using a stoichiometric amount of external oxidant, leading to the straightforward formation of stable enantiomerically enriched complexes, first of their kind. Their structural properties were fully analysed by IR, NMR and UV-Vis spectroscopy. The solid-state structure, further elucidated by X-ray diffraction analysis, confirmed that ITU act as an N-donor ligand by forming, as expected, linear and square planar compounds, respectively for the +1 and +3 metal oxidation states.

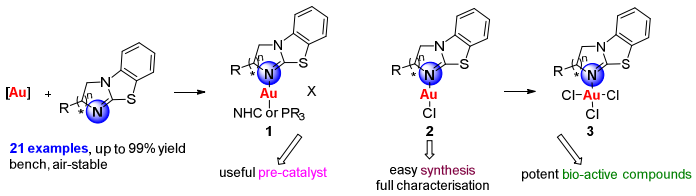

Figure 1: Synthesis and uses of [Au(ITU)(L')][X], [Au(ITU)(Cl)] and [Au(ITU)(Cl_3)] complexes; ITU = HyperBTM, BTM, DHPB; L' = IPr, PPh_3; X = BF_4, NTf_2; R =H, Ph, n = 2.

Moreover, **1**, **2** and **3** were tested in a series of Au(I) and Au(III) catalysed reactions with excellent results. The compounds showed high activity towards alkynes by improving existing reports in some instances and avoiding the use of silver salts; e.g. Au(I) catalysed hydroalkoxylation/Claisen rearrangement,[6] Au(III) catalysed synthesis of allenes,[7] and Au(I) catalysed rearrangement of sylliloxyexynes.[8] All the pre-catalysts tested could be activated by use of acids or Na salts, to release the active catalyst in solution.

References:

1. L. C. Morrill and A. D. Smith, *Chem. Soc. Rev.*, 2014, **43**, 6214-6226.
2. C. Joannesse, C. P. Johnston, C. Concellón, C. Simal, D. Philp and A. D. Smith, *Angew. Chem. Int. Ed.*, 2009, **48**, 8914-8918.
3. X. Yang, G. Lu and V. B. Birman, *Org. Lett.*, 2010, **12**, 892-895.
4. M. Kobayashi and S. Okamoto, *Tetrahedron Lett.*, 2006, **47**, 4347-4350.
5. Manuscript in preparation.
6. A. Gómez-Suárez, D. Gasperini, S. V. C. Vummaleti, A. Poater, L. Cavallo and S. P. Nolan, *ACS Cat.*, 2014, **4**, 2701-2705.
7. C.-F. Xu, M. Xu, L.-Q. Yang and C.-Y. Li, *J. Org. Chem.*, 2012, **77**, 3010-3016.
8. J.-F. Brazeau, S. Zhang, I. Colomer, B. K. Corkey and F. D. Toste, *J. Am. Chem. Soc.*, 2012, **134**, 2742-2749.

Artificial Hydrogenases for Asymmetric Reduction of Polarized C=X Bonds

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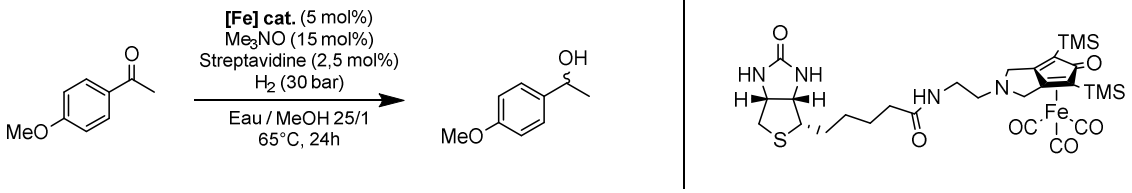
Recently, efficient phosphine-free iron based catalysts[1] have been reported for hydrogenation or hydrogen transfer. Thus, our group developed bifunctional tricarbonyl iron complexes bearing cyclopentadienone ligand.[2] These catalysts have showed interesting and valuable activity in hydrogenation reactions in water, in reductive amination and bicarbonate hydrogenation as well. In another hand, the most challenging part of catalysis is to be able to perform enantioselective hydrogenation, and only few examples have been reported so far. Instead of tuning the ligand, which is in some case appears as difficult and a waste of time, the solution is to use an external environment to bring the selectivity. In the past years, Ward's research group has highlighted the efficiency of this concept (merging organometallic and biotechnology) and developed many enantioselective processes. Thanks to artificial metallo-enzyme catalyst,[3] several example based on this technology for hydrogenation metal based catalyst were reported using metallic hydride species (hydrogenation, oxidation, C-H activation and olefin metathesis). However, until now, most of the catalytic system involves noble metal hydride as active species. Joining the knowledge and the expertise of both groups, we expect to cross our respective chemistry in order to enhance enantioselectivity of the cyclopentadienone tricarbonyl iron complex.



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References:

1. a) Casey, C.P.; Guan, H. *J. Am. Chem. Soc.* **2007**, *131*, 2499. b) Casey, C.P.; Guan, H. *J. Am. Chem. Soc.* **2009**, *129*, 5816. c) Tlili, A.; Neumann, H.; Beller, M. *Chem. Eur. J.*, **2012**, *18*, 15935. d) Fleischer, S.; Zhou, S.; Junge, K.; Beller, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 5120. e) Plank, T.N.; Drake, J.L. ; Jim, D.k.; Funk, T.W. *Adv. Synth. Catal.* **2012**, *354*, 597

2. a) Thai, T.-T.; Merel, D.S.; Poater, A.; Gaillard, S.; Renaud, J-L. *Chem. Eur. J.* **2015**, *21*, 7066. b) Merel, D.S.; Gaillard, S.; Ward, T.R.; Renaud, J.-L. *Catal. Lett.* **2016**, *146*, 564.

3. a) Skander, M.; Humbert, N.; Collot, J.; Gradinaru, J.; Klein, G.; Loosli, A.; Sauser, J.; Zocchi, A.; Gilardoni, F.; Ward, T.R. *J. Am. Chem. Soc.* **2004**, *126*, 14411. b) Lo, C.; Ringenberg, M.R.; Gnandt, D.; Wilson, Y.; Ward, T.R. *Chem. Commun.* **2011**, *47*, 12065. c) Hyster, T.K.; Knörr, L.; Ward, T.R.; Rovis, T. *Science*, **2012**, *338*, 500

Synthesis and Biological Activity of Novel Acylhydrazide Derivatives of 2,3-Dichloro-1,4-naphthoquinone

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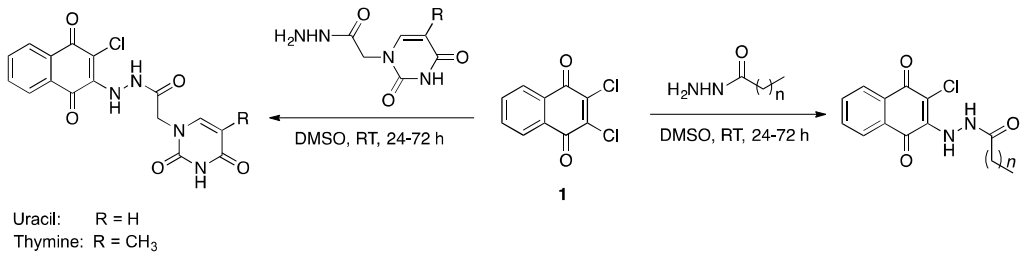
Naphthoquinones have been reported to possess a variety of pharmacological properties including antibacterial, antifungal, antiviral, anti-inflammatory, anti-artherosclerotic and anticancer effects.[1] 1,4-Naphthoquinone encompasses the quinone pharmacophore which is typically associated with most of the biological activity of related molecules.[2] Hydrazides are also an important class of compounds utilized in pharmaceutical products.[3] Interestingly, 1,4-naphthoquinones possessing an amino or a substituted amino group in the 2-position, have been used in a variety of medical and biological applications, including as antituberculars, antimalarials, antibacterials, antitumor agents, larvicides and molluscicides, herbicides, and fungicides.[4] For this reason, we investigated the preparation of series of novel naphthoquinone acylhydrazides. The straightforward and high yielding synthesis of these molecules involves a coupling reaction between 2,3-dichloro-1,4-naphthoquinone **1** and several alkyl and aromatic hydrazides and the hydrazides of the pyrimidine nucleobases, uracil and thymine. The product hydrazides were isolated in good to excellent yields and completely characterized by spectroscopic analysis. Biological evaluation against human colon cancer HCT116 cells and human breast cancer MCF-7 cells indicated that the novel hydrazides possessed significant anticancer activity and warrant investigation into their possible molecular mechanism of action.



Scheme 1: Synthesis of novel acylhydrazide derivatives of 2,3-dichloro-1,4-naphthoquinone

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References:

1. Pinto, A.; de Castro, S. *Molecules* **2009**, 14, 4570-4590.
2. Ashe, C. *Mini Rev. Med. Chem.* **2005**, *5*, 449–467.
3. Toliwal, S.; Jadav, K.; Patel, K. *Indian J. Pharm. Sci.* **2009**, *71*, 144–148.
4. a) Silver, R. F.; Holmes, H. L. *Can. J. Chem.* **1968**, *46*, 1859-1864. b) Oeriu, I. *Biokhimiia* **1963**, *28*, 380-383. c) Prescott, B. Potent antimalarial agents. *J. Med. Chem.* **1969**, *12*, 181-182. d) Hodnett, E. M.; Wongwiechintana, C.; Dunn, W. J. 3rd; Marrs, P. *J. Med. Chem.* **1983**, *26*, 570-574. e) Clark, N. G. *Pestic. Sci.* **1984**, *15*, 235-240.

Synthesis of Spirocyclohexadienones through Radical Cascade Reactions featuring 3-fold Carbon-Carbon-Bond Formation

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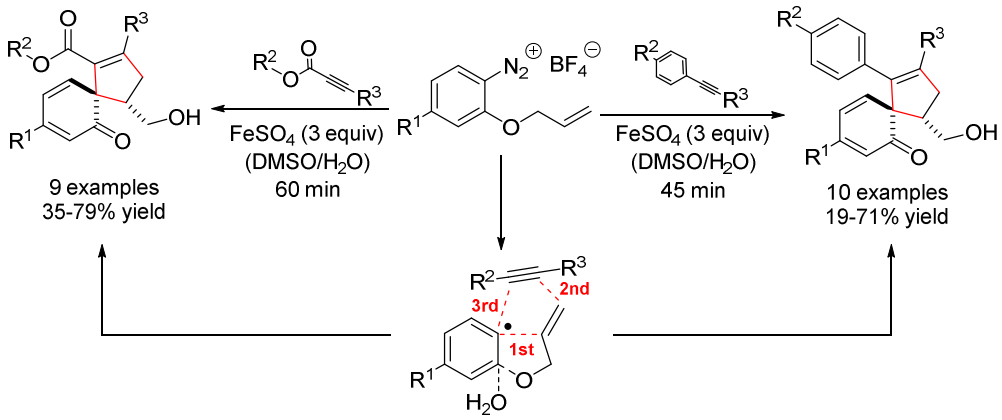
Spirocyclohexadienones are present as substructures in many natural products, pharmaceuticals, and compounds for diverse other applications.[1] A variety of synthetic methods that have recently been investigated mainly features an intramolecular dearomatization of phenols or other suitably substituted benzenes.[2]
In our approach highly functionalized spirocyclohexadienones were synthesized from readily available aryldiazonium salts and alkynes under simple reaction conditions. These spirocyclic systems were obtained through a radical [2 + 2 + 1] cycloaddition starting from 2-allyloxybenzenediazonium ions. Through a 5-*exo* cyclization, a consecutive addition to the alkyne and an *ipso* attack onto the original position of the diazonium derived aryl radical three carbon carbon bonds were formed with full diastereoselectivity.[3]



Scheme 1: Synthetic strategy for spirocyclohexadienones.

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References:

1. a) Bai, Y.; Davis, D. C.; Dai, M.; *J Org Chem* **2017**, *82*, 2319; b) Roche, S. P.; Porco, J. A. Jr.; *Angew Chem Int Ed Engl* **2011**, *50*, 4068; c) Undheim, K.; *Synthesis* **2016**, *49*, 705.
2. a) Godoi, B.; Schumacher, R.F.; Zeni, G.; *Chem Rev* **2011**, *111*, 2937; b) Magdziak, D.; Meek, S. J.; Pettus, T. R.; *Chem Rev* **2004**, *104*, 1383; c) Pouységu, L.; Deffieux, D.; Quideau, S.; *Tetrahedron* **2010**, *66*, 2235; d) Zhdankin, V. V.; Stang, P. J.; *Chem Rev* **2008**, *108*, 5299.
3. Hegmann, N.; Prusko, L.; Heinrich, M. R.; *Org Lett* **2017**, *19*, 2222.

Construction of All-carbon Quaternary Centres using Tandem Cyclisation/Suzuki Cross-coupling and Halocarbocyclisation

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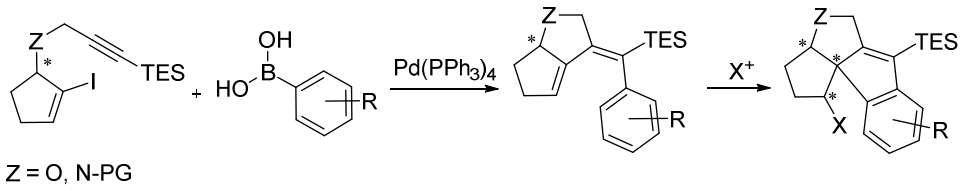
Although quaternary carbon centres are present in many biologically active natural products, their enantioselective formation still represents one of the most challenging tasks in organic chemistry. Herein, a method for synthesis of polycyclic compounds containing all-carbon quaternary centres is presented.
The key transformations of the reaction sequence are tandem cyclisation/Suzuki cross-coupling and halocarbocyclisation **(Scheme 1)**. The aim of this work was to explore the scope of the method using oxygen and nitrogen substrates, various boronic acids and different halocyclisation reagents, such as BDSB.[1]



Scheme 1: Tandem cyclisation/Suzuki cross-coupling and subsequent halocarbocyclisation.

The resulting structural pattern around the quaternary centre is similar to that encountered in natural products, such as alkaloids of *Amaryllidaceae* plant family, which are attractive synthetic targets for their significant biological activities[2] **(Figure 1)**.

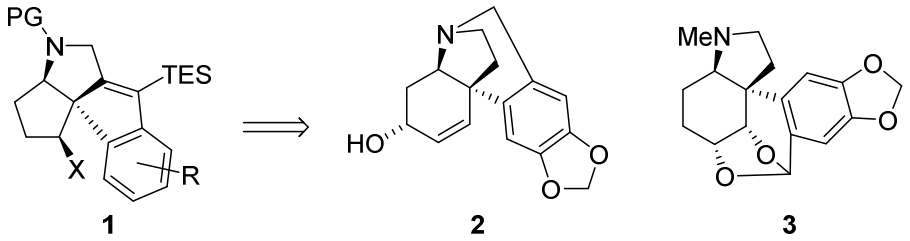


Figure 1: Comparison of our scaffold (1) with *Amaryllidaceae* alkaloids crinine (2) and augustamine (3).

Acknowledgements: We thank The Czech Science Foundation (No. 16-22419Y) for financial support.

References:

1. Snyder S. A.; Treitler D. S.; Brucks A. P. *J. Am. Chem. Soc.* **2010**, *132*, 14303.
2. Jin Z. *Nat. Prod. Rep.* **2016**, *33*, 1318

Cobalt-Catalyzed Direct α-Arylation of α-Amino Ester Compounds with Indoles

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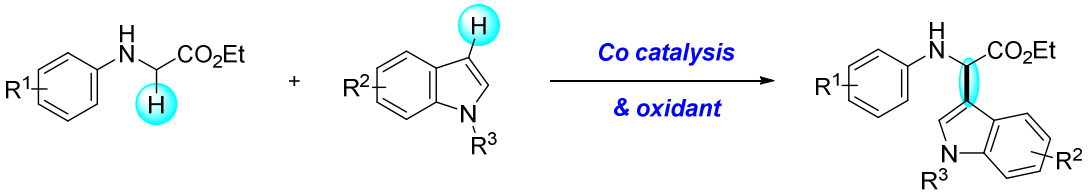
Metal-catalyzed C−H functionalization is a hot topic in the modern organic synthesis.[1] Among these chemical processes, the activation of C(sp^3)−H centers of amino acid derivatives has been extensively studied owing to the wide presence of the resulting α-amino carbonyl units in many structures of natural products and biomolecules.[2] In particular, the α-arylation of glycine derivatives with indoles have been recently explored upon transition-metal-catalysis (Ru, Fe and Cu).[3] In this communication, we report an alternative, yet novel, mild route to the C−H oxidative/cross-coupling of α-aminoester compounds with indoles catalyzed by cost-efficient cobalt salts[4] (***Scheme 1***). Remarkably, this new protocol for the α-arylation of α-aminoesters, which proceeds with a high functional group tolerance, represents an efficient synthetic route for the assembly of a wide range of biologically interesting compounds.



Scheme 1: Co-catalyzed α-arylation of glycine derivatives.

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References:

1. Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900.
2. a) Hunt, S. *Chemistry and Biochemistry of the Amino Acids*; Barret, G. C., Ed.; Chapman and hall: London, 1985, p 55. b) Ohfune, Y. *Acc. Chem. Res*. **1992**, *25*, 360. c) Gellman, S. H. *Acc. Chem. Res*. **1998**, *31*, 173.
3. a) Dai, C.; Meschini, F.; Narayanam, J. M. R.; Stephenson, C. R. J. *J. Org. Chem*. **2012**, *77*, 4425. b) Wu, J. C.; Song, R. J.; Wang, Z. Q.; Huang, X. C.; Xie, Y. X.; Li, J. H. *Angew. Chem. Int. Ed*. **2012**, *51*, 3453. c) Wang, Z. Q.; Hu, M.; Huang, X. C.; Gong, L. B.; Xie, Y. X.; Li, J. H. *J. Org. Chem*. **2012**, *77*, 8705. d) Huo, C.; Wang, C.; Wu, M.; Jia, X.; Xie, H.; Yuan, Y. *Adv. Synth. Catal*. **2014**, *356*, 411. e) Zhang, Y.; Ni, M.; Feng, B. *Org. Biomol. Chem*. **2016**, *14*, 1554. f) Li, K.; Tan, G.; Huang, J.; Song, F.; You, J. *Angew. Chem. Int. Ed.* **2013**, *52*, 12942.
4. For selected reviews, see: a) Cahiez, G.; Moyeux, A. *Chem. Rev.* **2010**, *110*, 1425. b) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208. c) Wei, D.; Zhu, X.; Niu, J.-L.; Song, M.-P. *ChemCatChem* **2016**, *8*, 1242. d) Wang, S.; Chen, S.-Y.; Yu, X.-Q. *Chem. Commun.* **2017**, *53*, 3165.

Cobalt-Catalyzed CDC Reactions of Amino Ester and Peptide Derivatives with Cyclic Ethers

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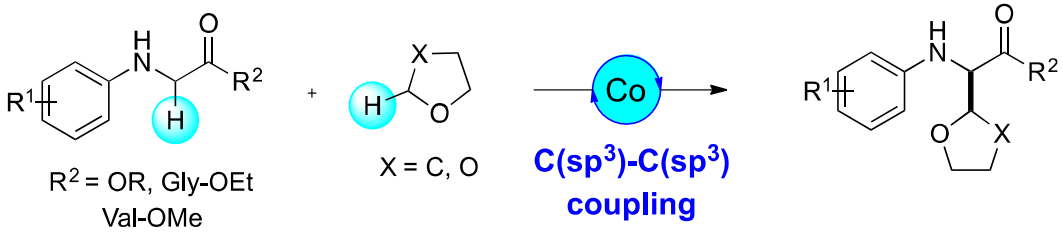
Metal-catalyzed "*Cross-Dehydrogenative Coupling*" (CDC) reactions have attracted tremendous interest owing to their capacity to activate inert C–H bonds.[1] Despite the extended use of copper catalysts in these chemical processes, the high potential of cobalt catalysis has lately received a great deal of attention.[2] In this communication, we describe unprecedented cobalt(II)–catalyzed CDC reactions for the α–functionalization of amino ester and peptide derivatives with cyclic ethers (***Scheme* 1**). The key feature relies on the dual C(sp^3)–H activation of cheap and readily available cyclic ethers, which are mainly used as common organic solvents in synthetic chemistry, and glycine derivatives.[3] Notably, our α–alkylation reactions proceed with total regioselectivity when starting from peptide derivatives containing multiple C–H bonds. Furthermore, the configuration of preexisting chiral centers within the peptides could be maintained. This method provides a straightforward, yet practical, access to a wide variety of peptide mimetics, which are privilege motifs in pharmaceuticals, bioactive molecules and natural products.



Scheme 1: Direct Co-catalyzed C(sp^3)–C(sp^3) coupling.

Acknowledgements: A.C. thanks MINECO for a Ramón y Cajal research contract (RYC-2012-09873). We are grateful to the Gobierno Vasco (ELKARTEK_KK-2015/0000101; IT_1033-16) and MINECO (CTQ2016-78395-P) for financial support. Cost-CHAOS action is also acknowledged.

References:

1. For selected reviews, see: a) Lv, L.; Li, Z. *Top. Curr. Chem.* **2016**, *374*, 38. b) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem. Int. Ed.* **2014**, *53*, 74. For recent achievements in metal-free CDC processes, see: c) Wu, X.-F.; Gong, J.-L.; Qi, X. *Org. Biomol. Chem.* **2014**, *12*, 5807.
2. For selected reviews, see: a) Cahiez, G.; Moyeux, A. *Chem. Rev.* **2010**, *110*, 1425. b) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208. c) Wei, D.; Zhu, X.; Niu, J.-L.; Song, M.-P. *ChemCatChem* **2016**, *8*, 1242. d) Wang, S.; Chen, S.-Y.; Yu, X.-Q. *Chem. Commun.* **2017**, *53*, 3165.
3. a) Congde, H.; Fengjuan, C.; Yong, Y.; Haisheng, X.; Yajun, W. *Org, Lett.* **2015**, *17*, 5028. b) Zhao, L.; Baslé, O.; Li, C.-J. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106,* 4107. c) Yanrong, L.; Mengshi, W.; Wei, F.; Fen, Q.; Guigen, L.; Hongjian, L. *J. Org. Chem.* **2016**, *81*, 11743. d) Longyang, D.; Hui, Z.; Daisy, N.; Yunfei, D. *Adv. Synth Catal.* **2016**, *358*, 2422. e) Wei, W. T.; Song, R. J.; Li, J. H. *Adv. Synth. Catal.* **2004**, *356*, 1703.

New Organocatalysts for Light Activated Asymmetric Catalysis

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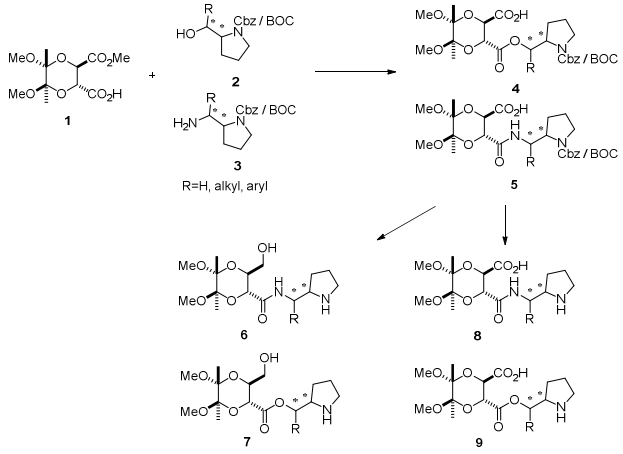
Organocatalysis is an important area of modern catalysis that complements the more traditional metal catalysis and enzyme catalysis.[1–3] Synthetic chemists have started to look at organocatalysis as a valuable tool for the asymmetric total synthesis of natural products and biological active compounds.[3]
However, there are still many classes of products that are difficult to obtain by enantioselective catalysis. One example is the reactions that require photochemical activation. These light driven reactions are a powerful tool for organic chemistry as they include important chemical transformations that are not available by conventional thermal activation. Additionally, visible light is abundant, inexpensive and appropriate for sustainable and green chemical processes.[4,5] However, photochemical reactions involve excited states with very short lives which are challenging to stereochemically control to afford products with high enantio- and/or diastereostereoselectivity.
Very recently, it has been reported some strategies for asymmetric organocatalysis activated by visible light, either using dual catalysis, organocatalyst plus photoredox catalyst, or a single organocatalyst.[6–8] In this work we describe preliminary results of the synthesis of new organocatalysts derived from readily available D- and L-tartaric acid and their use in photochemical asymmetric reactions.



Scheme or Figure 1: Summarised synthetic process to obtain the new organocatalysts.

Acknowledgements: This work is being supported by Fundação para a Ciência e Tecnologia (FCT) through a grant of the Doctoral Programme Catalysis and Sustainability (CATSUS) (PD/BD/114196/2016), by the prize "Programa de Estímulo à Investigação" of Fundação Calouste Gulbenkian (FCG), and by Instituto deTecnologia Química e Biológica (ITQB). The NMR spectrometers are part of The National NMR Facility, also supported by FCT (RECI/BBBBQB/0230/2012).

References:

1.Dalko, P. I. & Moisan, L. *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 5138.
2.MacMillan, D. W. C. *Nature,* **2008**, 455, 304–8.
3.Grondal, C., Jeanty, M. & Enders, D. *Nat. Chem.,* **2010**, 2, 167–78.
4.Narayanam, J. M. R. & Stephenson, C. R. J. *Chem. Soc. Rev.,* **2011**, 40, 102–13.
5.Meggers, E. *Chem. Commun.,* **2015**, 51, 3290–3301.
6.Nicewicz, D. A. & Macmillan, D. W. C. *Science,* **2008**, 322, 77–80.
7.Melchiorre, P., Arceo, E., Jurberg, I. D. & Ana, A. *Nat. Chem.,* **2013**, 5, 750–756.
8.Silvi, M., Arceo, E., Jurberg, I. D., Cassani, C. & Melchiorre, P. *J. Am. Chem. Soc.,* **2015**, 137, 6120–3.

Organocatalytic Synthesis of δ-Lactones Bearing a Cyclohexenone Scaffold

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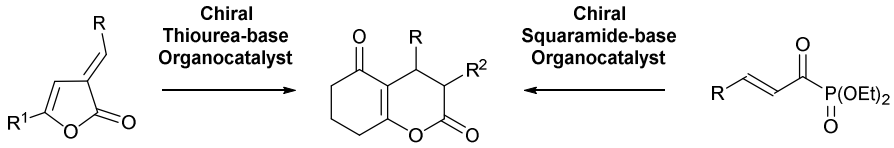
γ-Lactones and δ-lactones represent an important class of biologically active compounds.[1] The development of highly efficient and enantioselective methodologies for the synthesis of compounds containing the lactone ring is a very important goal in organic and medical chemistry due to its cytotoxic, antitumoral, and often antibacterial properties.

Herein, we report a novel approach to biologically relevant δ-lactones using readily available (*E*)-5-aryl-3-arylidenefuran-2(3*H*)-ones or β,γ-unsaturated-α-ketophosphonates and cyclohexane-1,3-dione as the starting materials. Interestingly, this approach is promoted by readily available bifunctional catalysts.The developed synthetic strategies benefit from the high efficiency, and the optically active target products are obtained in a highly enantioselective manner.



Acknowledgements: This work was made possible by a financial support from the Young Scientists' Fund at the Faculty of Chemistry, Lodz University of Technology (grant W-3/FMN/18G/2016) and within *Iuventus Plus* programme from the Minister of Science and Higher Education (grant number 0008/IP3/2015/73).

References:

1. John, E. V. O.; Israelstam, S. S. *J. Org. Chem.* **1961**, *26*, 240.
2. Mullowney M.W.; Ainmhire E.; Tanouye U.; Burdette J.E.; Pham V. C.; Murphy B.T. *Mar. Drugs* **2015**, *13*, 5815-5827;
3. Shi F.; Dai A.-X.; Zhang S.; Zhang X.-H.; Tu S.-J. *Eur. J. Med. Chem.* **2011**, *46*, 953-960.

Decarboxylative Aminocatalytic Cascade in the Synthesis of Xanthone and Chromanone

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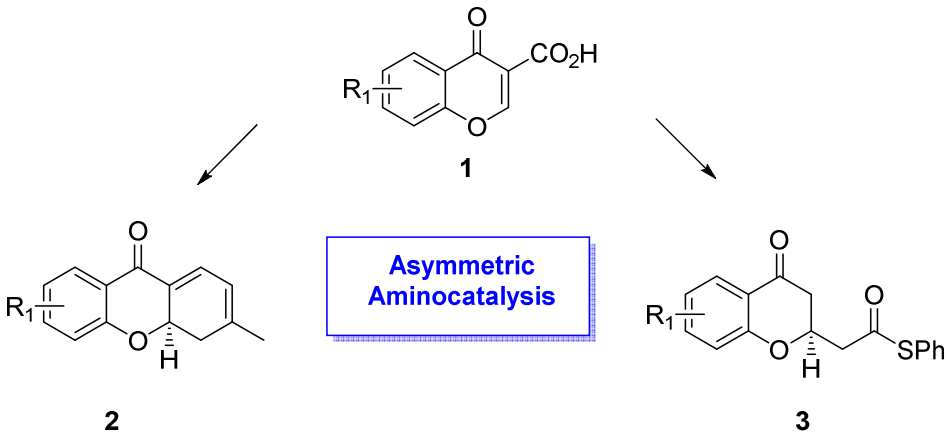
Development of stereocontrolled strategies leading to molecules of biological interest is of key importance in the contemporary organic chemistry.[1] A xanthone and chromanone structural units are constituents of many natural products exhibiting diverse and useful biological properties.[2]

Herein, we report a novel and straightforward approach to dihydroxanthones **2** and chomanones **3** based on a cascade reactivity of chromone-3-carboxylic acids **1** with □,□-disubstituted enals or malonic acid half thioester (MAHT). The synthesis of 4,4a-dihydroxanthone **2** is realized under aminocatalytic conditions and involves the formation of dienamine intermediate that participates in the [4+2]-cycloadditon. Subsequent decarboxylative deamination is a key step of the cascade enabling the turnover of the aminocatalyst and the formation of the 4,4a-dihydroxanthone derivatives **2** (**Scheme 1**).[3] The synthesis of chromanones **3** has been realized through an enantioselective doubly decarboxylative conjugate addition of MAHT to chromone-3-carboxylic acids **1**. The reaction was catalyzed by cinchona-alkaloid-derived catalyst to afford **3** in good yield and enantioselectivity.



Scheme 1

Acknowledgements: This project was financially supported by the National Science Centre, Poland within the "Sonata" programme realized in the period 2017-2020, project number: UMO-2016/21/D/ST5/01668. A.A. acknowledges Lodz University of Technology for a scholarship (Własny Fundusz Stypendialny PŁ programme).

References:

1. a) E. N. Jacobsen, A. Pfaltz, H. Yamamoto, *Comprehensive Asymmetric Catalysis*, Springer, Berlin, **1999**; b) K. Mikami, M. Lautens, *New Frontiers in Asymmetric Catalysis*, Wiley-Interscience, New Jersey, **2007**.
2. a) D. P. Kamat, S. G. Tilve, V. P. Kamat, J. K. Kirtany, *Org. Prep. Proc. Int.* **2015**, *47*, 1-79; b) K.-S. Masters, S. Bräse, *Chem. Rev.* **2012**,*112*, 3717-3776.
3) A. Albrecht, J. Bojanowski, *Adv. Synth. Catal.* **2017**, DOI: 10.1002/adsc.201700400.

Aerobic Oxidation of Lignin Model Compound Catalyzed by a $VO(acac)_2$/Triazole System

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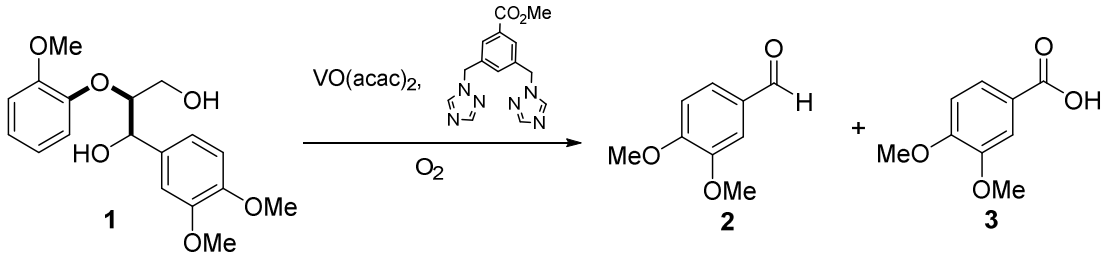
In a world aware of environmental issues, finding renewable sources of energy and chemicals has become a priority. The use of biomass for that purpose is an obvious and attractive option. Lignin is one of the most abundant components of biomass and, therefore, the development of methods for its transformation into valuable aromatic chemicals has attracted broad attention in recent years.[1] Lignin is a natural aromatic polymer produced by random polymerization of oxyphenylpropane units by C-O-C bond linkages. A methodology for breaking the ether bonds of its structure would constitute a good way of depolymerizing. Among other strategies for achieving this goal, the oxidative cleavage of lignin or model compounds has emerged as a promising strategy.[2]

Recently, we have found that very low amounts of vanadyl acetylacetonate and a triazole based pincer type ligand system catalyses aerobic oxidative debenzylation of ethers in green media.[3] We dediced to evaluate this catalytic system in the aerobic oxidative cleavage of lignin. Since lignin is a structurally complex polymer we prepared 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol **1** (Scheme 1), a model that contains the β-O-4 linkage present in the natural polymer, in order to use it as substrate in oxidative cleavage assays. In this communication, we wish to report our preliminary results on this matter.



Scheme 1: Aerobic oxidative cleavage of lignin model catalyzed by a vanadyl acetylacetonate/bis-triazolyl ligand system.

Acknowledgements: We thank Basque Government (IT-774-13), the Spanish Ministry of Economy and Competitiveness (CTQ2013-46970-P) and the University of the Basque Country (UFI QOSYC 11/12) for financial support. G.U thanks the Basque Government for a postdoctoral scholarship. Finally, technical and human support provided by SGIker of UPV/EHU is gratefully acknowledged.

References:

1. See for example: a) Calvo-Flores, F. G.; Dobado, J. A. *ChemSusChem*, **2010**, *3*, 1227. b) Bozell, J. J. *Top. Curr. Chem*., **2014**, *353*, 229. c) Xu, C. P.; Arancon, R. A ; Labidi, J.; Luque, R. *Chem. Soc. Rev*., **2014**, *43*, 7485. d) Li, C. Z.;. Zhao, X. C; Wang, A. Q.; Huber, G. W.; Zhang, T. *Chem. Rev*. **2015**, *115*, 11559.
2. a) Zakzeski, J.; Bruijnincx, P. C. A.; Jongerius, A. L.; Weckhuysen, B. M.. *Chem. Rev*. **2010**, *110*, 3552. b) Deuss, P. J.; Barta, K.; de Vries, J. G. *Catal. Sci. Technol*. **2014**, *4*, 1174. c) Rinaldi, R.; Jastrzebski, R.; Clough, M. T.; Ralph, J.; Kennema, M.; Bruijnincx, P. C. A.; Weckhuysen, B. M. *Angew. Chem., Int. Ed*. **2016**, *55*, 8164. d) Kärkäs, M. D.; Matsuura, B. S.; Monos, T. M.; Magallanes, G.; Stephenson, C. R. *Org. Biomol. Chem*. **2016**, *14*, 1853.
3. Urgoitia, G.; SanMartin, R.; Herrero, M.T.; Dominguez, E. *Adv. Synth. Catal*. **2016**, *358*, 3307.

Electrochemical Oxidation of Dithenylphosphine Oxide and Acetylenes Catalyzed by Ag Salts

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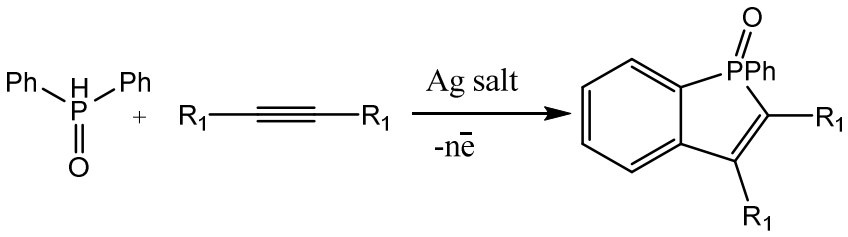
Phosphine oxides are successfully used as building blocks, specifically, for the synthesis of substituted vitamin D3 analogs. Tertiary phosphine oxides are key targets in the chemistry of organophosphorus compounds. They are widely used as ligands for metal complex catalysts, special solvents for stabilization of nanosystems in the synthesis of semiconductors, extractants for noble, rare-earth, and transuranium elements, fire-retardants and photochromic and luminescent materials.

Of particular interest are functionalized tertiary phosphine oxides; however, their synthesis involves some difficulties. A convenient synthetic approach to such compounds is based on the addition of secondary phosphine oxides to functionally substituted alkynes at high temperature by using equivalent amounts of oxidant and catalyst.

In our work the synthesis of different diphenylphosphine oxide derivatives in electrocatalytic conditions have been performed. Our approach provides an efficient way to construct different phosphorus-containing products, including bisphosphonates, benzo[b]phosphole oxides, alkynyl(diaryl)phosphine oxides with high yield at room temperature in oxidant-free media. The mechanism includes forming silver complexes with diphenylphosphine oxide, their electrochemical oxidation leads to binding with acetylene and obtaining target products.



Acknowledgements: This work was supported by Russian Science Foundation no. 14-23-00016.

Brønsted Acid Catalyzed Nitrile Synthesis from Aldehydes via Transoximation under Mild Conditions

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We recently focused on the transoximaze isolated from the pupae of silkworm and developted a Brønsted acid catalyzed transoximation.[1] In the present research, we demonstrate that the stable oxime is equivalent to explosive hydroxylamine. On the contray, *O*-protecting hydroxylamines containing electron-withdrawing groups are known to exhibit high reactivity for the amination reaction, however their reagents also showed explosive and unstable properties (ex. MSH reagent and HOSA etc.). Herein, we expanded our concept and considered that more stable *O*-protecing oxime could be treated as an equivalent of explosive *O*-protecting hydroxylamines in order to solve the problem (**Figure 1**).

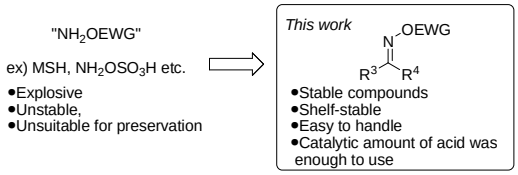

Figure 1. Advantages of using oxime instead of hydroxylamine derivatives

Based on the above concept, we atempted the reaction with aldehydes and *O*-sulfonyl oxime catalyzed by various Brønsted acid. As a result, the reacton were successfully proceeded under very mild conditions and the corresponding nitriles were generated *via* transoximation with good yield (**Figure 2**)[2]. We will discuss with the details in this synposium.

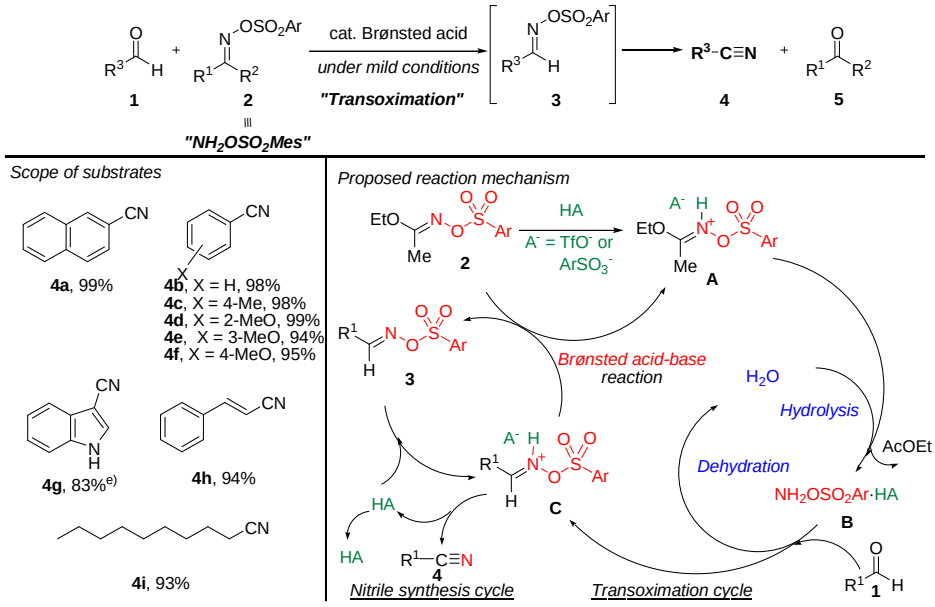

Figure 2. Brønsted acid catalyzed nitrile synthesis *via* transoximation.

Acknowledgements: We gratefully acknowledge the financial support from the Kaneka Award in Synthetic Organic Chemistry, Japan.

References:

1. Hyodo, K.; Togashi, K.; Oishi, N.; Hasegawa, G.; Uchida, K. *Green Chem.* **2016**, *18*, 5788.
2. Hyodo, K.; Togashi, K.; Oishi, N.; Hasegawa, G.; Uchida, K. *Org. Lett.* **2017**, *19*, 3005.

Small Molecule Transmembrane Anion Transporters

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The development of synthetic receptors capable of exchanging anions across the lipid bilayer is a field of growing interest in supramolecular chemistry.[1] Small molecules which show anion transport activity could have potential application in the treatment of diseases such as cystic fibrosis, caused by the defective regulation of chloride and bicarbonate transport.[2] Tambjamines and prodiginines, two families of natural products with anion transport properties, have served as an inspiration for the work described here. It has been shown that the ionophoric activity of these compounds, characterised by their unusual stability, due to the high electronic delocalisation throughout the aromatic structure, and the presence of hydrogen-bonding donor groups in their scaffolds, which allow interaction with anions, is related to their citotoxicity.[3]

Herein we report the synthesis, characterisation and anion transport studies of a series of new transmembrane anion transporters based on a 2,2'-bipyrrole core substituted with either a methoxy group (**Figure 1**, compound 1) or two alkyl chains (**Figure 1**, compounds 2 and 3) and containing a 7-aminoindole fragment. One of the most interesting features about these compounds is the presence of an additional hydrogen-bonding donor group in their structures, coming from the aminoindole moiety, which could enhance their interaction with anions. Anion transport activity was measured by studying the ability of the receptors to exchange Cl^- and NO_3^- and Cl^- and HCO_3^- across the membrane of model liposomes (POPC), employing a chloride selective electrode.

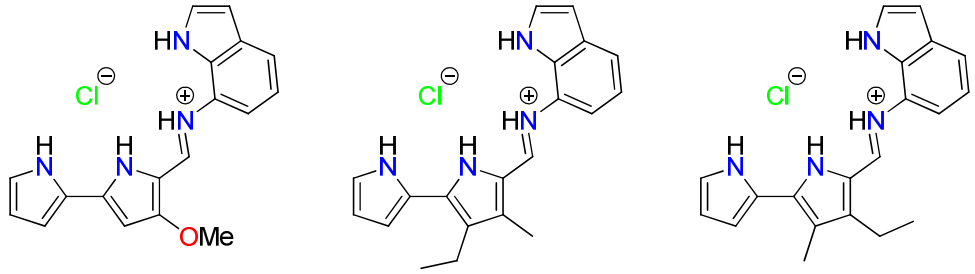

Figure 1: Receptors studied in the present work.

Acknowledgments: This work has been supported by the European Union's Horizon 2020 research and innovation programme (TAT-CF Project, Grant Agreement No. 667079).

References:

1. Gale, P. A.; Pérez-Tomás, R.; Quesada, R. *Acc. Chem. Res.* **2013**, *46*, 2801.
2. a) Ashcroft, F. M. *Nature* **2006**, *440*, 440; b) Ashcroft, F. M. *Ion Channels and Disease*. Academic Press, San Diego and London, **2000**.
3. Díaz de Greñu, B.; Iglesias-Hernández, P.; Espona, M.; Quiñonero, D.; Light, M. E.; Torroba, T.; Pérez-Tomás, R.; Quesada, R. *Chem.–Eur. J.* **2011**, *17*, 14074.

Adducts of $SbCl_5$ with Aromatic Nitrogen Bases as a Model System for the Description of Various Non-covalent Interactions

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Non-covalent interactions such as halogen bonding have become extremely important issues within the crystal engineering or studies of biological systems or processes.[1] The existence and nature of the halogen bonds due to the presence of the "σ-holes" has been reviewed recently.[2]

To the best of our knowledge, there are only several examples of antimony(V) pentachloride adducts with *N*-donor ligands which structures have been establisehd by SC-XRD techniques. These species include for example $CH_3C{\equiv}N{\bullet}SbCl_5$, [(*i*-Pr)N=C=N(*i*-Pr)]•$SbCl_5$, Cl-C≡N•$SbCl_5$, (*i*-Pr)$_2$N-C≡N•$SbCl_5$ or S_2N_2•$2SbCl_5$.[3] Pyrazine•$2SbF_5$ adduct is also known.[4] In all these cases, the central six-coordinate antimony atom adopts a distorted octahedral geometry with quite strong N→Sb co-ordination bond(s).

We now report on the synthesis of a set of adducts of antimony(V) pentachloride with various aromatic nitrogen bases (*i.e.* 4-dimethylaminopyridine, pyridine, pyrimidine, pyrazine and 1,3,5-triazine (Figure 1)). Structure of these species has been investigated by the help of multinuclear NMR spectroscopy in solution and SC-XRD techniques in the solid state. The poster presentation will further discuss the presence of several types of non-covalent intermolecular interactions (*e.g.* halogen bond or hydrogen bridges) within these adducts in detail. DFT calculations considering the nature of these interactions are in progress now and shall be discussed as well.

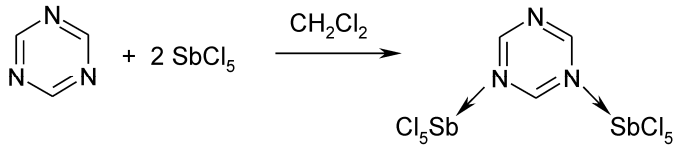

Figure 1: Preparation of the 1,3,5-triazine•$2SbCl_5$ adduct

Acknowledgements: The authors would like to thank the Czech Science Foundation for the financial support of this work (project 17-08045S).

References:

1. Politzer P.; Lane P.; Concha M. C.; Ma Y.; Murray J. S. *J. Mol. Model.* **2007**, *13*, 305.
2. Kolář M. H.; Hobza P. *Chem. Rev.* **2016**, *116*, 5072.
3. a) Binas H. *Z. Anorg. Allg. Chem*. **1967**, *352*, 271; b) Jochims J. C.; Abu-El-Halawa R.; Zsolnai L.; Huttner G. *Chem. Ber*. **1984,** *117*, 1161; c) Klapötke T. M.; Nöth H.; Schütt T.; Sutter M.; Warchhold M. *Z. Anorg. Allg. Chem.* **2001**, *627*, 1582; d) Hausen H. D.; Schwarz W.; Rajca G.; Weidlein J. *Z. Naturforsch*. **1986**, *41b*, 1223; e) Patton R. L.; Raymond K. N. *Inorg. Chem.* **1969***, 8,* 2426.
4. Sham I. H. T.; Patrick B. O.; Ahsen B.; Ahsen S.; Willner H.; Thompson R. C.; Aubke F. *Solid State Sci.* **2002**, *4*, 1457.

Structural Features and Catalytic Application of Enaminone/Carborane Zinc complexes

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The ring-opening polymerization (ROP) represents one of the most popular directions for preparation of biopolymers. Industrially, these type of reaction are promoted by the most popular tin(II) catalysts/initiators which could be strongly or weakly linked with toxic eventualities in final polymer. To address this issue, we have joined to mentioned afford[1] and designed heteroleptic zinc(II) complexes chelated by two types of β-enaminone ligand (BEN) containing electron rich groups (OMe or CH_2NMe_2) in side chain and substituted by alkyl, carborane, amido or alkoxo ligand on central zinc atom with coordination framework of TMEDA (**Figure 1**). The combination of carborane and BEN parts forming "chiral" vicinity of metal in one specie open new area of coordination chemistry and could contribute to study of complexes with higher added value.
The synthesis of target compounds can be described as a ligand exchange reaction between homoleptic zinc BEN complex and lithium precursor RLi (R: Me, Et, ^{i}Pr, ^{n}Bu, ^{s}Bu, ^{t}Bu, *o*-carborane) or as a substitution of alkyl moiety of heteroleptic zinc precursor by phenoxy (PhOH) or amide entity ($PhNH_2$, $^{t}BuNH_2$). Their structural features and catalytic properties during ROP reactions of lactide, caprolactone or trimethylene carbonate will be discussed.

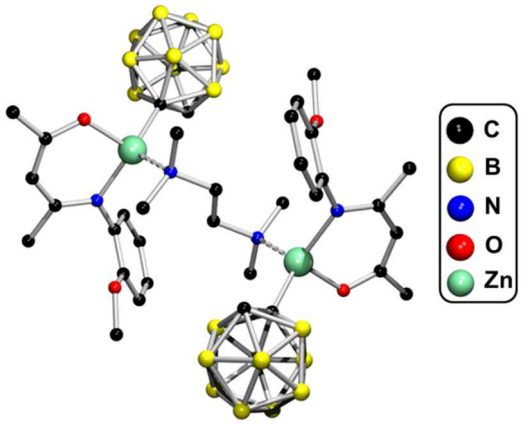

Figure 1: The structure of one of the compounds studied.

Acknowledgements: We gratefully acknowledged the financial support of the Czech Science Foundation (project no. GA CR 16-01618S).

References:

1. Gerling, K. A.; Rezayee N. M.; Rheingold A. L.; Green D. B.; Fritsch J. M. *Dalton Trans.* **2014**, *43*, 16498.
2. Olejník R.; Bílek M.; Růžičková Z.; Hoštálek Z.; Merna J.; Růžička A. *J. Organomet. Chem.* **2015**, *794*, 237.

Non Noble Metal Catalyzed Hydrogen Borrowing Reactions

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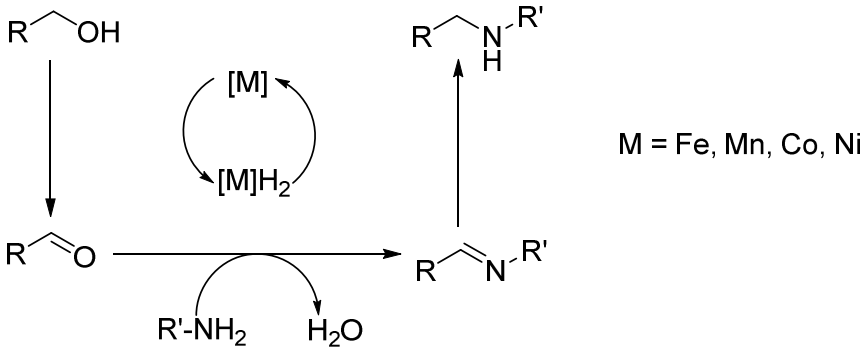
The development of more efficient and selective methodologies are prime importance to achieve the goals of green chemistry. Among the different eco-friendly approaches, hydrogen borrowing (hydrogen auto transfer) reactions are considered to be a greener and atom economical reaction since only water is produced as a side product. Based on these aspects, the borrowing hydrogen methodology received great attention in the last years.[1] Very interestingly, utilization of abundant and sustainable alcohols as the feedstocks for the production of fine chemicals is highly attractive in sustainable chemistry and this alcohols play an important role as H_2 donor, without necessity of external reductant.[2] Since the groups of Grigg[3] and Watanabe[4] reported transition-metal catalyzed *N*-alkylations of amines by means of alcohols as the alkylating agents, continuous efforts have been made towards both *N*-alkylation of amines and C-alkylation of ketones and related compounds through a hydrogen-autotransfer strategy. In the last decade, effective alkylation reactions were already reported with noble transition metals.[5] Obviously, in terms of sustainability, such precious transition metals should be replaced by more eco-friendly, inexpensive and widely abundant first row based metals. In recent years, Iron,[6] cobalt[7] and manganese[8] complexes have been well studied in hydrogen borrowing reactions.

Inspired from recent development based on non noble metals, we performed C-C and C-N bond formation with alcohols and currently we are studying their other applications.



Scheme 1: Hydrogen borrowing technology in the *N*-alkylation of amines with alcohols.

References:

1. J. Leonard, A. J. Blacker, S. P. Marsden, M. F. Jones, K. R. Mulholland, R. Newton, *Org. Process Res. Dev.* **2015**, *19*, 1400.
2. K. Barta,P. C. Ford, *Acc. Chem. Res.* **2014**, *47*, 1503.
3. R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit, N. Tongpenyai, *J. Chem. Soc., Chem. Commun*. **1981**, 611.
4. Y. Tsuji, R. Takeuchi, H. Ogawa, Y. Watanabe, *Chem. Lett* **1986**, 293.
5. Q. Yang, Q. Wanga, Z. Yu, *Chem. Soc. Rev*. **2015**, *44*, 2305.
6. Y. Tao, B. L. Feringa, K. Barta, *Nat. Commun.* **2014**, *5*, 5602.
7. S. Rosler, M. Ertl, T. Irrgang, R. Kempe, *Angew. Chem. Int. Ed*. **2015**, *54*, 15046.
8. S. Elangovan, J. Neumann, J.-B. Sortais, K. Junge, C. Darcel, M. Beller, *Nat. Commun*. **2016**, *7*, 12641.

Chiral Aminoaziridine Ligands in Asymmetric Addition of Arylzinc Reagents to Aldehydes

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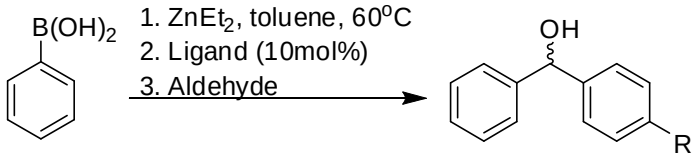
The enantioselective sunthesis of new carbon–carbon bonds is one of the most important and fundamental strategies in modern organic chemistry. Among them, the enantioselective aryl transfer to aldehydes is a current topic in synthetic organic chemistry.[1] Futhermore, diarylmethanols are precursors of many compounds which exhibit biological and pharmacological activity.[2]
We developed in our group new strategies for the synthesis of chiral ligands being 2-(aminomethyl)aziridine derivatives. The key starting material of aforementioned compounds have been used an optically pure ester derived from *N*-trityl-aziridine-2-carboxylic acid. All of the aminoaziridines were tested as chiral catalysts in the asymmetric addition of arylzinc system generated in situ from phenylboronic acid and diethylzinc to aldehydes (**Scheme 1**). The products were formed in high chemical yields and enantiomeric excess.



Scheme 1: Asymmetric addition of arylzinc generated from phenylboronic acid and Et_2Zn to aldehydes

Acknowledgements: Financial support by the National Science Center (Poland-Cracow) Grant PRELUDIUM 8 (UMO-2014/15/N/ST5/02897) is gratefully acknowledged.

References:

1. K Shimizu, H. Uetsu, T. Gotanda, K. Ito K. *Synlett* **2015**, 1238.
2. F. Schmidt, R. T. Stemmler, J. Rudolph, C. Bolm *Chem. Soc. Rev.* **2006**, *35*, 454.

Catalytic Transoximation to Aldehyde and Ketone

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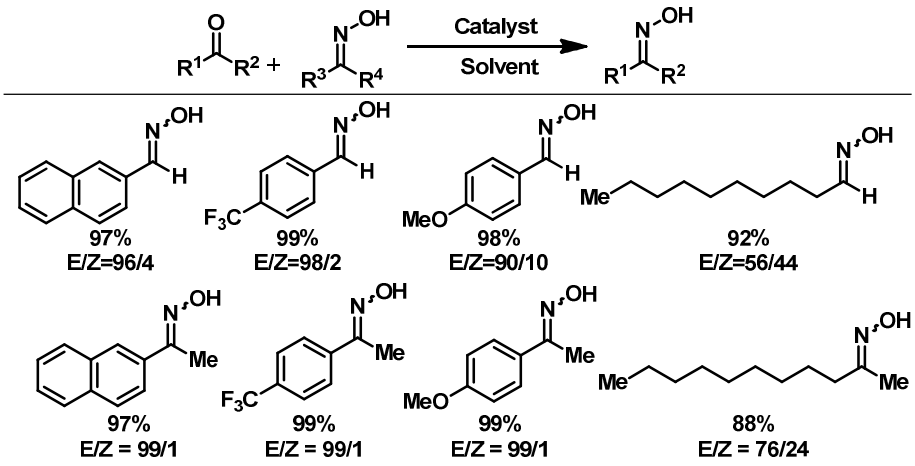
Oximes are highly stable, which are used for the protection of carbonyl compounds and also and important key intermediates in the generation of nitriles via dehydration[1)] and amides via Beckmann rearrangement. [2)] In particular, ε-caprolactam is produced from cyclohexanone oxime to provide a source of nylon 6 on an industrial scale. The dehydration of aldehydes and ketones with hydroxylamine is the typical synthetic method for oximes. [3)] However, hydroxylamine is explosive and unstable. To reduce these risks, hydroxylamine is often converted to various salt forms using acids such as hydrogen chloride, sulfuric acid, or phosphoric acid. The use of these salts for oxime synthesis requires the use of stoichiometric amounts of base, resulting in the generation of large amounts of byproducts such as ammonium sulfate. Ammoximation using a titanosilicate heterogeneous catalyst (TS-1) is an alternative method used in specific oxime syntheses on an industrial scale to avoid the direct use of hydroxylamine.[4)] However, TS-1 is not available commercially and is difficult to prepare.

Transoximation is one of the transamination and transoximaze observed from pupae of silkworm by Yamafuji *et al*.[5)] They suggested that the oximes were transformed to carbonyl compounds without proceeding through the hydroxylamine as an intermediate.[6)] Transoximation reaction from used acetoxime to carbonyl compounds catalyzed by acetic acid was developed.[7)] However, this reactions were required harsh conditions and specific equipment, therefore we attempted catalytic transoximation to aldehydes and ketones under mild conditions and report the details in this symposium (Scheme 1).[8)]



Scheme 1: Scope of substrates for catalytic transoximation

Acknowledgements: This work was financially supported by a Kaneka Award in Synthetic Organic Chemistry, Japan

References:

1. Selected examples: Ishihara K.; Furuya Y.; Yamamoto H. *Angew. Chem. Int. Ed.* **2002**, *41*, 2983–2986.
2. Beckmann E. *Ber. Dtsch. Chem. Ges.* **1886**, *19*, 988–993.
3. Sharghi H.; Hosseini M. *Synthesis* **2002**, 1057–1059.
4. Ichihashi H. *Catalysts Catal.* **2005**, *47*, 190–195.
5. Yamafuji K.; Omura H.; Yoshihara F.; Yoshitake M.; Oyama N. *Enzymol.* **1958**, *19*, 180–185.
6. Yamafuji K.; Omura H.; Miura M. *Enzymol.* **1953**, *16*, 75–80.
7. Newman M. S.; Lutz W. B. *J. Am. Chem. Soc.* **1956**, *78*, 2469–2473.
8. Hyodo K.; Togashi K.; Oishi N.; Hasegawa G.; Uchida K. *Green Chem.* **2016**, *18*, 5788–5793.

Dirhodium-Catalyzed Site-Selective C-H Amination

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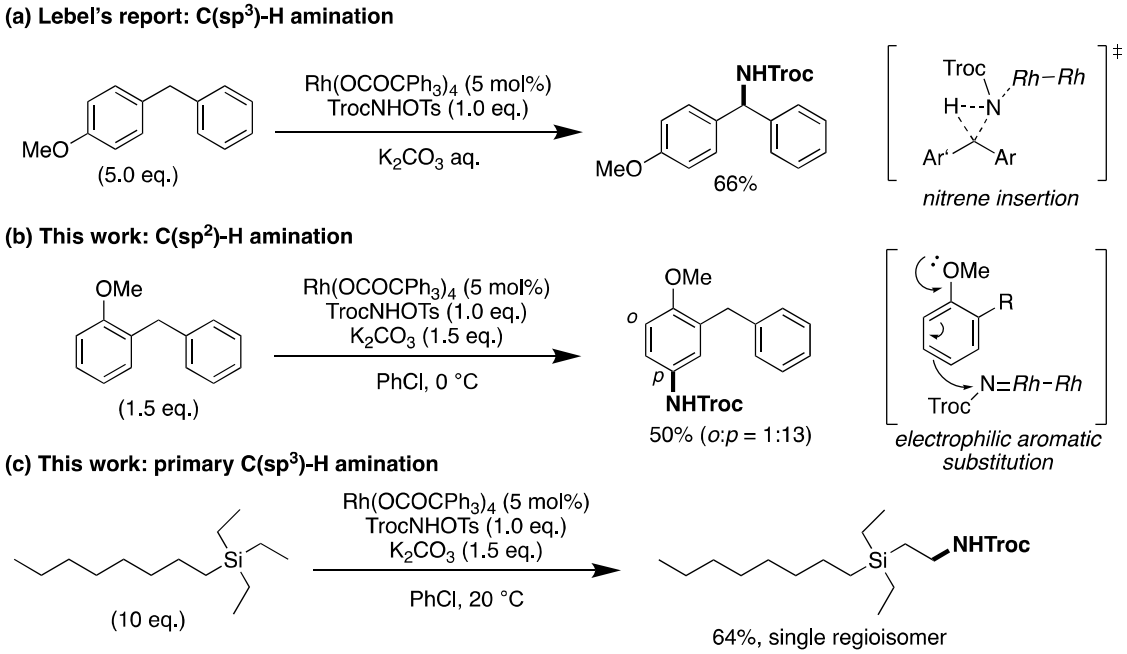
The development of catalytic procedures for the selective modification of unactivated C-H bonds has become a hot topic in modern organic synthesis due to its promise of streamlined and sustainable syntheses of high-value chemicals. In particular, C-N bond forming reaction attracts much attention from synthetic chemists since nitrogen-containing functional groups play key roles in bioactive molecules and functional materials.[1] Rhodium(II) nitrene-mediated C-H insertion reaction is one of the most powerful methods for unactivated C-H amination.[2] In 2007, lebel *et al.* reported C(sp^3)-H amination reaction by rhodium(II)-catalyzed nitrene transfer, using TrocNHOTs as a nitrogen source (Scheme 1a).[3] Here we report two types of site-selective C-H amination reaction using modified Lebel's methods. One is *para*-selective C(sp^2)-H amination of alkoxyarenes via electrophilic aromatic substitution[4] (Scheme 1b). The other is primary C(sp^3)-H amination at β-position of a silyl group, utilizing σ-donor ability of C-Si bonds (Scheme 1c). The details about reaction optimization and substrate scope will be discussed in the presentation.



Scheme 1:(a) Lebel's report: C(sp^3)-H amination via nitrene insertion. (b) This work: C(sp^2)-H amination via electrophilic aromatic substitution. (c) This work: primary C(sp^3)-H amination

Acknowledgements: This research was financially supported by Grants-in-Aids for Scientific Research S (26221301) and Scientific Research on Innovative Area 'Middle Molecular Strategy' (16H01148).

References:

1. Jiao, J.; Murakami, K.; Itami, K. *ACS Catal.* **2016**, *6*, 610.
2. For example, Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378.
3. Lebel, H.; Huard, K. *Org. Lett.* **2007**, *9*, 639.
4. Paudyal, M. P.; Adebesin, A. M.; Burt, S. R.; Ess, D. H.; Ma, Z.; Kürti, L.; Falck, J. R. *Science* **2016**, *353*, 1144.

Aminolytic Kinetic Resolution of α-Nitroepoxides: A DFT Study

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Optically active epoxides are among the most useful class of compounds in organic synthesis.[1] Asymmetric epoxidation of alkenes is undoubtedly a straighforward and deeply investigated approach to obtain a great variety of chiral epoxides.[2] However, the kinetic resolution of racemic epoxides demonstrated to be a powerful and unique tool when highly challenging epoxides are the required targets, as demostrated by the metal-complex based systems developed by Sharpless, Jacobsen and Katsuki. Biocatalytic kinetic resolutions of racemic epoxides are also useful in this respect, although being highly substrate-specific. We recently developed the first enantioselective synthesis of β-aryl-substituted α-nitroepoxides, exploiting an organocatalyzed aminolytic kinetic resolution (AKR). Racemic α-nitroepoxides are ring-opened by aniline in the presence of a readily available Cinchona alkaloid-derived thiourea to give unreacted epoxides in acceptable yied, up to 95% ee and α-amino ketones as products of interest (**Figure 1**).[3]. To shed light on the mechanism of the reaction and in view of improving the efficiency of this process, we started a DFT investigation of the AKR, whose results will be illustrated.

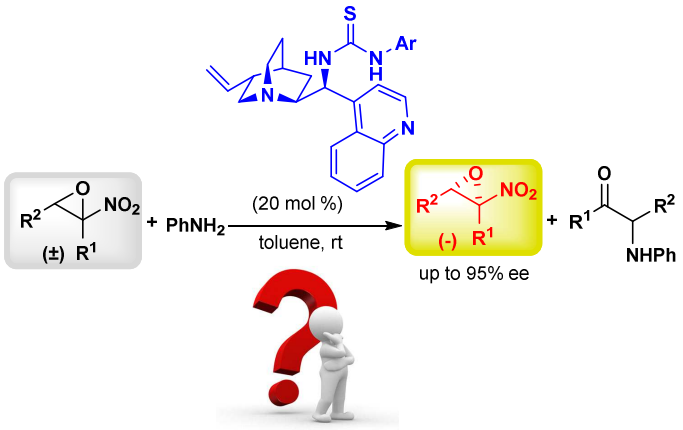

Figure 1: Aminolytic kinetic resolution of racemic β-aryl-substituted α-nitroepoxides.

Acknowledgements: We thank MIUR for financial support.

References:

1. *Aziridines and Epoxides in Organic Synthesis*, (Yudin, A. Ed.), Wiley-VCH, Weinheim, **2006**.
2. *Asymmetric Synthesis of Three-Membered Rings*, (Pellissier, H.; Lattanzi, A.; Dalpozzo, R. Eds.), Wiley-VCH, Weinheim, **2017**.
3. Meninno, S.; Napolitano, L.; Lattanzi, A. *Catal. Sci. Technol.*, **2015**, *15*, 124.

Normal vs. Abnormal Aluminum NHCs: Genesis, Synthesis, Structure, Theoretical Calculations and Reactivity

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Aluminium, a cheap microbiogenic element and the most abundant metal in the earth's crust plays an important role in organometallic/coordination compounds of main group elements both from the economic as well as from the environmental point of view. The first unusual example of congested Lewis adducts built up from the *N*-heterocyclic carbene as a σ-electron donating system and aluminium(III) species was reported by Arduengo[1] in early 1990s. Increasing interest of their applications in homogeneous catalysis, organic syntheses as well as material science has been recognized in last years. However, since then only a little attention has been directed toward aluminium-carbene complexes. In addition, a handful of examples of abnormal carbenes of main group metals[2] and zinc[3] (abnormal carbenes are mainly studied for d-block elements) are known.

The direct synthesis, structure and an interesting reactivity of normal vs. abnormal amidinato-aluminium *N*-heterocyclic carbenes supported by a series of theoretical calculations will be demonstrated.

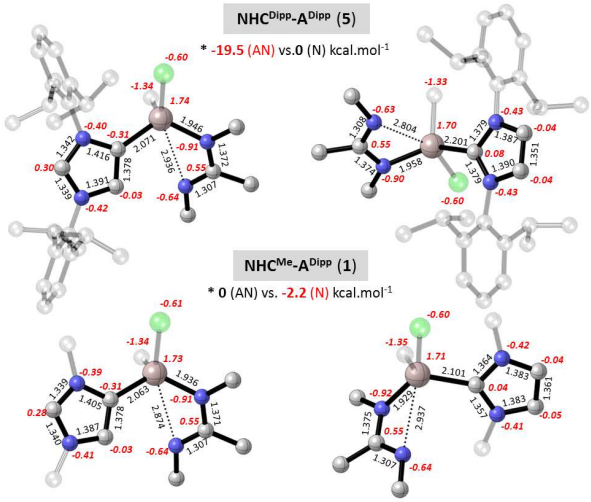

Figure 1: Comparison of normal(N)/abnormal(AN) type of aluminum NHC-amidinates **5** and **1** on the basis of DFT calculations. The Dipp groups of amidinato ligands are omitted for clarity. Selected interatomic distances are black in Å and NBO charges are red.

Acknowledgements: Financial support from the Czech Science Foundation (grant nr. 17-10377S) is acknowledged.

References:

1. Arduengo A. J.; Dias H. V. R.; Calabrese J. C.; Davison F. *J. Am. Chem. Soc.* **1992**, *114*, 9724.
2 for example: (a) Cui H.; Cui Ch. *Dalton Trans.* **2011**, *40*, 11937; (b) Cui H.; Shao Y.; Li X.; Kong L.; Cui Ch. *Organometallics* **2009**, *28*, 5191; (c) Whittell G. R.; Balmod E. I.; Robetson A. P. M.; Patra S. K.; Haddow M. F.; Manners I. *Eur. J. Inorg. Chem.* **2010**, 3967; (d) Turbervill R. S. P.; Goicoechea J. M. *Aust. J. Chem.* **2013**, *66*, 1131.
3. Jochmann P.; Stephan D. W. *Chem.-Eur. J.* **2014**, *20*, 8370.

Designing of New Nanostructured Zinc Oxide Materials for Coatings of Metallic Surfaces

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Zinc oxides particle have been paid more attention for their unique properties such as: unexpensive, n-type semiconductor with a wide band gap having optical transparency in the visible range. This study focuses on sol-gel method due to the following advantages: easiness of the synthesis, low temperature of decomposition and control on the chemical composition.[1] In this work, a simple sol gel method was used to prepare ZnO nanoparticles. The aim of this study was to synthesize hybrid nanomaterials based on zinc oxide, and to investigate the morphological properties and the silica precursor type effect on the particle size. Two types of silica precursors were used: phenyltrietoxysilane (PhTES) and octadecyltrietoxysiolane (ODTES) to obtain nanostructured zinc oxide materials. The final solutions were deposited on different mettalic substrates (aluminium, cooper and zinc) in order to realize coatings with variaous wettability. Detailed structural and morphological investigations were carried out using Dynamic Light Scattering (DLS) technique, microscopy analyses (TEM, SEM – **Figure 1**), Fourier transform infrared spectroscopy (FTIR) and contact angle measurement.

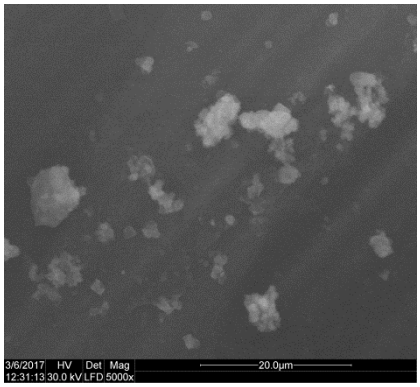

Figure 1: SEM image of the nanostructured zinc oxide particles modified with PhTES.

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References:

1. Jurablu S.; Farahmandjou M.; Firoozabadi T. P. *J. Sci. I. R. Iran* **2015,** *26(3)*, 281.

Intermolecular Aza-Diels-Alder Reaction for the Diastereoselective Synthesis of Tetrahydropyridines

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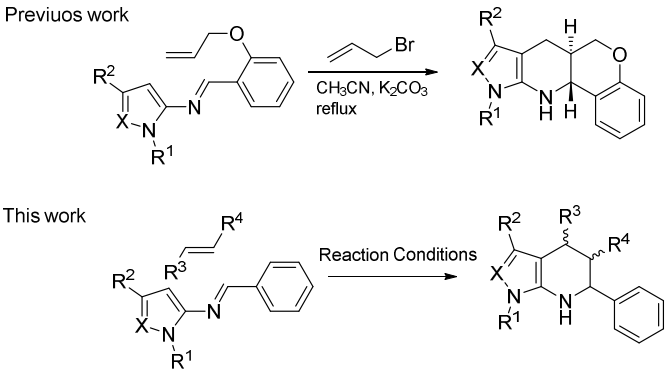
The aza Diels-Alder reaction is a subclass of the more general hetero Diels-Alder reaction and is one of the most valuable tools for the synthesis of heterocycles containing nitrogen. The reaction posses a general synthetic utility, up to three new stereogenic centers, one ring and two carbon-carbon bonds are formed.[1] Based on our previous experience using 5-amino-1-(*tert*-butyl)-1*H*-pyrrole-3-carbonitrile and 3-methyl-1-phenyl-1*H*-pyrazol-5-amine in the synthesis of chiral tetracyclic dihydrochromeno-pyrrolo- and dihydrochromenopyrazolo-tetrahydropyridines using an intramolecular aza-Diels-Alder reaction,[2] we decided to study the intermolecular version of this reaction.

We have previously postulated a normal electron demand aza-Diels-Alder mechanism restricted however to the fact that the use of frontier molecular orbital (FMO) theory to determine the type of interaction between diene and dienophile is not straightforward because the HOMO and LUMO concerned were in the same molecule.[3] The use of the intermolecular version, always based on the use of aminoheterocycles, has allowed us to confirm our mechanistic proposal and to broad the possible products to be obtained since different pairs diene-dienophile can be used. Regarding to the stereoselectivity we found out that non-covalent interactions play an important role in the control of the diastereo- and regio- selectivity of the reaction. Theoretical calculations have been performed to evaluate this contribution in terms of energy of intermediates transition states and final products.



Scheme 1. Inter- and intra- molecular aza-Diels-Alder reaction

Acknowledgements: We thank the Fundação para a Ciência e Tecnolgia for financial support....

References:

1. Domingo L.R., Aurell M.J., Sáez J.A. and Mekelleche S.M., *RSC Adv*., **2014**, 4, 25268.
2. Lezana N., Matus-Pérez M., Galdámez A., Lühr S. and Vilches-Herrera M. *Green Chem*., **2016**, 18, 3712.
3. Soto-Delgado J., Domingo L. and Contreras R., *Org. Biomol. Chem*., **2010**, 8, 3678.

Nickel-Catalyzed Reductive Dicarbofunctionalization of Olefins

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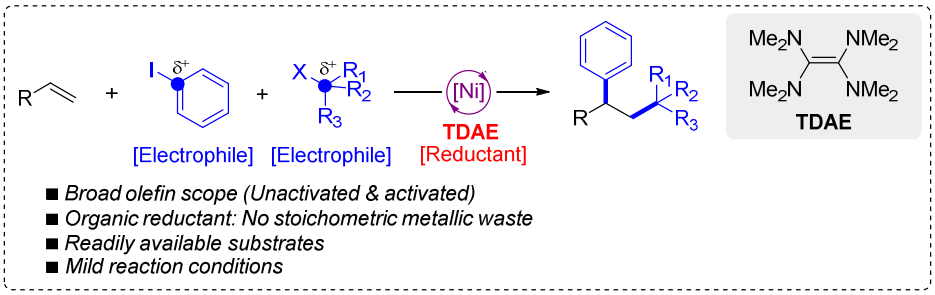
Intermolecular processes involving formation of two new C-C bonds across multiple bonds are in high demand as they provide a fast access to complex molecules from readily available substrates.[1] In this context, our group has previously developed metal catalyzed multicomponent dicarbofunctionalizations of terminal alkynes using boronic acids and alkyl halides as carbon sources.[2] Given our ongoing interest in the field and the scarce number of examples for efficient and general dicarbofunctionalization of double bonds with alkyl derivatives[3], we aimed to expand the applicability of these processes towards the use of alkenes. Here, we present the first example of an intermolecular, three-component reductive dicarbofunctionalization of olefins using nickel catalysis under reductive conditions with aryl iodides and alkyl iodides as reaction partners.[4] The involvement of alkyl radicals along the reaction pathway allows the regiocontrolled addition of the alkyl group exclusively at the terminal position of the alkene. In contrast to the previous methodologies, the reaction tolerates a wide range of olefins and the carbon sources do not require additional functionalizations. Moreover, the use of an organic reductant (TDAE) not only avoids the generation of stoichiometric metallic waste, but also proved to be crucial for the success of this transformation.



Acknowledgements: We thank the European Research Council (ERC Starting grant agreement no. 307948) and the Swiss National Science Foundation (SNF 200020_146853) for financial support. We also thank Prof. Anthony Linden for the X-ray diffraction analysis.

References:

1. a) E. Negishi, Z. Huang, G. Wang, S. Mohan, C. Wang, H. Hattori, *Acc. Chem. Res.* **2008**, *41*, 1474; b) A. B. Flynn, W. W. Ogilvie, *Chem. Rev.* **2007**, *107*, 4698; c) M. Ihara, K. Fukumoto, Angew. Chem. Int. Ed. **1993**, *32*, 1010; d) M. J. Chapdelaine, M. Hulce *Org. React.* **1990**, *38,* 225.
2. a) Z. Li, A. García-Domínguez, C. Nevado, *Angew. Chem. Int. Ed.* **2016,** *55*, 6938; b) Z. Li, A. García-Domínguez, C. Nevado, *J. Am. Chem. Soc.* **2015**, *137*, 11610.
3. For Ni-catalyzed reactions see: a) J.-W. Gu, Q.-Q. Min, L.-C. Yu, X. Zhang *Angew. Chem. Int. Ed.* **2016**, *55*, 12270; b) T. Qin, J. Cornella, C. Li, L. R. Malins, J. T. Edwards, S. Kawamura, B. D. Maxwell, M. D. Eastgate, P. S. Baran *Science* **2016**, *352*, 801; c) J. Terao, F. Bando, N. Kambe, *Chem. Commun.* **2009**, 7336.
4. A. García Domínguez, Z. Li, C. Nevado *J. Am. Chem. Soc.* **2017**, DOI: 10.1021/jacs.7b03195

Palladium(II) Pyrazolyl–pyridyl Complexes Containing a Sterically Hindered N-Heterocyclic Carbene Moiety for the Suzuki-Miyaura Cross-coupling Reaction

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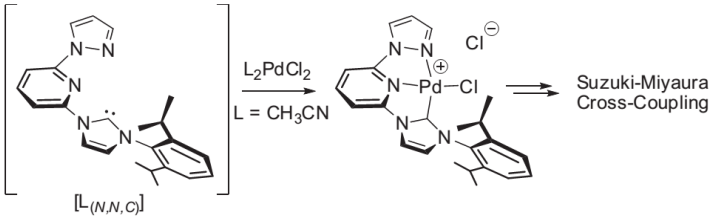
The design and synthesis of new ligands featured by a mixeddonor atom set and including one or more N-heterocyclic carbene (NHC) frameworks have received a great deal of attention in the last decade because of their high versatility in the fields of coordination chemistry and homogeneous catalysis.[1] The strong rdonor and relatively weakp-acceptor properties of NHCs make them valuable mimics of phosphines in transition-metal coordination chemistry.[2] In addition, NHC frameworks generally present higher donor capability and basicity than phosphines and offer more versatility to the easy tuning of their stereo-electronic properties compared to their P-based counterparts whose manipulation is often not trivial.[3]

In this work cationic palladium complexes stabilized by a tridentate neutral {N,N,C} ligand containing a sterically hindered N-heterocyclic carbene (NHC) moiety have been prepared and characterized.[4] The nature of the anionic counterion in the palladium complex has been varied to get crystals suitable for X-ray diffraction. The square planar structure of one of these complexes along with the axial contribution of the sterically hinderedNHCfragment has been confirmed by X-ray analysis. In addition, all the isolated [{κ^3-N,N,C}$Pd^{II}Cl]^+X^-$ [X^- = Cl, PF_6,BF_4, $B(C_6H_3Cl_2)_4$] ion pairs have been scrutinized as catalysts in the cross-coupling Suzuki-Miyaura reaction between phenylboronic acid and variably substituted halo-aryl acceptors. Selected issues from this series have shown improved catalyst turn-over frequencies (TOFs) with respect to structurally related catalytic systems of the *state-of-the-art* (**Scheme 1**).



Scheme 1: General sketch of ligand and complexes described in this work.

Acknowledgements: We thank the Bilateral CNR-RFBR Project (Italy-Russian Federation) and the common program of the Russian Foundation for Basic Research and the Government of the Republic of Tatarstan (project 15-43-02667) for the financial support of this work.

References:

1. G.C. Fortman, S.P. Nolan, *Chem. Soc. Rev*. **2011**, *40*, 5151.
2. R.H. Crabtree, *J. Organomet. Chem*. **2005**, *690*, 5451.
3. M.N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature*. **2014**, *510*, 485.
4. L. Luconi, Z. Gafurov, A. Rossin, G. Tuci, O. Sinyashin, D. Yakhvarov, G. Giambastiani, *Inorg. Chim. Acta*, doi.org/10.1016/j.ica.2017.03.026.

Synthesis of Polyfunctionalized Pyrazoles *via* (3+2)-Cycloadditions of Fluorinated Nitrile Imines and Enol Ethers

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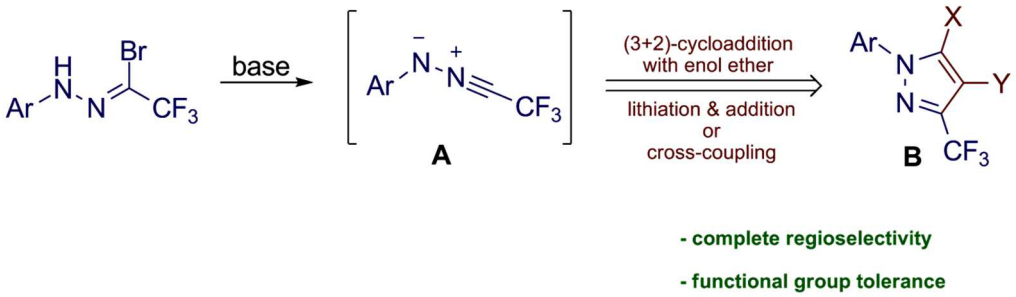
The [3+2]-cycloaddition reaction (Huisgen reactions) is considered as one of the most powerful method, which can be applied for the synthesis of manifold five-membered heterocycles. In this context, nitrile imines are classified as an important group of propargyl-type 1,3-dipoles widely applied for the preparation of various *N*-containing systems. Recently, trifluoroacetaldehyde arylhydrazones[1] have been recognized as suitable substrates for the generation of the CF_3-nitrile imines **A** *via* radical bromination and subsequent base-induced dehydrohalogenation.[2,3] Here, we report, that these 1,3-dipoles can be efficiently trapped with enol ethers to yield trifluoromethylated pyrazole derivatives **B**. Further transformations of **B** via cross-coupling reactions and lithiation/addition procedure will be also presented.



Scheme 1: Application of fluorinated nitrile imines **A** in the synthesis of pyrazoles **B**

Acknowledgements: Financial support by the National Science Centre (Poland; grant PRELUDIUM no 2016/21/N/ST5/01254)
is gratefully acknowledged.

References:

1. A. Wojciechowska, M. Jasiński, P. Kaszyński *Tetrahedron* **2015**, *71,* 2349.
2. G. Mlostoń, K. Urbaniak, G. Utecht, D. Lentz, M. Jasiński *J. Fluorine Chem.* **2016**, *192,* 147.
3. P. Grzelak, G. Utecht, M. Jasiński, G. Mlostoń *Synthesis* **2017**, *49,* 2129.

Straightforward Access to Trifluoromethylated 2,3-Dihydro-1,3,4-thiadiazoles by using Nitrile Imines Derived from Fluoral and C=S Dipolarophiles

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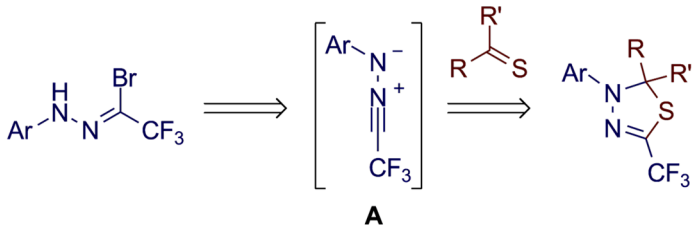
Nitrogen and sulfur containing heterocycles including 1,3,4-thiadiazole derivatives are extensively applied in pharmaceutical industry e.g. as anti-inflammatory, anticancer and antidepressant drugs.[1] In this context, special attention has been paid to fluorinated analogues as potential materials of unique properties. Here we report, that fluorinated nitrile imines **A,** readily available from the corresponding fluoral-derived hydrazonoyl bromides, smoothly react with C=S dipolarophiles (thioketones and thiochalcones) to give 1,3,4-thiadiazole derivatives in a fully chemo- and regioselective manner.[2] The title reactions proceeded with high efficiency and broad functional group tolerance.



A

Scheme 1: General synthesis of trifluoromethylated 2,3-dihydro-1,3,4-thiadiazoles

Acknowledgements: Financial support by the National Science Centre (Poland; grant MAESTRO no 2012/06/A/ST5/00219)
is gratefully acknowledged.

References:

1. Y. Hu, C.-Y. Li, X.-M. Wang, Y.-H. Yang, H.-L. Zhu *Chem. Rev*. **2014**, *114*, 5572.
2. a) G. Mlostoń, K. Urbaniak, G. Utecht, D. Lentz, M. Jasiński *J. Fluorine Chem.* **2016**, *192,* 147*; b)* P. Grzelak, G. Utecht, M. Jasiński, G. Mlostoń *Synthesis* **2017**, *49,* 2129.

Syntheses of Carolacton Derivatives as Highly Potent Biofilm Inhibitors

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Carolacton (**1a**) is a secondary metabolite of myxobacterium *Sorangium cellulosum* (*So ce960*). In 1988, it was discovered and isolated because of its antibiotic activity against *E. coli* strain *tolC* bacteria in the Helmholtz Centre for Infection Research in Braunschweig.[1,2]
In 2012, the first total synthesis of Carolacton (**1a**) was achieved in our laboratories which was based on key dissections depicted in figure 1.[3]
Carolacton (**1a**) distinguishes itself in its unique ability to inhibit biofilms of the caries- and endocarditis-associated bacterium *Streptococcus mutans* even at nanomolar concentrations. Biofilm-associated infections have become a major concern in clinical treatment since bacterial biofilms are inherently resistant to extreme pH- and temperature conditions as well as antimicrobial agents. The synthesis of natural products and derivatives with novel modes of actions is a promising way to inhibit biofilms. However, the exact mode of action of Carolacton (**1a**) is still not elucidated.[4]

Here we present our recent results towards the syntheses of highly active Carolacton derivatives including Carolactam (**1b**) and provide preliminary results on the relationship between structure and activity. In this regard, the syntheses of demethylated derivatives such as **2**-**4** are of particular interest to figure out the influence of the presence of methyl groups - widespread abundant in polyketides - on the global conformation of such macrolactons and link these data to biological activity (**Figure 1**).

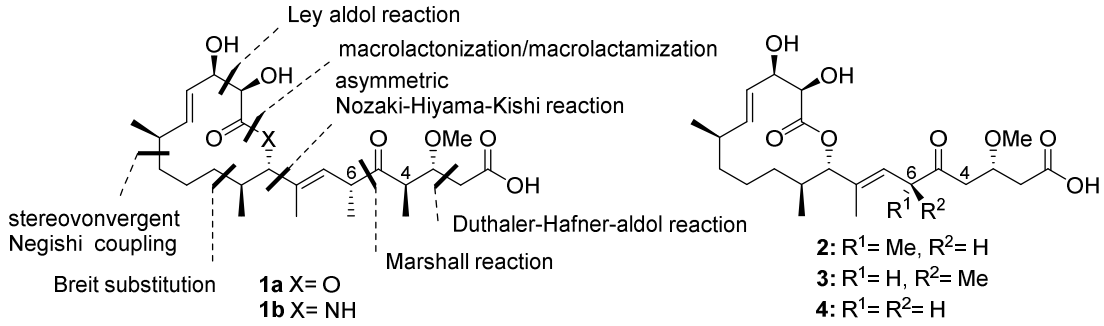

Figure 1: Retrosynthetic key dissections of Carolacton (**1a**) and Carolactam (**1b**) and new demethylated derivatives (**2**-**4**).

References:

1. G. Höfle, *Scientific Annual Report of the GBF*, **1998**, p. 101.
2. H. Irschik, R. Jansen, K. Gerth, *J. Antibiot.* **1987**, *40*, 7-13.
3. T. Schmidt, A. Kirschning, *Angew. Chem. Int. Ed.* **2012**, *51*, 1063-1066.
4. M. Reck, K. Rutz, B. Kunze, J. Tomasch, S. K. Surapaneni, S. Schulz, I. Wagner-Döbler, *J. Bacteriol*. **2011**, *193*, 5692–5706.

Alkyl Radical Addition to Simple Carbonyls Facilitated by Double Activation Catalysis

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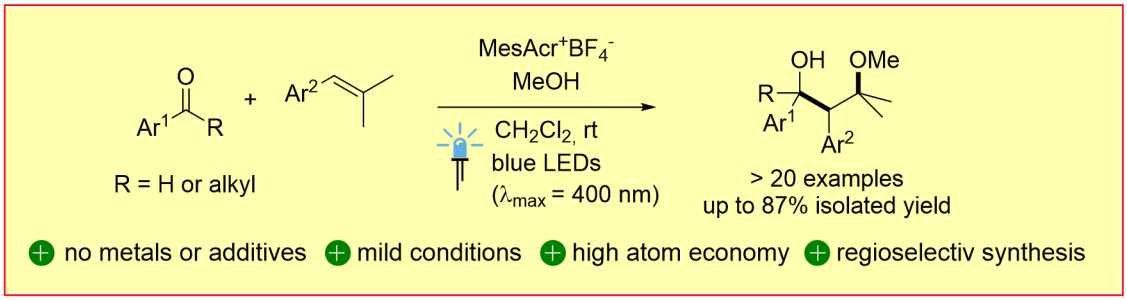
Over the last decade visible light photoredox catalysis has emerged as a powerful concept in the field of synthetic organic chemistry.[1] Based on the unique properties of the photoredox catalysts, open shell species can be selectively generated under mild conditions. Numerous reactions have been developed focusing mostly on the functionalization of the generated radicals or their trapping with weak C=X bonds (X = C or N) as radical acceptors. However, applying simple carbonyl compounds like aromatic aldehydes as intermolecular radical acceptors has yet not been described.[2] Utilizing 9-Mesityl-10-methylacridinium tetrafluoroborate ($MesAcr^+BF_4^-$) as a visible light photoredox catalyst we found that benzylic radicals, derived from styrenes after cation trapping with methanol, add regioselectively to the carbonyl carbon of aromatic aldehydes delivering the corresponding alcohols (see Scheme 1). The reaction proceeds under extremely mild conditions, without the need of any additives, is metal free, highly atom economical and gives the products in good yields. Using this three-component reaction versatile building-blocks can be obtained in a single step.



Scheme 1: Visible light mediated bisfunctionalization of olefins.

Acknowledgements: We thank the DFG (German Research Foundation) for financial support.

References:

1. For selected reviews, see: a) Prier C. K.; Rankic D. A.; MacMillan D. W. C. *Chem. Rev*. **2013**, *113*, 5322. b) Romero N. A.; Nicewicz D. A. *Chem. Rev*. **2016**, *116*, 10075. c) Skubi K. L.; Blum T. R.; Yoon T. P. *Chem. Rev*. **2016,** 116, 10035.
2. a) Miyabe H.; Ueda M.; Naito T. *Synlett* **2004**, 7, 1140. b) Hoffmann A. *Pure Appl. Chem.* **2007**, *79*, 1949. c) Liu D.; Liu C.; Lei A. *Chem. Asian J*. **2015**, *10*, 2040. d) Hippler H.; Viskolcz B. *Phys. Chem. Chem. Phys*. **2002**, *4*, 4663.

Dendrimeric Novel Perylene- Cyclophosphazene Dyad: Synthesis, Characterization and Photophyisical Properties

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Organic planar molecules that present strong π- π interaction have been used an appropriate structure to study the properties of thin solid films. Perylene derivatives exhibits comparably high electron affinity of the large band-gap material, large visible extinction coefficients, photostability, which make them candidates for applications in electronic and optical devices such as field-effect transistors, electrophotographic applications, and photovoltaic devices.[1]

In this study, we synthesized, characterized and invstigate photophyisical properties of novel denrimeric hexa substituted perylene derivative of cyclophosphazene compound. In the designed perylene-cyclophosphazene derivative (Figure 1), cyclophosphazene core act as thermally stable carrier where asymmetric perylene chromophore functionalized with branched aliphatic chain as solubilizing agent .

First of all, asymmetric perylene derivative was synthesized in three steps. Perylene derivative contain –OH functional group was reacted with hexachlorocyclotriphosphazatriene (trimer) to obtain perylene substituted cyclophosphazene derivative (Figure 1). All products that will be derived from the reactions were purified; and the structural qualities of them were analyzed by the mass spectrometry, ^{1}H, ^{13}C and ^{31}P NMR spectroscopic techniques. Additionally, fluorescence properties of the compounds were investigated by using UV-vis and fluorescence spectrophotometer.

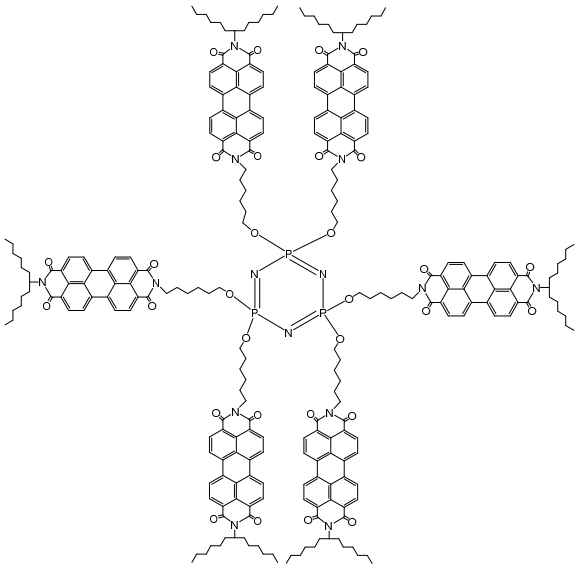

Figure 1: Molecular structure of Perylene- Cyclophosphazene compound

Acknowledgements: We thank the TUBITAK (Grant Number 215-Z-250) for financial support.

References:

1. Schmidt-Mende L.; Fechtenkotter A.;, Mullen K.; Moons E.; Friend R. H.;, MacKenzie J. D. *Science* **2001**, 293, 5532, 1119.

Preparation of 6-Substituted 1,7-Phenanthroline Derivatives as Novel Cross-Species GPR35 Agonists

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We prepared a large array of bufrolin **(Figure 1)** analogues using classical Suzuki-Miyaura coupling and a modified Conrad-Limpach reaction in the development of novel G protein-coupled receptor 35 agonists.

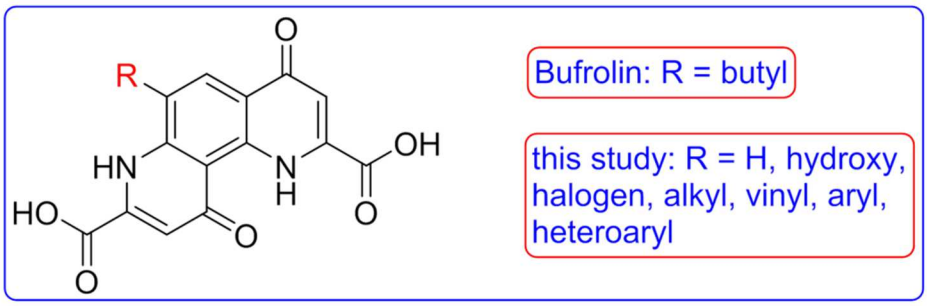

Figure 1: 1,7-phenanthroline-2,8-dicarboxylic acid scaffold

A Novel Hybrid Metalloporphyrin-Magnetic Nanoparticle Catalyst For Epoxidation of Olefins using Molecular Oxygen as Oxidant

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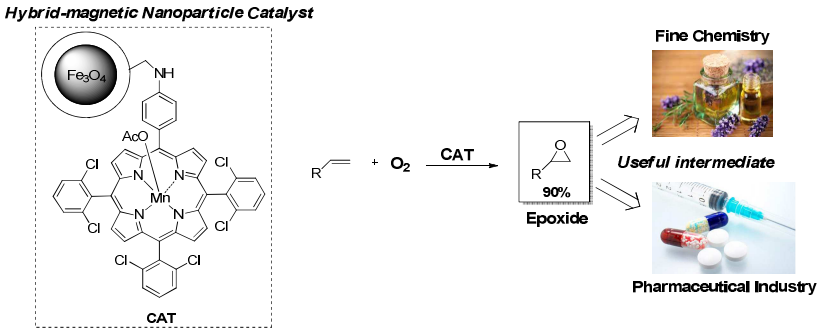
One of the most important challenges in organic synthesis is the development of ecologically/economically attractive and sustainable new catalytic synthetic approaches towards epoxides, which are highly useful intermediates for the synthesis of a variety of fine chemicals and pharmaceutical products.[1] Metalloporphyrins have been receiving increasing attention by scientific community,[2] regarding their efficiency as homogeneous oxidative catalysts,[3] particularly in epoxidation reactions, generally in the presence of non-sustainable oxidants. However, their susceptibility toward oxidative degradation has been a great challenge for chemists. In this way, their immobilization onto inorganic materials offers an interesting alternative to increase catalyst's stability, while providing several other benefits like the possibility of recycling and reuse.

Herein we present our recent results on the synthesis of a manganese-porphyrin bearing an appropriate functional group to promote its linkage to a functionalized magnetic nanoparticle. The new hybrid magnetic nanomaterial was evaluated in epoxidation of olefins, using molecular oxygen (O_2) and isobutylraldehyde as an ecological and sustainable oxygen source **(Scheme 1)**. A comparative study of the metalloporphyrins used either as homogeneous or heterogeneous catalyst and the optimization of reaction conditions to maximize the activity and selectivity of both catalysts were performed and will be discussed. Under optimized reaction conditions, yields up to 90% for epoxide formation were obtained, turning possible to enlarge the reaction scope to natural-based olefins (*e.g.* terpenes), whose epoxides encompass potential biological activity.



Scheme 1: Synthesis of epoxide using molecular oxygen catalyzed by hybrid-magnetic nanoparticle.

Acknowledgements: The authors are thankful to Fundação para a Ciência e Tecnolgia and PT2020 for financial support to Coimbra Chemistry Centre (Pest-OE/QUI/UI0313/2014) and (PTDC/QEQ-MED/3521/2014), respectively. LDD thanks CNPq (Brazil) for PhD grant 232620/2014-8/GDE. RMBC and MJFC thanks FCT for post-doc grant SFRH/BPD/100537/2014 and SFRH/BPD/99698/2014, respectively.

References:

1. Fingerhut, A.; Serdyuk, O.V.; Tsogoeva, S.B.; *Green Chem.* **2015**, 17, 2042.
2. Hiroto, S.; Miyake, Y.; Shinokubo, H. *Chem. Rev.* **2017**, 117, 2910.
3. Henriques, C.A.; Fernandes, A.; Rossi, L.M.; Ribeiro, M.F.; Calvete, M.J.F.; Pereira, M.M. *Adv. Funct. Mater*. **2016**, 26, 3359.

Sustainable Synthetic Approaches of Catalytic Carbonylation Reactions

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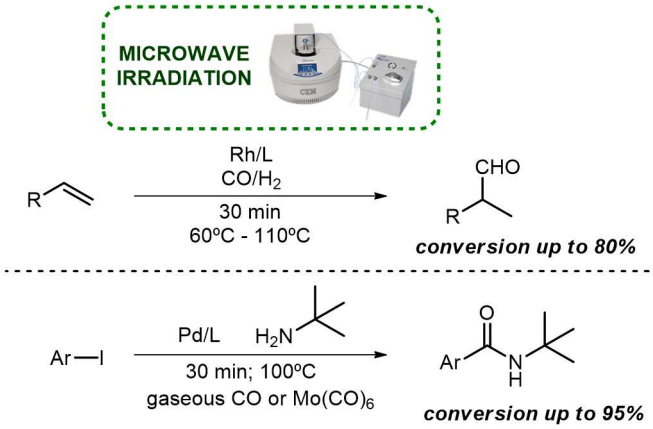
Carbonylation reactions have become a valuable tool for organic synthesis and have been extensively applied in the one-pot preparation of a wide range of chemical compounds. Among them, Pd-catalyzed aminocarbonylation and Rh-catalyzed hydroformylation are effective strategies to synthesize different products, such as amides and aldehydes, which can be used as versatile synthetic intermediates.[1]
Recently, the use of microwave irradiation has been demonstrated as an effective approach to accelerate catalytic carbonylation reactions.[2] Particularly, the hydroformylation of terminal alkenes[3] and sequential isomerization/hydroformylation of natural oils[4] under MW were reported with notable improvements regarding the reaction time, selectivity, atom economy and energy-saving of the process. In addition, Pd-catalyzed aminocarbonylation under MW irradiation has allowed the synthesis of a wide range of carboxamides with higher yields than conventional heating in shorter reaction times.[2]
Herein we present our recent results on the development of Rh-catalyzed hydroformylation of aryl olefins, using a CEM Discover® SP microwave apparatus connected to a gas addition kit. Furthermore, we present sustainable Pd-catalyzed approaches to perform the aminocarbonylation of iodoarenes under MW irradiation. The effect of substrate, nucleophile and reaction conditions will be presented. A comparative study to evaluate the use of high pressure carbon monoxide *versus* $Mo(CO)_6$ as an alternative CO source will be discussed.



Scheme 1: Carbonylation reactions under microwave irradiation

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References:

1. a) Wu, X.; Fang, X.; Wu, L.; Jackstell, R.; Neumann, H.; Beller, M. *Acc. Chem. Res.* **2014**, *47*, 1041−1053; b) Takács, A.; Marosvolgyi-Haskó, D.; Kabak-Solt, Z.; Damas, L.; Rodrigues, F.M.S.; Carrilho, R.M.B.; Pineiro, M.; Pereira, M.M.; Kollár, L. *Tetrahedron*, **2016**, *72*, 247-256
2. Pineiro, M.; Dias, L.D.; Damas, L.; Aquino, G.L.B.; Calvete, M.J.F.; Pereira, M.M. *Inorganica Chimica Acta,* **2017**, *455*, 364
3. Petricci, E.; Mann, A.; Schoenfelder, A.; Rota, A.; Taddei, M. *Org.Lett.*, **2006**, *8*, 3725-3727
4. Damas, L.; Costa, G.N.; Ruas, J.C.; Carrilho, R.M.B.; Abreu, A.R.; Aquino, G.; Calvete, M.J.F.; Pineiro, M.; Pereira, M.M. *Current Microwave Chemistry*, **2015**, *2*, 53-60

Exploring the Potential of One-dimensional Cu(II) Coordination Polymers as Catalysts in Organic Reactions

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Coordination polymers (CPs) have received huge attention as catalysts in various reactions. They offer a unique opportunity to connect Inorganic and Organic Chemistry, providing invaluable information on the catalytic system or the mechanism. In most cases, porous three-dimensional CPs (also known as MOFs) are studied. However, they can present significant drawbacks (difficult to synthesize, low yields and stability). As a result, our group has instead focused on the one-dimensional CPs and their catalytic potential, which has been studied less extensively.[1]

In the present work, a novel semi-rigid benzotriazole-based ligand (**Figure 1, left**) was employed to afford Copper (II) coordination compounds. We obtained two one-dimensional CPs formulated as $[Cu(L)_2(MeCN)_2]\cdot 2(ClO_4)\cdot MeCN$ (**1**) and $[Cu(L)_2(CF_3SO_3)_2]$ (**2**), under easily reproducible conditions and in good yields. Both compounds contain an octahedral Cu(II) center which includes a symmetrical $\{N_4\}$ plane (**Figure 1, right**). Initial studies indicate that both compounds retain their polymeric structure in solution, while cyclic voltammetry showed a quasi-reversible reduction process, assigned to the $[Cu^{II}]\leftrightarrow[Cu^{I}]$ couple.

In this work, we showcase the effectiveness of these coordination polymers towards a) a novel one-step synthesis of 5-aryl-1-(benzylideneamino) 1,4-dihydropyridines,[2] b) the synthesis of propargyl amines through the multi-component reaction (MCR) of an aldehyde, an amine and an alkyne, also known as the A^3 coupling,[3] c) the MCR synthesis of alkyl substituted pyrroles.[4]

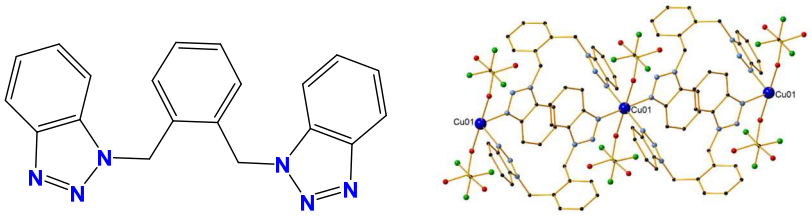

Figure 1: (left) The ligand L used in this study. (right) The 1D framework of compound 2.

Acknowledgements: We thank the EPSRC UK National Crystallography Service at the University of Southampton for the collection of crystallographic data for selected compounds, and the EPSRC UK National Electron Paramagnetic Resonance Service at the University of Manchester for providing magnetic measurements of selected compounds. We also thank Dr. Nikolaos Tsoureas (University of Sussex) for CV data of compound **2**.

References:

1. a) Karmakar A., Rubio G. M. D. M., Guedes da Silva M. F. C.,́Hazra S., Pombeiro A. J. L., *Cryst. Growth Des.*, **2015**, *15,* 4185–4197. b) Mendes, R. F.; Silva, P.; Antunes, M. M.; Valente, A. A.; Almeida Paz, F. A., *Chem. Commun.* **2015**, *51*, 10807–10810.
2. Kallitsakis M.[£], Loukopoulos E.[£], Abdul-Sada A., Tizzard G. J., Coles S. J., Kostakis G. E., Lykakis I. N., *Adv. Synth. Cat*., 2017, **359**, 138. (£ = equal contribution)
3. Loukopoulos E., Kallitsakis M., Tsoureas N., Abdul-Sada A., Chilton N. F., Lykakis I. N., Kostakis G. E., *Inorg. Chem.*, 2017, **56**, 4898–4910.
4. Kallitsakis M., Loukopoulos E., Andreou D., Abdul-Sada A., Kostakis G. E., Lykakis I. N., *to be submitted*.

New Reactions of Molybdenum-Containing Enzymes: Reduction of Nitrite

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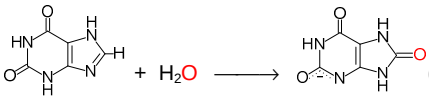
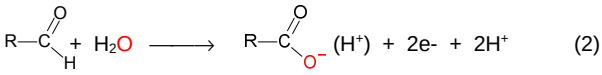
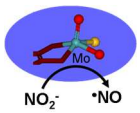
The molybdenum's chemistry is dominated by the formation of oxides and sulfides. Yet, the strong tendency of molybdenum to bind oxo groups is balanced by its ability to easily lose a single oxygen atom, a property that makes molybdenum complexes excellent "oxygen atom exchangers", as long as the thermodynamics of the reaction is favorable - the "oxo transfer hypothesis" coined by Holm and others in the 1980s.[1] Living organism exploited this rich chemistry and developed several oxidoreductases to catalyze oxygen atom transfer reactions essential to fulfill different cellular functions. Typically, the molybdoenzymes catalyze the transfer of an oxygen atom from water to product (oxygen atom insertion) or from substrate to water (oxygen atom abstraction) in reactions that entail a net exchange of two electrons, in which the molybdenum atom cycles between Mo^{6+} and Mo^{4+}, and, most importantly, where the metal is the direct oxygen atom acceptor or donor.[1,2] During the last decade, several *in vivo* and *in situ* evidences suggested that the mammalian molybdoenzymes, present in cells to carry out other functions, namely xanthine catabolism (xanthine oxidase (eq. 1)), aldehyde and sulfite oxidation (aldehyde oxidase (eq. 2) and sulfite oxidase), could also catalyze the nitrite reduction to nitric oxide radical, •NO, an oxygen abstraction reaction (eq. 3).[2,3] In this work, we demonstrated that xanthine oxidase and aldehyde oxidase are the most promising mammalian nitrite reductases and proposed a unified molecular mechanism to explain the simultaneous oxygen atom insertion and abstraction by the enzymes' molybdenum center.[4,5] The physiological relevance of this surprising activity was also discussed.







Acknowledgements: LBM thanks to Fundação para a Ciência e a Tecnologia, MCTES, for a fellowship grant (SFRH/BPD/111404/2015, which is financed by national funds and co-financed by FSE). This work was supported by the Unidade de Ciências Biomoleculares Aplicadas-UCIBIO, which is financed by national funds from FCT/MEC (UID/Multi/04378/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER-007728).

References:

1. Maia, L.; Moura, I.; Moura, J.J.G. "Molybdenum and tungsten-containing enzymes: an overview", in "*Molybdenum and Tungsten Enzymes: Biochemistry*", RSC Metallobiology Series No. 5. Eds Hille, R., Schulzke, C., Kirk, M., The Royal Society of Chemistry, Cambridge, **2017**, 1-80 (doi: 10.1039/9781782623915-00001).
2. Maia L.; Moura, J.J.G. *Chem. Rev.* **2014**, *114*, 5273 (doi: 10.1021/cr400518y)
3. Maia L.; Moura J.J.G. *J. Biol. Inorg. Chem.* **2015**, *20*, 403 (doi: 10.1007/s00775-014-1234-2).
4. Maia L.; Moura, J.J.G. *J. Biol. Inorg. Chem.* **2011**, 16, 443 (doi: 10.1007/s00775-010-0741-z).
5. Maia L.; Moura J.J.G. *Biochemistry* **2015**, *54*, 685 (doi: 10.1021/bi500987w).

Abundant Metal Catalyzed C–H Activation Utilizing Cobalt and Manganese Complexes

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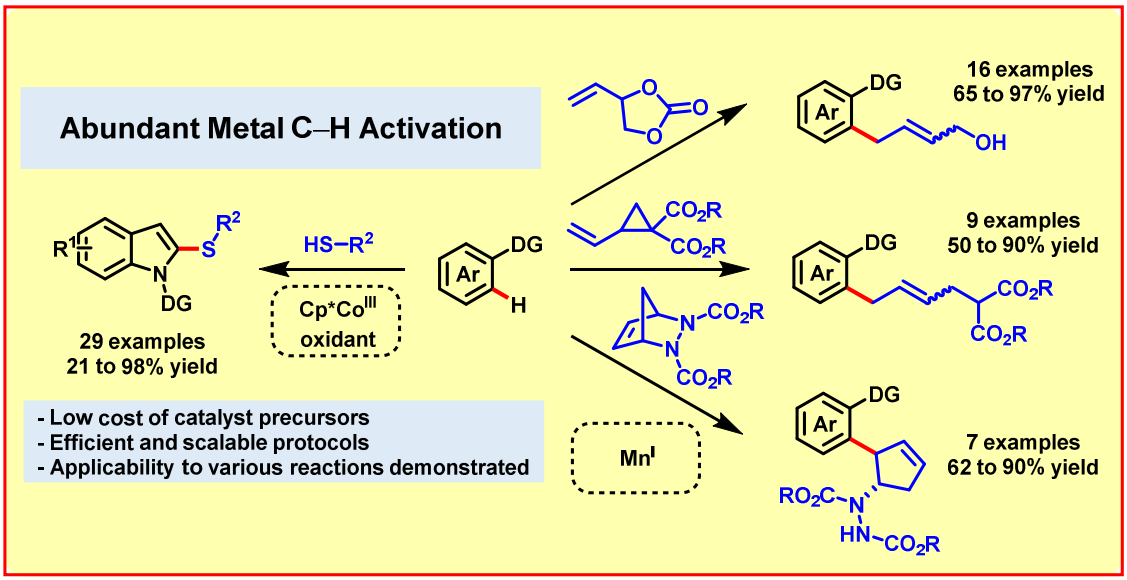
The research area of metal catalyzed C–H activation has evoked a variety of transformations for the efficient synthesis of complex molecular scaffolds. However, only recently researchers started to explore abundant metal catalysts to activate C–H bonds.[1] In this context we reported on C–S and C–C bond forming processes using Co and Mn complexes, respectively. We found that the Cp*Co(III)$(CO)I_2$ complex resembles an efficient pre-catalyst for the dehydrogenative thiolation of indoles. The transformation was shown to possess a broad functional group tolerance.[2] A manganese catalyzed sequential C–H bond activation and subsequent C–C/C–Het bond cleavage to synthesize allylic alcohols, allylated arenes, functionalized cyclopentenes and skipped dienes has been found. Complimentary to the standard solution-based protocols, the reactions also proceeded efficiently under neat conditions. The allylated aromatics were formed in good to excellent yields employing $Mn(CO)_5Br$ or $Mn_2(CO)_{10}$ as catalysts.[3]



Scheme 1: Co(III) catalyzed thiolation and Mn(I) catalyzed ring-opening allylation.

Acknowledgements: This work was supported by the Fonds der Chemischen Industrie (F. J. R. K.), the European Research Council under the European Communitys Seventh Framework Program (FP7 2007–2013)/ERC Grant Agreement 25936, by the DFG (Leibniz Award for F. G.) and the Alexander von Humboldt Foundation (Q. L.).

References:

1. For Co catalyzed C–H activation: a) Yoshino T.; Ikemoto H.; Matsunaga S.; Kanai M. *Angew. Chem. Int. Ed.* **2013**, *52*, 2207. b) Yoshino T.; Matsunaga S. *Adv. Synth. Catal.* **2017**, *359*, 1245. c) Wang S.; Chen S.−Y.; Yu X.−Q. *Chem. Commun.* **2017**, *53*, 3165. For Mn catalyzed C–H activation: d) Kuninobu Y.; Nishina Y.; Takeuchi T.; Takai K. *Angew. Chem. Int. Ed.* **2007**, *46*, 6518. e) Liu W.; Ackermann L. *ACS Catal*. **2016**, *6*, 3743.
2. Klauck F. J. R.[§]; Gensch T.[§]; Glorius F. *Angew. Chem. Int. Ed.* **2016**, *55*, 11287. ([§] Both authors contributed equally)
3. Lu Q.; Klauck F. J. R.; Glorius F. *Chem. Sci.* **2017**, *8*, 3379.

Understanding the Role of Hydrogen Bonding in the N-Heterocyclic Carbene-catalyzed Benzoin Condensation

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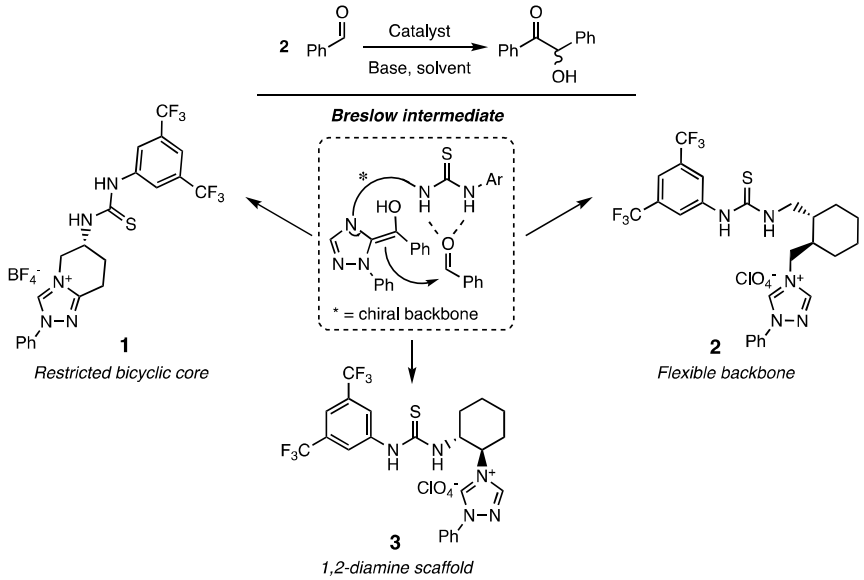
N-heterocyclic carbenes (NHCs) are an important class of organocatalysts which catalyse the benzoin condensation, among other reactions. Although much progress has been made over the past 50 years with respect to the asymmetric benzoin condensation, there are still limitations to the catalysts used. Traditionally, NHC catalysts exploit bulky substituents in order to promote chiral selectivity. However, this results in reactions that are typically slow, taking several days to achieve acceptable yields. It is hypothesised that introduction of H-bonding groups in the catalyst would provide an alternative source of stereoselective control, by co-ordination of the Breslow intermediate to the second molecule of benzaldehyde. Preliminary investigations have shown that catalysts incorporating H-bonding can demonstrate high ee's and good yields[1], but little is understood about the effect of the positioning of the H-bonding moiety relative to the active carbene centre. To investigate this idea, a range of novel chiral NHC catalysts featuring H-bonding moieties such as (thio)urea have been designed, to understand the effects of distance and free rotation on yield and ee. Herein we discuss the syntheses of a range of novel NHC catalysts featuring different chiral backbones, and with varying distance of the (thio)urea from the carbene centre (**Scheme 1**). The synthetic routes are all designed from commercially available chiral starting materials, and initial testing of the 1,2-diamine-derived catalyst **3**, inspired by Takemoto's catalyst[2], has proved promising with 62% ee.



Scheme 1: NHC catalysts featuring H-bonding moieties designed for use in the asymmetric benzoin condensation.

Acknowledgements: We thank the EPSRC for financial support.

References:

1. a) S. E. Toole *et al.*, *Org. Biomol. Chem.* **2009**, 7, 3584. b) L. Baragwanath *et al., J. Org. Chem.* **2009,** 74, 9214. c) J. Waser *et al*., *Synlett* **2010**, 6, 881.
2. Y. Takemoto *et al., J. Am. Chem. Soc.* **2003**, 125, 12672.

C-H Trifluoromethylation of Aromatic Compounds under Conditions of Heterogeneous and Homogeneous Catalysis

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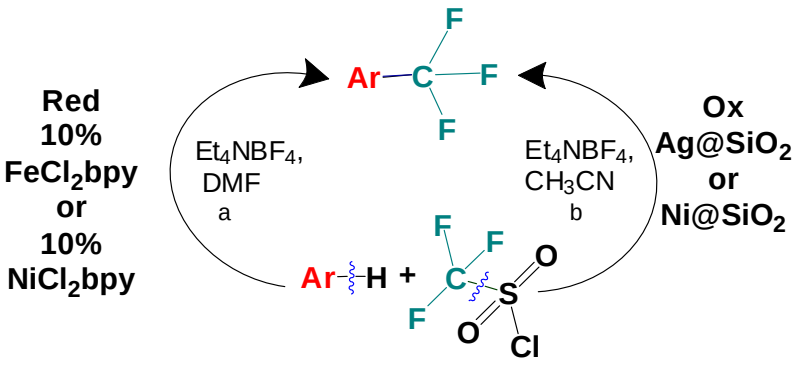
Trifluoromethylated aromatic compounds are widely used in medicinal chemistry, agriculture chemistry and materials science. For many decades, formation of aryl-CF_3 compounds has been limited to a few traditional technologies, especially the perchlorination of aromatic methyl-groups followed by exhaustive chlorinefluorine exchange using anhydrous HF (AHF) or SbF_5, or the deoxofluorination of carboxylic acids using sulfur tetrafluoride.[1]

The aim of this work is to develop new simple approach to obtain trifluoromethylated aromatic compounds via electrochemical activation of aromatic C-H bonds.

As a result of the research, catalytic systems have been developed that can be divided into two approaches: heterogeneous and homogeneous catalysis. Initial study was focused on obtaining trifluoromethylated aromatics using $Ni(BF_4)_2$bpy or $FeCl_2$bpy as catalysts. Different aromatic compounds such as benzene, coumarin, caffeine, etc. were chosen as substrates. The reactions proceeded under electrochemical mild condition (room temperature), with separation using Pt anode or without separation using Zn anode. In a series of experimentts the disered products of trifluoromethylation were obtained in one stage in good yields (to 75%) [2]

Another way of obtaining trifluoromethylated aromatic compounds is the use of silver or nickel nanoparticles in a silicate shell as a catalyst under oxidizing conditions in acetonitrile. **Scheme 1** shows the reaction of obtaining trifluoromethylated aromatic compounds under homogeneous (a) or heterogeneous catalytic conditions (b). [3]



Scheme 1. Trifluoromethylation of aromatic compounds under homogeneous (a) or heterogeneous (b) conditions.

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References:

1. Steiner H. *Chim. Oggi-Chem. Today*, **2015**, *33*, 3.
2. Khrizanforov M; Strekalova S.; Khrizanforova V.; Grinenko V.; Kholin V.; Kadirov M.; Burganov T.; Gubaidullin A.; Gryaznova T.; Sinyashin O.; Xu L.; Vicic D. A.; Budnikova Y. *Dalton Trans*., **2015**, *44*, 19674.
3. Khrizanforov M. N.; Fedorenko S. V.; Strekalova S. O.; Kholin K. V.; Mustafina A. R.; Zhilkin M. Ye.; Khrizanforova V. V.; Osin Y. N.; Salnikov V. V.; Gryaznova T. V. ; BudnikovaY. H. *Dalton. Trans*., **2016,** *45*, 11976.

Various Approaches to Phosphorylation of Aromatic Compounds

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Aryl and heteroaryl phosphonates form an important class of substrates because of their broad application in medicinal chemistry, synthetic chemistry, material chemistry and catalysis. There are several methods to obtain phosphorylated aromatic and heteroaromatic substrates such as cross-coupling, nucleophilic addition or reactions catalyzed by metals. However, it should be noted that in majority of papers organic halides are used as aromatic substrates, while examples of substitution of C-H bonds where the leaving group is hydrogen are much smaller.[1]

The aim of our work was to develop simple and environmentally friendly approach to phosphorylation of aromatic and heteroaromatic compounds via electrochemical activation of aromatic C-H bonds using transition metal complexes as catalysts ($CoCl_2$bpy, $Ni(BF_4)_2$bpy, $MnCl_2$bpy, $Ni(BF_4)_2$bpy/$MnCl_2$bpy). The synthesis of arylphosphonates via direct phosphorylation of aromatic C-H bonds under electrochemical mild conditions is regarded as one of the most important approaches because it meets the generally accepted criteria of "green chemistry" such as atom-economy, short time and low waste of reaction compared to traditional approaches when organic halides are often used.[1,2]

We carried out a series of experiments to obtain phosphorylated aromatic compounds (benzene and its derivatives, coumarins, pyridine, etc.) under electrochemical oxidative conditions using bimetallic catalytic system $Ni(BF_4)_2$bpy/$MnCl_2$bpy and under electrochemical reduction conditions using $CoCl_2$bpy as catalyst. The distinctive feature of the process is an equimolar ratio of aromatic compound and phosphorylation reagent (1:1) and the room temperature. In both cases phosphorylated products were obtained in one step in good yield (up to 80%) and 100 % conversion of H-phosphonate (**Figure 1**). Although it was impossible to obtain ferrocenyl phosphonate under these conditions so we developed a non-catalytic method using Pb electrode and α-hydroxyalkylphosphonate as "masked" phosphorylating agent. Reaction proceeded at -50 °C, phosphorylated ferrocene was obtained in one step and in yield up to 90%.[2]

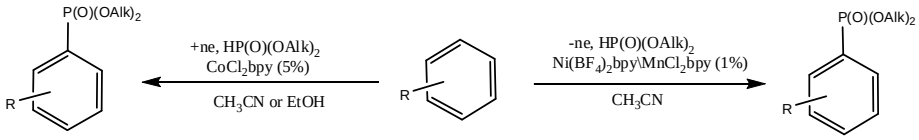

Figure 1: Electrochemical phosphorylation of aromatic compounds.

Thus new electrochemical approach to phosphorylation of aromatic compounds under mild conditions was proposed.

Acknowledgements: We thank the Russian Science Foundation, grant 14-23-00016 for financial support.

References:

1. a) Budnikova Y. H.; Sinyashin O. G. *Russ. Chem. Rev.* **2015**, *84(9)*, 917. b) Budnikova Y. H.; Gryaznova T. V.; Grinenko V. V.; Dudkina Y. B.; Khrizanforov M. N. *Pure Appl. Chem*. **2017**, *89*(3), 311.

2. a) Khrizanforov M. N.; Strekalova S. O.; Gryaznova T. V.; Khrizanforova V. V.; Budnikova Y. H. *Russ. Chem. Bull.* **2015**, 8, 1926. b) Khrizanforov M. N.; Strekalova S. O.; Kholin K. V.; Khrizanforova V. V.; Kadirov M. K.; Gryaznova T. V.; Budnikova Y. H. *Catal. Today*. **2017**, *279*, 133. c) Khrizanforov M.; Strekalova S.; Kholin K.; Khrizanforova V.; Grinenko V.; Gryaznova T.; Budnikova Y. *RSC Adv.* **2016**, *6*(48), 42701.

Borate Esters: Simple Catalysts for the Sustainable Synthesis of Complex Amides

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Chemical reactions for the formation of amide bonds are among the most commonly employed transformations in organic chemistry. Amides feature in 25% of industrially important pharmaceuticals, as well as a wide selection of bioactive natural products. However, limitations to amide bond formation reactions remain, especially with regard to finding improved catalytic, waste-free and chemoselective methods. These problems must be addressed in order to make this chemistry more sustainable on a process scale. Herein, we report a novel protocol for amidation using a simple borate ester catalyst. The process presents significant improvements over other catalytic amidation methods in terms of process efficiency and safety, with an unprecedented substrate scope including functionalized heterocycles and even unprotected amino acids. An aspect that makes this chemistry especially applicable to the current industrial needs is the use of a simple solid-phase work-up with commercially available resins avoiding wasteful work-ups or column chromatography.

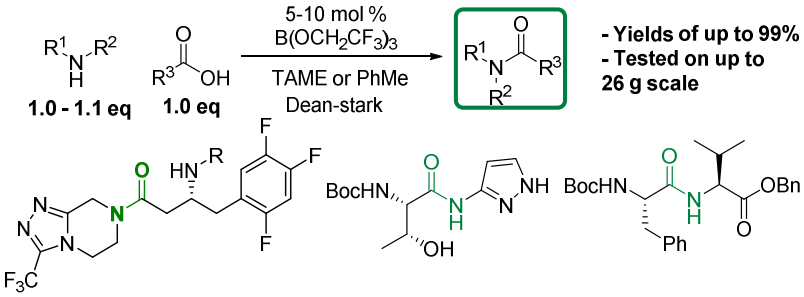

Figure 1: Scope of borate catalysed amide bond formation.

The method was used to access a wide range of functionalized amide derivatives, including pharmaceutically relevant targets, important synthetic intermediates, a catalyst, and a natural product.

Acknowledgements: We would like to thank GSK and UCL Chemistry for providing funding to support a PhD studentship.

References:

1. M. T. Sabatini; L. Boulton; T. Sheppard. *manuscript submitted*
2. R. M. Lanigan; V. Karaluka; M. T. Sabatini; P. Starkov; M. Badland; L. Boulton; T. D. Sheppard. *Chem. Commun*., 2016, 52, 8846 (b) highlighted in Synfacts, 2016, 12, 0967

Rediscovering the Isospecific Ring-Opening Polymerization of Racemic Propylene Oxide with Dibutylmagnesium

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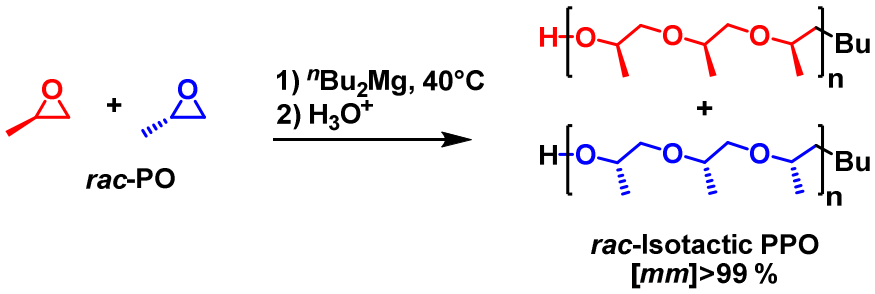
Aliphatic polyethers have become an important class of materials due to their large variety of applications, e.g., as matrixes for controlled drug delivery systems,[1,2] nonionic surfactants,[3] lithium polymer batteries,[4] polyurethane production, and many others. These polyethers are generally synthesized either by ring-opening polymerization (ROP) of epoxides using metal complexes as initiators or via metal-free polymerization.[5]

In this studies we used simple $^{n}Bu_2Mg$ as catalyst, which showed good activity in the isoselective bulk ring opening polymerization (ROP) of racemic propylene oxide (*rac*-PO), yielding isotactic PO (*mm* triad > 99%) with high yield and high number average molecular weight (M_n) in a living fashion without any co-catalyst or additive even at high temperatures. Powder *X*-ray and DSC analysis confirm the high crystallinity of the obtained polymers. Kinetic data analysis shows that the ROP of PO by this system is first order in both monomer and catalysts concentration. Analyses of low molecular weight oligomers revealed that the butyl group is incorporated as one of the end terminal groups in the polymer chain and initiates the polymerization. To the best of our knowledge, this is the simplest achiral catalytic system yielding the highest isotacticity in the ROP of *rac*-PO. DFT calculations ruled out the role alkyl-alkoxy magnesium complexes as the catalytically active species as well as the involvement of monometallic intermediates and tetrametallic clusters. For the time being, both the active species and the origin of the isotactic selectivity remain elusive. More experimental as well as computational work is indeed required in order to shed light in this chemistry.[6]



References:

1. Knop K.; Hoogenboom R.; Fischer D.; Schubert U. S. *Angew. Chem., Int. Ed*. **2010**, *49*, 6288−6308. b) Müller S. S.; Moerst C.; Frey H. *Macromolecules* **2014**, *47*, 5492−5500.
2. Schmolka I. *J. Am. Oil Chem. Soc.* **1977**, *54*, 110−116.
3. Barteau K. P.; Wolffs M.; Lynd N. A.; Fredrickson G. H.; Kramer E. J.; Hawker C. J. *Macromolecules* **2013**, *46*, 8988−8994.
4. Childers I. M.; Longo J. M.; Van Zee N. J.; La Pointe A. M.; Coates G. W.; *Chem. Rev*. **2014**, *114*, 8129−8152.
5. Labbé A.; Carlotti, S.; Billouard C.; Desbois P.; Deffieux A. *Macromolecules* **2007**, *40*, 7842–7847.
6. Ghosh S.; Lund H.; Jiao H.; Mejía E. *Macromolecules* **2017**, *50*, 1245−1250.

Phosphazenes as Organosuperbases for Darzens Reaction

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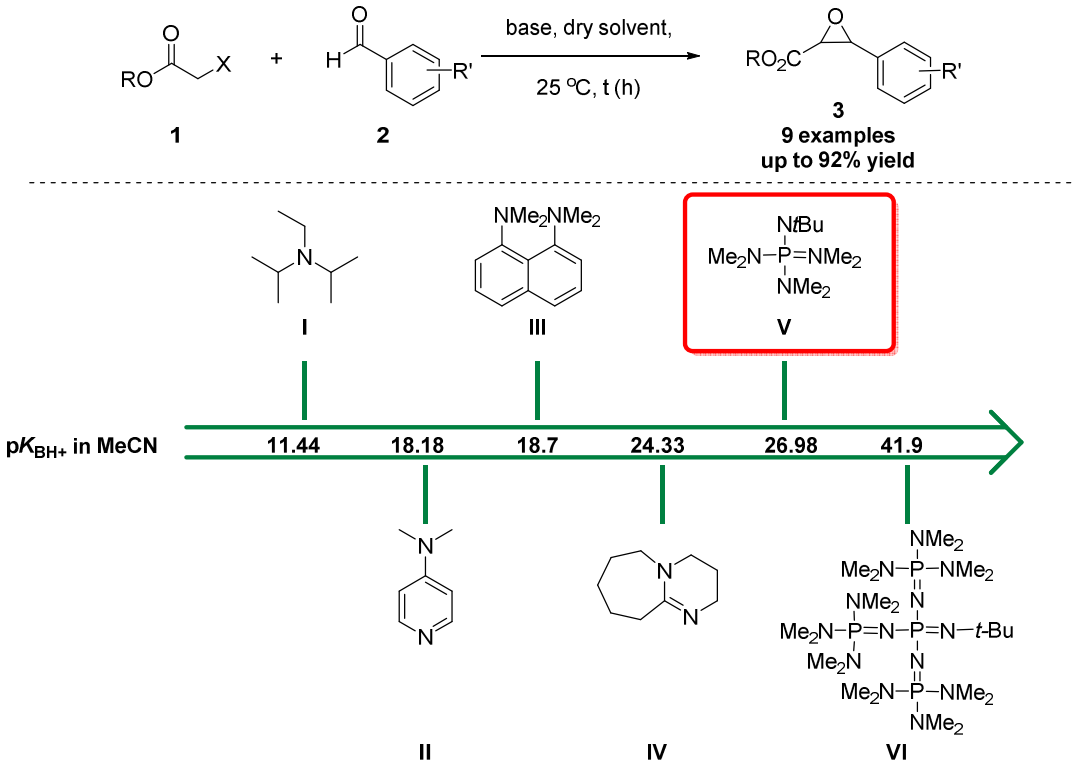
Driven by the relevance of Darzens reaction for the preparation of multifunctional intermediates in the synthesis of fine chemicals or API, we assess the suitability of 'organosuperbases' in the synthesis of α,β-epoxycarbonyl compounds.[1] The Darzens condensation between the α-halo esters **1** and aromatic aldehydes **2** was investigated using neutral organobases **I-VI** with different pK_{BH^+} (Scheme 1).[2] The reaction, under mild condition, proceeds in the presence of phosphazene P$_1$-*t*-Bu **V** to give the corresponding *cis*- and *trans*-epoxides **3** in good yield and short reaction time. Base **V** outperformed all other bases. With optimised reaction conditions, P$_1$-*t*-Bu **V** provided to be tolerant to both variations in the structure and electronic properties of the aromatic aldehydes and α-halo esters used. In these reactions, addition of chiral quaternary ammonium salts did not display effects on the stereoselectivity.[3] In addition, the stability of *trans*-epoxide **3** in the presence of P$_1$-*t*-Bu **V** was tested and no epimerization was observed.



Scheme 1: Development of Darzens reaction in the presence of organobases **I-VI**.

References:

1. a) Bakó, P.; Rapi, Z.; Keglevich, G. *Curr. Org. Chem.* **2014**, *11*, 361. b) Ishikawa, T. *Superbases for Organic Synthesis* Ed.; John Wiley & Sons: Chippenham, **2009**.
2. Kaljurand, I.; Kütt, A.; Sooväli, L.; Rodima, T.; Mäemets, V.; Leito, I.; Koppel, I. A. *J. Org. Chem.* **2005**, *70*, 1019.
3. O`Donnell, M.J.; Delgado, F.; Hostettler, C.; Schwesinger, R. *Tetrahedron Lett.* **1998**, *39*, 8775.

Synergetic Bimetallic Oxidative Esterification of 5-Hydroxymethylfurfural (HMF) under Mild Conditions

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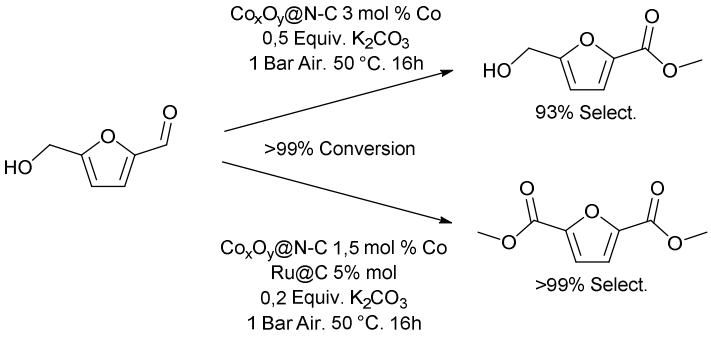
The need of 2,5-Furandicarboxylic Acid (FDCA) or its esters analogues (e.g. dimethyl furan-2,5-dicarboxylate, FDCM) to synthesize bio-based polymers has dragged attention to the oxidation of 5-hydroxymethylfurfural (HMF).[1] There are several reports about the use of heterogeneous catalysts in the oxidation of HMF to FDCA, using different metals, combinations of them and several types of supports;[2] but only a few for the selective synthesis of FDCM.[3] When FDCA is used as starting material in the polymer synthesis, the first step is to make ester derivatives, and then a transesterification reaction is needed to obtain the desired products. The advantage of having FDCM as a starting material is that the step for the esterification of FDCA is avoided, and is possible to proceed to the transesterification step directly.[4] The reported systems require high pressures of oxygen, high temperatures or stoichiometric amounts of additives to achieve full conversion or selectivity.

Herein, we report the oxidative esterification of HMF to FDCM made by a cooperative reaction using the heterogeneous catalyst Co_xO_y@N-C and commercial Ru@C catalyst, and the selective synthesis of one of the intermediaries under mild conditions (see Scheme 1). Moreover, the selective synthesis of methyl 5-(hydroxymethyl)furan-2-carboxylate, an important monomer for the synthesis of bio-based polyesters, was also achieved. Also the role and performance of each catalyst is investigated.



Scheme 1: Selective Oxidative Esterification of HMF under mild conditions.

References:

1. I. Delidovich, P. J. C. Hausoul, L. Deng, R. Pfützenreuter, M. Rose, R. Palkovits, *Chemical Reviews* **2016**, *116*, 1540-1599.
2. a) C. Zhou, W. Deng, X. Wan, Q. Zhang, Y. Yang, Y. Wang, *ChemCatChem* **2015**, *7*, 2853-2863; b)Z. Gui, W. Cao, S. Saravanamurugan, A. Riisager, L. Chen, Z. Qi, *ChemCatChem* **2016**, *8*, 3636-3643; c)X. Han, L. Geng, Y. Guo, R. Jia, X. Liu, Y. Zhang, Y. Wang, *Green Chemistry* **2016**, *18*, 1597-1604; d)Y. Wang, K. Yu, D. Lei, W. Si, Y. Feng, L.-L. Lou, S. Liu, *ACS Sustainable Chemistry & Engineering* **2016**, *4*, 4752-4761; e)G. Yi, S. P. Teong, Y. Zhang, *Green Chemistry* **2016**, *18*, 979-983; f)D. K. Mishra, H. J. Lee, J. Kim, H.-S. Lee, J. K. Cho, Y.-W. Suh, Y. Yi, Y. J. Kim, *Green Chemistry* **2017**, *19*, 1619-1623; g)X. Tong, L. Yu, H. Chen, X. Zhuang, S. Liao, H. Cui, *Catalysis Communications* **2017**, *90*, 91-94.
3. a)O. Casanova, S. Iborra, A. Corma, *Journal of Catalysis* **2009**, *265*, 109-116; b)J. Deng, H.-J. Song, M.-S. Cui, Y.-P. Du, Y. Fu, *ChemSusChem* **2014**, *7*, 3334-3340; c)F. Menegazzo, M. Signoretto, D. Marchese, F. Pinna, M. Manzoli, *Journal of Catalysis* **2015**, *326*, 1-8; d)Y. Sun, H. Ma, X. Jia, J. Ma, Y. Luo, J. Gao, J. Xu, *ChemCatChem* **2016**, *8*, 2907-2911.
4. A. F. Sousa, C. Vilela, A. C. Fonseca, M. Matos, C. S. R. Freire, G.-J. M. Gruter, J. F. J. Coelho, A. J. D. Silvestre, *Polymer Chemistry* **2015**, *6*, 5961-5983.

Manganese(I)-Catalyzed Regioselective Synthesis of Highly Substituted Allenes and Isoquinolines via C–H Activation

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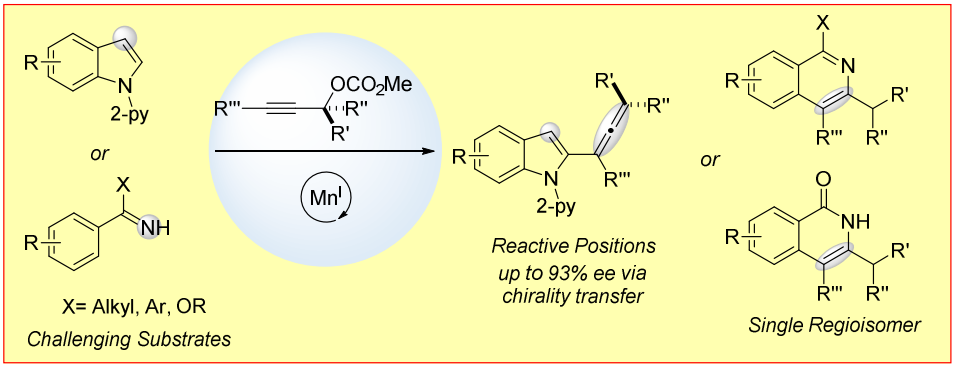
Manganese(I)-catalyzed C–H activation reactions have gained serious interest in the last few years. Due to its low toxicity, air stability, low price as well as its potential to promote new reactivity, it has become an interesting extension to the well-established precious transition metal catalysts.[1] Here, we present a Mn(I)-catalyzed regioselective synthesis of 2-allenylindoles (**Scheme 1**).[2] Allenes have been demonstrated to be a powerful building block and intermediate in modern synthetic chemistry. However, the selective synthesis of these reactive compounds via C–H activation is still underdeveloped. It has recently been shown that Mn(I) catalysts can facilitate β-heteroatom elimination.[3] Therefore a combination of a low valent Mn(I) catalyst and propargylic carbonates and indoles led to the desired, highly substituted heteroaromatic allenes in excellent yields. This method was further extended to nucleophilic directing groups, so that N-H imines and amidates can be transferred to isoquinolines and isoquinolin-1-ones in perfect selectivity (**Scheme 1**).[4] The insertion of alkynes as C2 building block into carbon–metal bonds has been widely applied.[5] However, the control of the selectivity for the insertion remains challenging, so that either symmetrical alkynes are used, or the intrinsic reactivity and product mixtures must be accepted. The perfect selectivity in this case is proposed to be caused by a pre-coordination of the carbonate oxygen to the catalyst prior to the insertion into the manganese-carbon bond.[6]



Scheme 1: Regioselective Synthesis of 2-Allenylindoles, Isoquinolines and Isoquinolin-1-ones by Manganese(I)-Catalysis.

Acknowledgements: This work was supported by the European Research Council under the European Community's Seventh Framework Program (FP7 2007–2013)/ERC Grant Agreement 25936.

References:

1. For a recent review on Mn catalyzed C–H activation, see: W. Liu, L. Ackermann *ACS Catal.* **2016**, *6*, 3743 – 3752; for an introduction to C–H activation, see J. A. Labinger, J. E. Bercaw *Nature* **2002**, *417*, 507 – 514.
2. Q. Lu, S. Greßies, F. J. Klauck, F. Glorius *Angew. Chem. Int. Ed.* **2017**, *56*, 6660 – 6664, *Angew. Chem.* **2017**, *129*, 6760 – 6764.
3. Q. Lu, F. J. Klauck, F. Glorius *Chem. Sci.* **2017**, *8*, 3379 – 3383.
4. Q. Lu[†], S. Greßies[†], S. Cembellín, F. J. R. Klauck, F. Glorius *Manuscript Submitted* ([†] both authors contributed equally).
5. Selected examples with Mn-catalysts: R. He, Z.-T. Huang, Q.-Y. Zheng, C. Wang *Angew. Chem. Int. Ed.* **2014**, *53*, 4950 – 4953.
6. S. Wu, X. Huang, W. Wu, P. Li, C. Fu, S. Ma *Nat. Commun.* **2015**, *6*, 7946.

Synthesis of Functionalized NHC-CO_2 Adducts for Self-Assembled Monolayers: Applications in SERS Sensing

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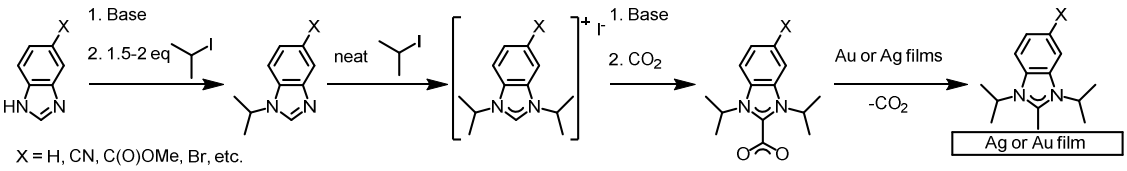
Thiol functionalized self-assembled monolayers (SAMs) have been key in stabilizing nanostructures and controlling properties on metal surfaces. This technology has been used extensively in local surface resonance plasmonic (LSPR) based sensing, specifically surface enhanced Raman spectroscopy (SERS).[1] SERS has revolutionized optical based analytical detection; by carefully regulating surface properties, feats such as single molecule detection can be performed. Nonetheless, one major challenge for further developing this analytical method is that the stability of the thiol coated SAMs is poor since sulfur is easily dissociated.

Recently, *N*-heterocyclic carbenes (NHCs) have attracted intense interest as potential replacements for thiol SAMs.[2] Monolayers that have been formed by using NHCs shows much greater resistance compared to thiol SAMs in thermal stability, pH extremes, oxidation, and ligand exchange. However, for NHC-modified surfaces to replace thiol-coated examples, improved synthesis of stable NHCs precursors is necessary.

We are developing new synthetic methods for preparing air stable "masked" carbenes, referred to as NHC-CO_2 adducts. Our synthetic goals are three-fold: developing synthetic methodologies for preparing bifunctional imidazolium precursors effectively, standardizing methods to prepare the critical CO_2 adducts, and determining effective conditions for liberation of CO_2 to yield NHC-coated metal surfaces (Scheme 1). Since SAMs for SERS applications require a bifunctional ligand (one functional group for metal surface and one for analyte), we have developed a pair of general methodologies for creating a wide library of bifunctional imidazoliums. These molecules are air-stable in the solid state and can generally be fully characterized by typical organic chemistry techniques. Finally, we showcase methods for release of CO_2 to yield the NHC-SAMs. Initial SERS spectra are included for demonstration purposes.



Scheme 1: Synthesis of CO_2 adduct NHCs and their deposition on metal films.

Acknowledgements: We thank the National Science Foundation and the PDRD program (DOE) for support of this work.

References:

1. Sun, F.; Galvin, D. D.; Jain, P.; Yu Q. *Chem. Commun.* **2017**, *53*, 4550.
2. Crudden, C. M.; Horton, J. H.; Narouz, M. R.; Li, Z.; Smith, C. A.; Munro, K.; Baddeley, C. J.; Larrea, C. R.; Drevniok, B.; Thanabalasingam, B.; McLean, A. B.; Zenkina, O. V.; Ebralidze, I. I.; She, Z.; Kraatz, H.; Mosey, N. J.; Saunders, L. N.; Yagi, A. *Nat. Commun.* **2016** 7:12654.

The Use of Dispersion-created Concentration Gradients to Optimise Reactions and Probe Reaction Scope in Flow

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We report a method using flow chemistry to obtain information on the effect of a wide range of concentrations of one or more components on the outcome of a reaction in a single short experiment. Under continuous flow conditions, Taylor dispersion spreads a plug of one component along tube creating a concentration gradient. Mixing in-line with a steady state of other reagents, passing through a reactor, and continuously monitoring the outcome provides data from all reactions from zero to a set maximum concentration of the dispersed component in one reaction (Figure 1). We used in-line spectroscopic techniques such as IR or UV, as well as off-line monitoring of collected fractions by GC or HPLC (Figure 2). The concentration gradient method was used to optimise the photocycloaddition of 3,4-dihydropyran with diphenylacetylene with respect to diphenylacetylene concentration giving three different optimal concentrations for formation of mono and bis addition products and a phenanthrene compound. It was also used to probe the effect of additives on a Heck reaction showing inhibition from addition of ligands, inhibition from thiols, sulfoxide, disulphide, thioanisole, furan, pyridine, imidazole, terminal alkyne and primary amines. No effect was observed on addition of amides, aldehydes, esters, ketones, primary alcohols, carboxylic acids, cyano, and thiophene.

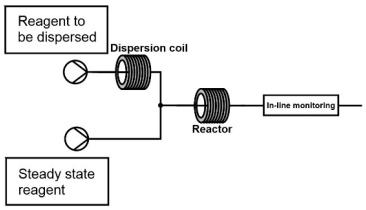

Figure 1: Flow diagram for the formation of a dispersion created concentration gradient. Plug flows through dispersion coil where it undergoes Taylor dispersion creating the gradient.

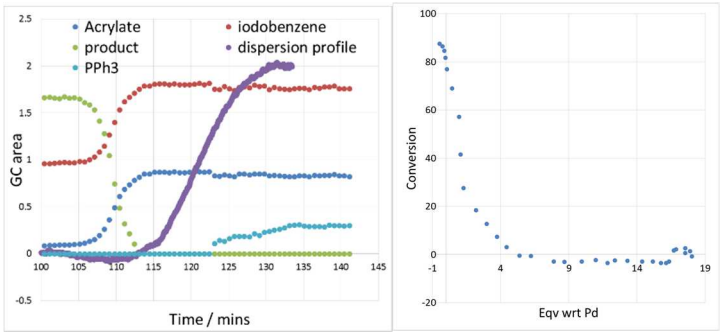

Figure 2: Left: Raw GC data from concentration gradient experiment dispersing PPh_3 against Heck reaction. Right: GC data converted to equivalents of PPh_3 against conversion showing inhibitory effect

Acknowledgements: We would like to thank Syngenta and the EPRSC for funding of this project and Matthew Hughes from Syngenta for his interest in the project.

References:

1. G. Taylor, *Proc. R. Soc. Lond. Ser. Math. Phys. Sci.*, 1953, **219**, 186.

Zirconium-Mediated Reactions for Synthesis of Orphan Nuclear Receptor Agonists

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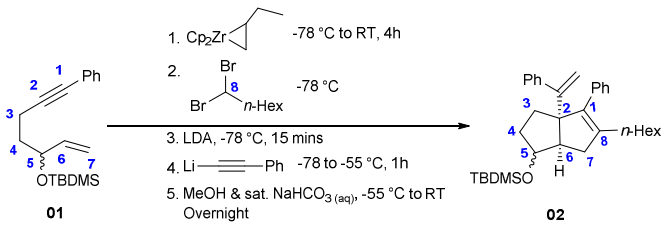
Orphan nuclear receptors (ONRs) behave as transcriptional factors with no known natural ligands.[1] Liver receptor homolog-1 (LRH-1), expressed in tissues of endodermal origin, is involved in processes such as modulation of cholesterol transport and cell differentiation during embryonic development.[1, 2] Evidence of its association with cancer cell proliferation and tumour pathogenesis is also emerging.[2] Steroidogenic factor-1 (SF-1) is a key regulator of endocrine function and an essential factor in sex determination; particularly for the function and development of the gonad and adrenal glands.[3] Despite LRH-1 and SF-1 being known as ONRs, structural analysis show they can accommodate ligands and, therefore, have potential as pharmaceutical targets.

In this work we show how small molecule agonists have been synthesised for receptors LRH-1 and SF-1 *via* a complex tandem zirconium cyclisation reaction from an enyne compound to form compounds with a *cis*-bicyclo[3.3.0]octa-2-ene backbone (**Scheme 1**). Furthermore, we show how new analogues of our current most potent compound, RJW100, have been synthesised following potency and selectivity data of previously synthesised compounds and the crystal structure of RJW100 bound in the LRH-1 receptor (**Figure 1**).[4, 5]



Scheme 2: Example of a zirconium tandem cyclisation reaction to synthesise a *cis*-bicyclo[3.3.0]octa-2-ene compound.

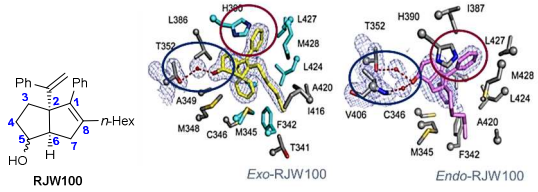


Figure 1: Structure of RJW100 and its interaction with LRH-1 residues shown in the crystal structure.[4]

Acknowledgements: We thank EPSRC for their financial support of this project.

References:

1. K. A. Lazarus, D. Wijayakumara, A. L. Chand, E. R. Simpson and C. D. Clyne, *J. Steroid Biochem. Mol. Biol.*, 2012, **130**, 138-146.
2. S. Stein and K. Schoonjans, *Curr. Opin. Cell Biol.*, 2015, **33**, 26-34.
3. E. A. Hoivik, A. E. Lewis, L. Aumo and M. Bakke, *Mol. Cell. Endocrinol.*, 2010, **315**, 27-39.
4. S. G. Mays, C. D. Okafor, R. J. Whitby, D. Goswami, J. Stec, A. R. Flynn, M. C. Dugan, N. T. Jui, P. R. Griffin and E. A. Ortlund, *J. Biol. Chem.*, 2016, **291**, 25281-25291.
5. R. J. Whitby, J. Stec, R. D. Blind, S. Dixon, L. M. Leesnitzer, L. A. Orband-Miller, S. P. Williams, T. M. Willson, R. Xu, W. J. Zuercher, F. Cai and H. A. Ingraham, *J. Med. Chem.*, 2011, **54**, 2266-2281.

Emergent Applications of Acyclic Diaminocarbenes

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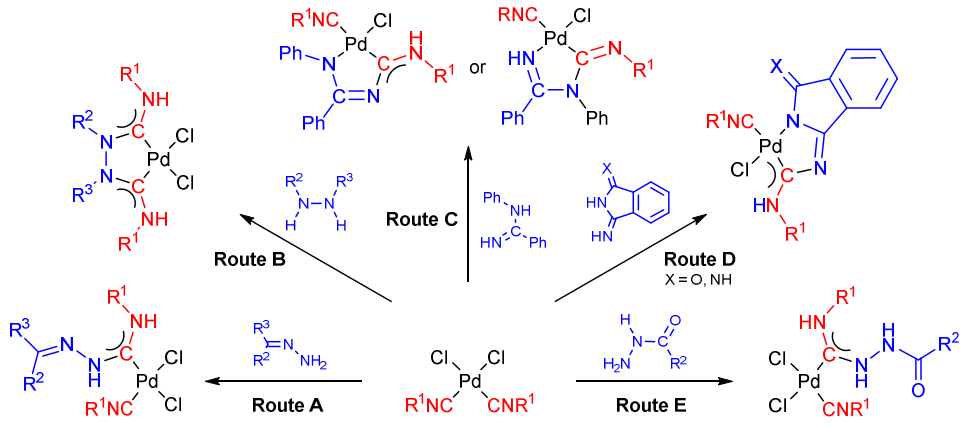
Acyclic diaminocarbenes (ADCs) represent a contemporary class of ancillary ligands for catalytic applications.[1,2] Being structural analogues of *N*-heterocyclic carbenes, ADC species possess comparable electronic and steric properties, and their metal complexes can be prepared via several synthetic approaches including nucleophilic addition to metal-bound isocyanides, recognized as the most versatile route.

In pursuit of our studies on chemistry of metal-aminocarbenes, we have developed a route leading to a range of novel types of metal-ADC complexes starting from isocyanides (**Figure 1**).[3,4] Prepared M-ADCs were employed as catalysts for various transition metal-catalysed reactions demonstrating outstanding efficiencies. Identification of the true catalytic species allowed to shed light on mechanisms of the catalytic action of aminocarbene catalysts and to extend the frontiers of their application.[1,3,4]



Scheme 1. Examples of metal-ADC species prepared from metal-bound isocyanides.

The essential goals of this report are: (i) to provide an overview of recent data on preparation of metal-ADC complexes, (ii) to compare the catalytic properties of M-ADCs against M-NHCs and M-PR_3 species, and (iii) to draw attention to the advantages that application of ADC catalysts give to synthetic organometallic chemistry and catalysis.

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References:

1. Boyarskiy V. P.; Bokach N. A.; Luzyanin K. V.; Kukushkin V. Yu. *Chem. Rev.* **2015,** *115*, 2698.
2. Boyarskiy V. P.; Luzyanin K. V.; Kukushkin, V. Yu. *Coord. Chem. Rev.* **2012,** *256*, 2029.
3. Rocha B. G. M.; Valishina E. A.; Chay R. S.; Guedes da Silva M. F. C.; Buslaeva T. M.; Pombeiro A. J. L.; Kukushkin V. Yu.; Luzyanin, K. V. *J. Catal.* **2014,** *309*, 79.
4. Kinzhalov M. A.; Timofeeva S. A.; Luzyanin K. V.; Boyarskiy V. P.; Yakimanskiy A. A.; Haukka M.; Kukushkin V. Yu. *Organometallics* **2016,** *35*, 218.

(1,2,3-Triazol-4-yl)-7-Deazapurines and Purines: Synthesis and Optical Properties

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Purine and 7-deazapurine heterocycles have been recognized as an important class of compounds widely spread in nature and exhibiting diverse biological activities. On the other hand, heterocycles containing 1,2,3-triazole moiety have found application in fields of material science, chemical sensors, drug discovery and related areas.[1] Recently, we have shown that triazole – 7-deazapurine conjugates exhibit strong fluorescence and are promising candidates as functional materials.[2] In view of the growing importance of highly efficient light-emitting materials we present herein the synthesis and photopysical properties of novel 2,6-bis(1-aryl-1,2,3-triazol-4-yl)- and 2-aryl-6-(1-phenyl-1,2,3-triazol-4-yl)-7-deazapurines and purines (**Figure 1**).

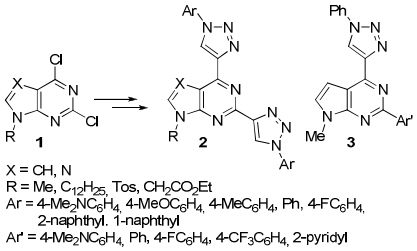

Figure 1: (1,2,3-Triazol-4-yl)-7-deazapurines and purines.

The synthetic strategy for the target compounds **2** was based on the Sonogashira cross-coupling reactions of 2,6-dichloro-(7-deaza)purines **1** and following Cu(I)-catalyzed azide-alkyne cycloaddition reactions of the formed ethynyl(deaza)purines with the appropriate arylazides. Synthesis of 2-aryl-7-deazapurines **3** was achieved under the microwave irradiation by using Stille cross-coupling reaction of 2-chloro-6-(1-phenyl-1,2,3-triazol-4-yl)-7-deazapurine with the corresponding aryl(tributyl)stannanes in the presence of $Pd(PPh_3)_2Cl_2/AsPh_3$ as a catalyst system.

Optical properties of the synthesized 7-deazapurines and purines (**2**, **3)** were assessed by performing absorption and fluorescence spectroscopy, fluorescence quantum yield and fluorescence lifetime measurements. Most of the studied compounds exhibited blue fluorescence with fluorescence quantum yield ranging from 1% to 64%.

Peculiarities of reactivity of 2-chlorine group of (7-deaza)purines in cross-coupling reactions and the photophysical properties in conjunction with DFT calculations of the synthesized molecules will be discussed, as well.

Acknowledgements: The research was funded by a grant (No. TAP-LLT-01/2015) from the Research Council of Lithuania.

References:

1. a) Moses J. E.; Moorhouse A. D. *Chem. Soc. Rev.* **2007**, *36*, 1249. b) Lau Y. H.; Rutledge P. J.; Watkinson M.; Todd M. H. *Chem. Soc. Rev*. **2011**, *40*, 2848.
2. Bucevicius J.; Skardziute L.; Dodonova J.; Kazlauskas K.; Bagdziunas G.; Jursenas S.; Tumkevicius S. *RSC Adv*. **2015**, *5*, 38610.

Old Compounds and New Applications: Pd, Base, and Ligand-free Sonogashira Coupling Cyclization Reactions for Phthalide Synthesis

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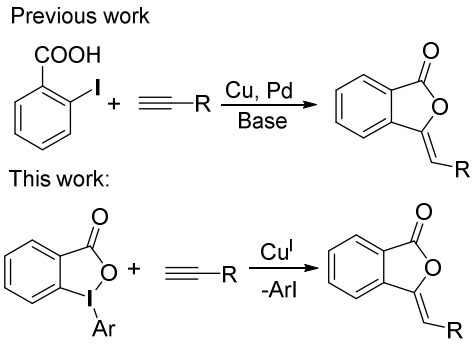
Hypervalent iodine (III) five-membered heterocycles have found broad application as "atom-transfer" reagents for organic synthesis.[1] 1-Phenylbenziodoxole[2] is known as a traditional benzyne precursor under heating,[3] but not further synthetic applications have been reported. Traditionally, phthalide-containing products can be prepared by the reaction of phthalic anhydride with acetic anhydride or acetic acid at high temperature,[4] and by the metal-catalyzed 5-exo-dig or 6-endo-dig cyclization of 2-alkynylbenzoic acid/esters which are available[5] or synthesized in situ[6] *via* Sonogashira-type coupling reactions. These are perhaps the most attractive methods for the synthesis of phthalides and isocoumarins, although having high substrate scopes, but these methods often suffer from low regioselectivity, and also using strong bases, which affect the yield,[7] the integrity of the product,[8] and limit the substrates scope specially in total synthesis, which requires further protecting/deprotecting steps (scheme 1).[9] In literature, there are few reactions involving Pd-free Sonogashira coupling for the synthesis of heterocycles and carbocycles,[10] and to the best of our knowledge there is no report involving Pd and base-free Sonogashira coupling cyclization reactions.[11]

Herein, we report the first synthetic application of 1-phenylbenz-idoxole to the synthesis of Phthalides using only Cu^{I} as catalyst. High regioselectivity and yield were achieved under mild reaction condition with good functional group tolerance. During our investigations, the efficiency of different Cu^{I} and Cu^{II} catalysts under various conditions (temperature and solvent) were studied. The nature of the leaving group, the substituents on the substrate and temperature play an important role on both yield and regioselectivity. We proposed a rational pathway for this transformation based on previous reports and our experimental work.



Scheme 1: Synthesis of phthalide by Sonogashira type cross coupling reactions.

References:

1. J. Charpentier, N. Früh, A. Togni, *Chemical Reviews* **2015**, *115*, 650-682.
2. M. S. Yusubov, R. Y. Yusubova, V. N. Nemykin, V. V. Zhdankin, *The Journal of Organic Chemistry* **2013**, *78*, 3767-3773.
3. D. Del Mazza, M. G. Reinecke, *The Journal of Organic Chemistry* **1988**, *53*, 5799-5806.
4. M. Lácová, J. Chovancová, E. Veverková, Š. Toma, *Tetrahedron* **1996**, *52*, 14995-15006.
5. H. Sashida, A. Kawamukai, *Synthesis* **1999**, *1999*, 1145-1148.
6. A. Duchêne, J. Thibonnet, J.-L. Parrain, E. Anselmi, M. Abarbri, *Synthesis* **2007**, *2007*, 597-607.
7. M. R. Kumar, F. M. Irudayanathan, J. H. Moon, S. Lee, *Advanced Synthesis & Catalysis* **2013**, *355*, 3221-3230.
8. M. Uchiyama, H. Ozawa, K. Takuma, Y. Matsumoto, M. Yonehara, K. Hiroya, T. Sakamoto, *Organic Letters* **2006**, *8*, 5517-5520.
9. K. Tatsuta, S. Hosokawa, *Chemical Reviews* **2005**, *105*, 4707-4729.
10. S. Dhara, R. Singha, M. Ghosh, A. Ahmed, Y. Nuree, A. Das, J. K. Ray, *RSC Advances* **2014**, *4*, 42604-42607.
11. R. Chinchilla, C. Nájera, *Chemical Reviews* **2007**, *107*, 874-922.

Utilizing New Planar Chiral Copper Complex in Asymmetric Conjugated *β*-Borylation and One Pot Tandem Metathesis-Asymmetric *β*-Borylation

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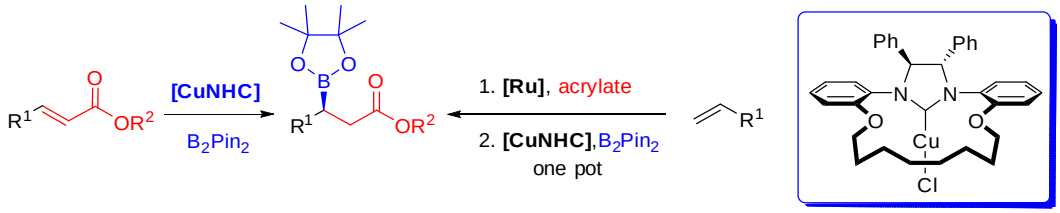
Since the first attempt to catalyse the asymmetric *β*-boration of *α,β*-unsaturated esters was made by Yun *et al*[1] synthesis of chiral organoboranes remains an attractive area of research in chemical synthesis because the C−B bond can be converted into a wide variety of functional groups without loss of enantiopurity.[2] Fernández et al. first successful applied the N-heterocyclic carbene (NHC)-copper complex in enantioselective boration reaction.[3] Since then, catalysis mediated by N-heterocyclic carbenes (NHCs) based metal complexes, has emerged as a powerful tool for the synthesis of chiral organoboron compounds[4] because these catalysts have several significant advantages over their phosphine counterparts[5]. Despite the fact that few results have been reported, most of investigated cases NHC ligands and copper salts were used to generate *in situ* copper-NHC complex. Hence, high loading of ligand and copper salt may limit their application in pharmaceutical and fine-chemical industries. Therefore, we have designed new type of chiral copper catalyst **1** (Scheme 1) having planar chiral ligand and in which the alkyl chain remains quite closer to metal centre exhibiting an exceptionally high reactivity and enantioselectivity in the asymmetric boration of unsaturated esters by virtue of its special arrangement. This methodology is employed in the synthesis of chiral *β*-borylated ester from simple unconjugated alkenes through unpecedenced one- pot tandem cross metathesis-asymmetric borylation sequence.



Scheme 1: Cu-NHC Catalyzed Asymmetric Borylation

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References:

1. a) Lee, J. E.; Yun, J. *Angew. Chem., Int. Ed*. **2008**, *47*, 145.
2. a) Xi, Y.; Hartwig, J. F. *J. Am. Chem. Soc.* **2016**, *138*, 6703. b) Hall, D. G. Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials, 2nd ed.; Wiley-VCH: Weinheim, **2011**. c) Scott, H. K.; Aggarwal, V. K. *Chem. Eur. J.* **2011**, *17*, 13124.
3. Lillo, V.; Prieto, A.; Bonet, A.; Díaz-Requejo, M. M.; Ramírez, J.; Pérez, P. J.; Fernández, E. *Organometallics* **2009**, *28*, 659.
4. a Tarrieu, R.; Dumas, A.; Thongpaen , J.; Vives, T.; Roisnel, T.; Dorcet, V.; Crévisy, C.; Baslé, O.; Mauduit, M. *J. Org. Chem*. **2017**, *82*, 1880−1887 b) Park, J. K.; Lackey, H. H.; Rexford, M. D.; Kovnir, K.; Shatruk, M.; McQuade, D. T. *Org. Lett*., **2010,** *12,* 5008-5011. c) O'Brien, J. M.; Lee, K. S.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2010**, *132*, 10630.
5. a) Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev*. **2009**, *109*, 3612. b) Cohen, D. T.; Scheidt, K. A. *Chem. Sci*. **2012**, *3*, 53. c) Bugaut, X.; Glorius, F. *Chem. Soc. Rev*. 2012, 41, 3511. d) Grossmann, A.; Enders, D. *Angew. Chem., Int. Ed*. **2012**, *51*, 314.

Fast Selective Oxidation of Styrene in Benzaldehyde Catalyzed by a Copper(II) Scorpionate Complex

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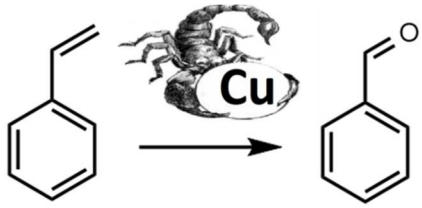
Oxidation reactions are one of the most studied in terms of catalysis to obtain different products with added value or transform products that can be used in industry. In order develop economic and greener catalytic systems, selective and efficient metal-complexes have been used due to their activity in this type of reaction. However, selectivity in oxidation reactions is one of the biggest difficulties.

Over the last years, the chemistry of scorpionate ligands has been developed due to their coordinative versatility that allows the electronic and steric features at a metal center to be tuned. The appearance of new ligands, which can improve some characteristics of their metal complexes, such as hydro-solubility, led to enhanced catalytic activity and selectivity.[1]

The styrene oxidation is one of the most studied reactions due to problems of selectivity, when the desired product is the benzaldehyde.[2] In order to try to solve this issue, a Cu(II) complex bearing homo-scorpionate ligands was tested (**Scheme 1**) and exhibits excellent activity after only 5 minutes of reaction. Benzaldehyde is the major product, being possible to obtain 100 % of selectivity in certain conditions.



Scheme 1 – Representation of the sytyrene oxidation catalysed by a Cu(II) scorpionate complex.

Acknowledgements: This work has been partially supported by the Foundation for Science and Technology (FCT), Portugal (UID/QUI/00100/2013, PTDC/QEQ-ERQ/1648/2014, PTDC/QEQ-QIN/3967/2014 and UID/MULTI/00612/2013). Tiago A.G. Duarte is thankful to FCT for his CATSUS Ph.D fellowship (PD/BD/105993/2014).

References:

1. Martins L. M. D. R. S.; Pombeiro A. J. L. *Coord. Chem. Rev.* **2014**, *265*, 74.
2. Zhang L.; Zhang Z.; He X.; Zhang F., Zhang Z. *Chem. Eng. Res. Des.* **2017**, *120*, 171.

Novel Sulfonation Method of Hydrochars for Esterification Catalysis

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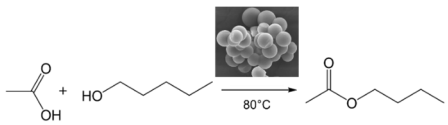
Hydrochars are carbon materials easily prepared by hydrothermal treatment of various types of carbohydrates, namely, glucose, sucrose, fructose, xylose and even starch. These materials have spherical morphology and have been successfully applied in different areas especially due to their high electrical conductivity and excellent chemical stability. There are also studies reporting the use of as-synthesised, or further activated, hydrochars as adsorbents, catalysts or catalyst supports.[1]

The aim of the present study was to use sucrose, glucose and fructose derived hydrochars as catalysts for esterification of butanol and acetic acid (**Scheme 1**). According to the literature this transformation needs the presence of the surface sulfonic groups[2] that can be introduced by a post-synthesis treatment with concentrated sulfuric acid, the most commonly reported methodology to tune surface chemistry for this purpose.

In fact, our results proved that even though the as-synthesied hydrochars present acid surface properties, as demonstrated by the Boehm titration results and pH_{PZC} values of *ca.* 2.0, they are not active, leading to only 15% conversion. Thus, hydrochars were modified by sulphuric acid treatment and by an innovative strategy consisting in the impregnation of the hydrochars with a source of sulfonic groups (*p*-toluenesulfonic acid, isethionic acid sodium salt, and 4-sulfophtalic acid) followed by a second hydrothermal treatment.

Despite in the literature glucose derived hydrochars are the most commonly used, we opted to start the catalytic study testing sucrose derivatives since with this carbohydrate a higher preparation yield is achieved. From the 6 h conversion values it can be concluded that, with the material obtained by impregnation with *p*-toluenesulfonic acid a small decrease is observed when compare with the value achieved with the sulfuric acid treated material (77% against 93 %). In the case of glucose and fructose modified hydrochars the sulphuric acid modified materials presented lower conversion yields (78 %) while the *p*-toluenesulfonic acid impregnated samples presented only a small decrease when compared to the value achieved with sucrose (70 %). Regarding the modification with the two other sulfonic sources the results of sucrose functionalized samples show that materials impregnated with 4-sulfophtalic acid reaches a conversion of 73 %, while that treated with isethionic acid sodium salt achieved only 36 % of conversion.

The results prove that impregnation method with *p*-toluenesulfonic acid and 4-sulfophtalic acid are potential alternatives to the sulphuric acid treatment, although optimization studies are still needed.



Scheme 1 – Representation of catalytic butyl acetate synthesis

Acknowledgements: This work has been partially supported by the Foundation for Science and Technology (FCT), Portugal (UID/QUI/00100/2013, PTDC/QEQ-ERQ/1648/2014, PTDC/QEQ-QIN/3967/2014 and UID/MULTI/00612/2013). Tiago A.G. Duarte is thankful to FCT for his CATSUS Ph.D. fellowship (PD/BD/105993/2014).

References:

1. White R. J., Budarin V., Luque R., Clark J. H., Macquarrie D. J. *Chem. Soc. Rev.* **2009**, 38, 3401.
2. Li Y., Zeng D. *Matt. Letters* **2017**, 193, 172.

Microwave-assisted Peroxidative Oxidation of Toluene Catalysed by Copper Metalloporphyrins

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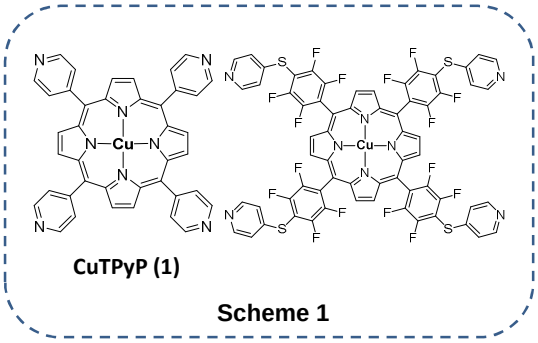
New Cu(II)-based metalloporphyrins CuTPyP (**1**) and $CuTPPF_{16}(SPy)_4$ (**2**) were prepared in a $CHCl_3$/MeOH (2:1) mixture, using 1.5 equiv. of $Cu(AcO)_2{\cdot}H_2O$ and the corresponding free base porphyrins H_2TPyP or $H_2TPPF_{16}(SPy)_4$ (Scheme 1) and characterized by UV-Vis, infrared (ATR-FTIR) and electron paramagnetic resonance (EPR) [1,2].

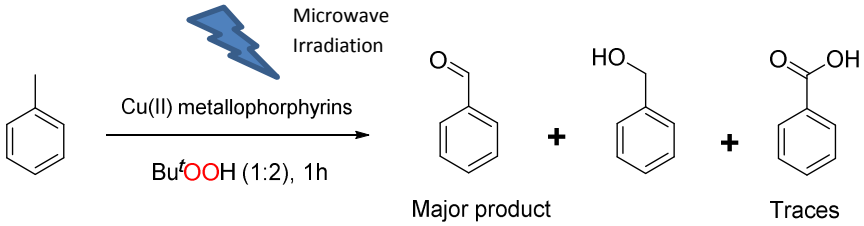
Both Cu(II) complexes act as catalyst for the microwave-assisted peroxidative oxidation of toluene. Benzaldehyde (BzH), the main product of toluene oxidation, is an important starting material in the industry of dyes, perfumes and pharmaceuticals [3]. Recently, catalytic systems involving metalloporphyrins [4,5] were successfully tested in solvent-free aerobic oxidation of toluene. However, MW assisted peroxidation of this substrate has not been explored.



Scheme 1

Complexes **1** and **2** can provide selectively benzaldehyde product with yield up to *ca*. 21% in a short period and in the absence of any added solvent (Scheme 2).

The influence of various parameters, such as, reaction time, amount of catalyst, temperature and presence of additives, was also evaluated.



Scheme 2 - Microwave-assisted oxidation of toluene

Acknowledgements: Thanks are due to FCT/MEC for the financial support to CQE (FCT UID/QUI/0100/2013) and QOPNA (FCT UID/QUI/00062/2013) research units, through national funds and where applicable cofinanced by the FEDER, within the PT2020 Partnership Agreement.

References:

1. Castro K.; Rodrigues J.; Mendes R.; Neves M.; Simões M.; Cavaleiro J.; Paz F.; Tomé J.; Nakagaki S.; *J. Catal.;* **2016**, *344*, 303.
2. Gomes M.; Woranovicz-Barreira S.; Faustino M.; Fernandes R.; Neves M.; Tomé A.; Gomes N.; Almeida A.; Cavaleiro J.; Cunha A.; Tomé J.; *Photochem. Photobiol. Sci.;* **2011**, *10*, 1735
3. F. Brühne, E. Wright, Benzaldehyde, Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH Verlag GmbH & Co. KGaA, 2011, vol. 5, pp 223-233.
4. Guo C.C.; Liu, Q.; Wang, X.T.; Hu, H.Y. *Appl Catal A*. **2005**, *282*, 55.
5. Huang, G.; Wang, A.P.; Liu, S.Y.; Guo, Y.A.; Zhou, H.; Zhao, S.K. *Catal Lett*. **2007**,*114*,174.

Friedel-Crafts Acylation/Benzolylation with *N*-Acetylpyrazine-2-Carbohydrazide-Fe(III)-Chloro Catalysts

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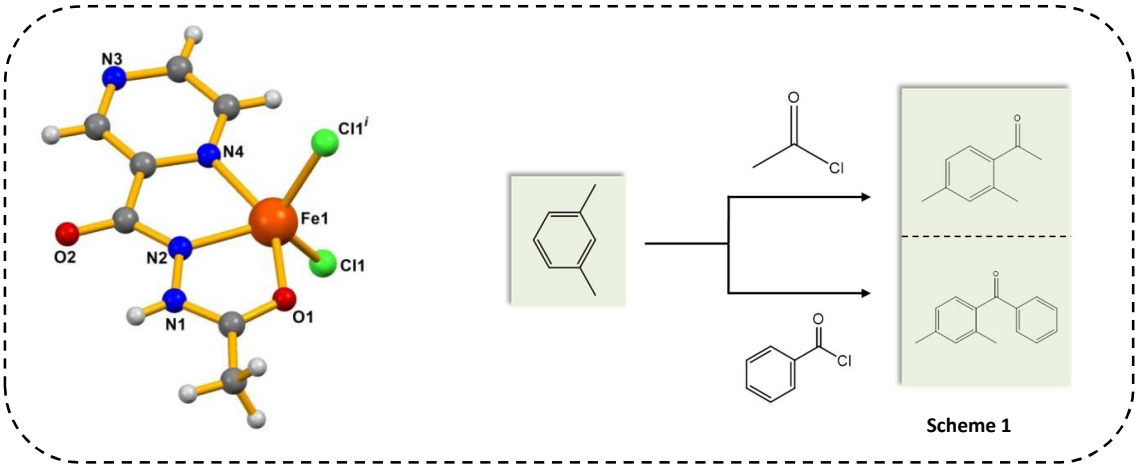
Reaction of *N*-acetylpyrazine-2-carbohydrazide with anhydrous $FeCl_2$ in two different solvents (CH_3CN and MeOH) leads to mononuclear [Fe((κ*NN'O*-HL)Cl_2] (**1**) and binuclear [Fe((κ*NN'O*-HL)Cl(μ-OMe)]$_2$ (**2**) Fe(III) complexes having chloride as an auxiliary ligand. Both the complexes **1** and **2** have been characterized by elemental analysis, various spectroscopic techniques and X-ray crystallography (**Figure 1** for complex **1**). The catalytic activity of **1** and **2** was screened towards Friedel-Crafts acylation and benzolylation of *m*-xylene. (**Scheme 1**).[1,2] The reaction conditions, such as catalyst concentration, time and temperature, were optimized. Complex **1** exhibits the highest activity in both reactions. The obtained results will be presented.



Scheme 1

Acknowledgements: Authors are grateful to the Fundação para a Ciência e a Tecnologia: FCT (projects UID/QUI/00100/2013, PTDC/QEQ-ERQ/1648/2014 and PTDC/QEQ-QIN/3967/2014), Portugal, for financial support. M.S. acknowledges the FCT, Portugal for a postdoctoral fellowship (SFRH/BPD/86067/2012).

References:

1. Mu, M.; Fang, W.; Liu, Y.; Chen, L. *Ind. Eng. Chem. Res*. **2015**, 54, 8893.
2. Cardoso, L.A.M.; Alves. W.; A.R.E. Gonzaga, A.R.E; Aguiar, L.M.G.; Andrade, H.M.C. *J. Molec. Cat. A: Chem*. **2004**, 209, 189.
3. Valkenberg, M.H.; de Castro, C.;. Hölderich, W.F. *Appl. Catal. A: Gen*. **2001**, 215, 185.

Catalytic Activity of Cu(II) Diethanolamine-based Complexes in Radical Cyclohexane Amidation

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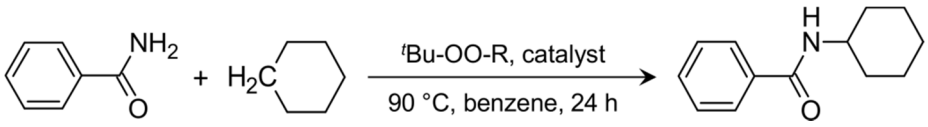
The amide group is a widespread linking fragment in nature (for example, peptide bond represents an amide), artificial compounds of industrial importance, such as polyamides (nylons), as well as pharmaceutical chemicals.[1] Among the known methods for synthesis of amides, direct amidation of saturated C–H bond is still under exploring and is hampered by the inertness of alkanes.[2] Formation of amides *via* highly reactive alkyl radical intermediates is a promising approach.[3-5] Cu(II) complexes are of special importance in a broad range of catalytic reactions,[6] which include the radical functionalization of inert alkanes where an sp^3 C–H bond undergoes hydrogen abstraction to produce a carbon-centered alkyl radical. However, the study of such processes is still rather limited. Series of aminoalcohol Cu(II) compounds are known catalysts in radical oxidation of alkanes with peroxides in polar solvents (CH_3CN/H_2O),[6] and now we propose to use bulky N- and *tert*-butyl diethanolamine-based Cu(II) complexes, which ligands should favor the solubility in a non-polar medium to achieve homogeneous catalysis in such a type of medium. The novel coordination compounds $[Cu_2(HtBuDea)_2(OAc)_2]$ (**1**) and $[Cu_2(HBuDea)_2Cl_2]$ (**2**) have been prepared through the self-assembly reaction of the respective copper(II) salts with N-*tert*-butyldiethanolamine ($H_2tBuDea$) (**1**) or N-butyldiethanolamine (H_2BuDea) (**2**) in methanol solution. Crystallographic analysis reveals that in spite of the same binuclear $\{Cu_2(\mu\text{-}O)_2\}$ core, in **1**, binuclear molecules are linked together by H-bonds into 1D chains, while in **2** the neighboring pairs of molecules are H-bonded forming tetranuclear aggregates. Complexes **1** and **2** were tested as catalysts in the reaction of amidation of cyclohexane with benzamide, in benzene medium (**Scheme 1**):



Scheme 1: Catalytic amidation of cyclohexane, catalysed by **1** and **2** (R = ^{t}Bu or H).

The maximum achieved conversion of benzamide (20%, after 24 h reaction time) was observed in the **1**/^{t}BuOO^{t}Bu system. In the cases of ^{t}BuOO(O)CPh (*tert*-butyl perbenzoate) or ^{t}BuOOH oxidants, no amidation product was significantly observed, while the oxidative dehydrogenation of cyclohexane occurred (for ^{t}BuOO(O)CPh) to afford the allylic ester (cyclohex-2-en-1-yl benzoate) as the main reaction product.

Acknowledgements: This work was supported by Fundação para a Ciência e Tecnologia (FCT), Portugal (projects PTDC/QEQ-QIN/3967/2014 and UID/QUI/00100/2013; fellowship SFRH/BPD/99533/2014).

References:

1. Wan J. P.; Jing Y. F. *Beilstein J. Org. Chem.* **2015**, *11*, 2209.
2. Hartwig J. F. *J. Am. Chem. Soc.* **2016**, *138*, 2.
3. Tran B. L.; Li B. J.; Driess M.; Hartwig J. F. *J. Am. Chem. Soc.* **2014**, *136*, 2555.
4. Kamon T.; Irifune Y.; Tanaka T.; Yoshimitsu T. *Org. Lett.* **2011**, *13*, 2674.
5. Yamaguchi J.; Yamaguchi A. D.; Itami K. *Angew. Chem. Int. Edit.* **2012**, *51*, 8960.
6. Kirillov A. M.; Kirillova M. V.; Pombeiro A. J. L. *Coord. Chem. Rev.* **2012**, *256*, 2741.

Microwave-assisted Peroxidative Oxidation of Toluene and 1-Phenylethanol with Aroylhydrazone Cu(II) Catalysts

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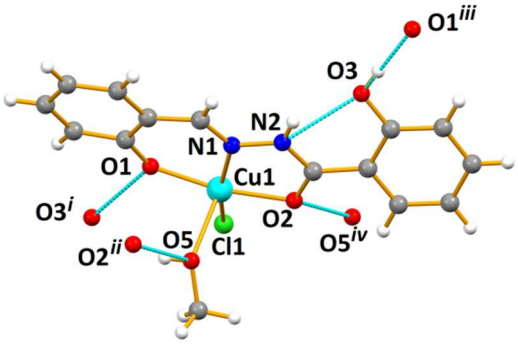
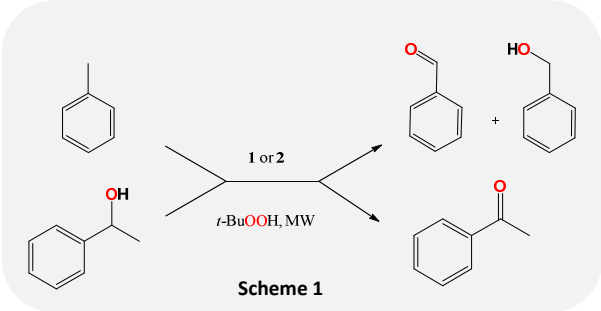
The aroylhydrazone Schiff base 2-hydroxy(2-hydroxybenzylidene)benzohydrazide (H_2L)[1] has been used to synthesize Cu(II) complexes in two different tautomeric forms (keto and enol). While the Cu(II) complex with the enol form of the ligand exists as the 1D polymer $[Cu(1\kappa NOO',2\kappa O',3\kappa O''\text{-}L)]_n$ (**1**), that with the keto form of the ligand occurs as the monomer $[Cu(\kappa NOO'\text{-}HL)Cl(CH_3OH)]$ (**2**) (**Figure 1**). Both **1** and **2** have been characterized by elemental analysis, IR spectroscopy, ESI-MS and single crystal X-ray crystallography. In the last decade, microwave (MW) irradiation in catalytic reactions has received a great attention.[2] In this study, both complexes act as good catalysts for the MW-assisted peroxidative oxidation of toluene and 1-phenylethanol with *tert*-butyl hydroperoxide (**Scheme 1**). Complex **2** exhibits the highest activity in both reactions, leading selectively to a maximum product yield of 39 and 92%, respectively.





Scheme 1

Figure 1: Structural representation of **2** with partial atom labelling

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References:

1. Sutradhar, M.; Mukherjee, G.; Drew, M. G. B.; Ghosh, S. *Inorg. Chem.* **2007**, *46*, 5069–5075.
2. Kopylovich, M. N.; Ribeiro, A. P. C.; Alegria, E. C. B. A.; Martins, N. M. R.; Martins, L. M. D. R. S.; Pombeiro, A. J. L. *Adv. Organometal*. Chem. **2015**, *63*, 91-174.

Bimetallic Nickel - Rare Earth Oxides: a New Approach for the Methanation of CO_2

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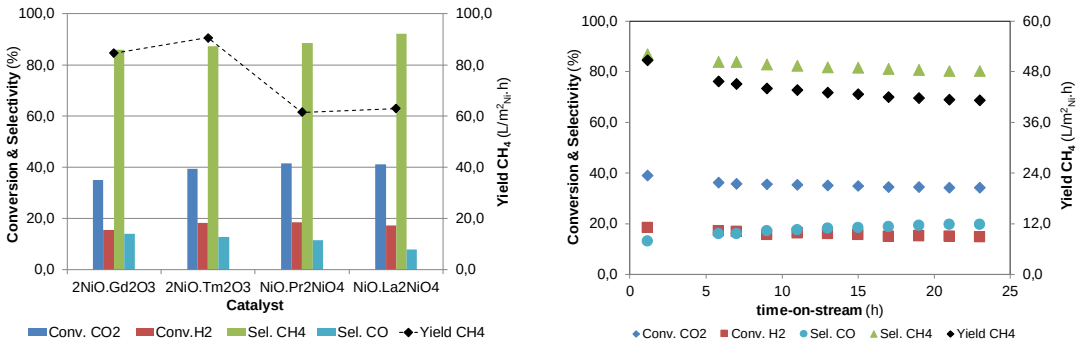
In the last decades, the number of studies aiming the development of processes able to decrease the emissions of greenhouse gases (e.g. CO_2, CH_4 and N_2O) using them as feedstock for the production of value-added chemicals (e.g. hydrocarbons and alcohols) increased exponentially. Currently, the use of CO_2 as chemical feedstock is limited to a few processes: synthesis of urea (for nitrogen fertilizers and plastics), salicylic acid (a pharmaceutical ingredient), and polycarbonates (for plastics).[1]

In this context, the hydrogenation of CO_2 to methane is a major catalytic goal. The methanation of carbon dioxide has a range of applications including: i) the purification of synthesis gas for the production of ammonia, ii) the production of syngas or iii) their use to convert the Martian CO_2 atmosphere into CH_4 and H_2O for fuel and astronaut life support systems.[2]

Herein, we present the study of the methanation of CO_2 using bimetallic nickel - *f* block element oxides as catalysts. The results obtained show good catalytic performance, e.g. selectivity >80% (Fig. 1A) and unusual long-term stability in the gaseous stream (Fig. 1B). All samples were characterized by different techniques (XRD, SEM/EDS, H_2-TPR).



(A) (B)

Figure 1: (A) Methanation of CO_2 over bimetallic nickel-lanthanide oxides at 350 ºC, without pre reduction; (B) Stability study over NiO.Pr_2NiO_4 at 350 ºC. (CO_2 / H_2 =1:4 mol/mol; GHSV=15000 mL of CO_2 per g of catalyst and per h)

Acknowledgements: C^2TN/IST authors gratefully acknowledge also the FCT support through the UID/Multi/04349/2013 project.

References:

1. Centi, G.; Perathoner, S.; *Catal. Today* **2009**, 148, 191-205.
2. Wang W.; Gong J.; *Front. Chem. Sci. Eng.* **2011**, 5(1), 2-10.

Valorisation of Primary Pollutants using Nanostructured Bimetallic *f*-Block Element Oxides Obtained by Electrospinning

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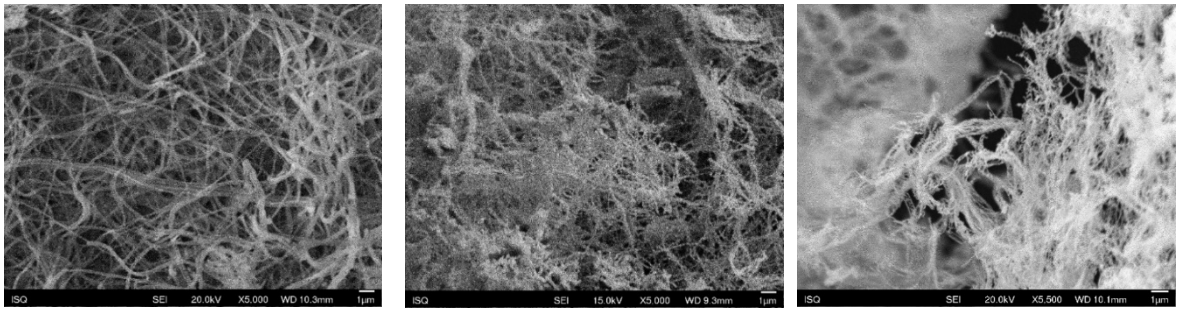
Electrospinning is a simple and versatile technique that is capable of producing nanofibers with diameters ranging from 50 to 500 nm [1].This preparation method has the advantages of easy and versatile deposition in the manufacture of polymeric materials, composites, and ceramics [1-3].
The goal of this work was to prepare bimetallic oxides nanofibers/nanoparticles containing *f*-block elements using the electrospinning technique, and to study their catalytic properties for the valorization of primary pollutants (e.g.CH_4, CO_2 or N_2O) to obtain value-added products such as syngas, hydrocarbons or alcohols. The preparation of bimetallic of $NiO.LaNiO_3$, $Co_3O_4.SmCoO_3$ and $Fe_2O_3.DyFeO_3$, with a crystallite size around 30 nm, was successfully undertaken. All nanostructured bimetallic oxides were characterized by XRD and SEM-EDS. Figure 1 shows SEM images of the nanofibers of bimetallic oxides containing f block elements.
The best catalytic results for the methanation of CO_2 were those obtained over $NiO.LaNiO_3$ that presents an activity and selectivity comparable to that of standard commercial catalysts (5% Rh, Pt /Al_2O_3). The influence of the nanostructure in the catalytic activity will be discussed.



(A) (B) (C)

Figure 1: SEM Images of bimetallic oxide nanofibers of (A) $NiO.LaNiO_3$ (B) $Co_3O_4.SmCoO_3$ (C) $Fe_2O_3.DyFeO_3$.

Acknowledgements: C^2TN/IST authors gratefully acknowledge also the FCT support through the UID/Multi/04349/2013 project.

References:

1. Chronakis, I.S. *Journal of Materials Processing Technology* 167, **2005**, 283-293.
2. Fong, H., Liu, W., Wang, C.S., Vaia, R.A., *Polymer* **2002** 43,775.
3. Chronakis, I.S., *Micro-/Nano-Fibers by Electrospinning Technology: Processing, Properties and Applications,* in Y. Quin (Ed.), *Micro-manufacturing Engineering and Technology*, Elsevier, Oxford, **2010**, pp. 264.

A Cooperative Metal-Ligand Effect in Intramolecular Hydromination Catalysis

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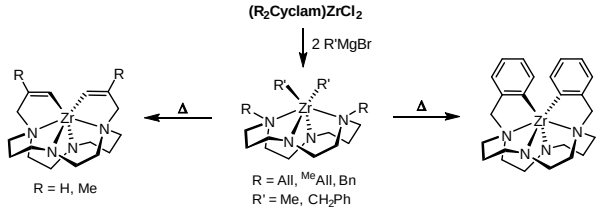
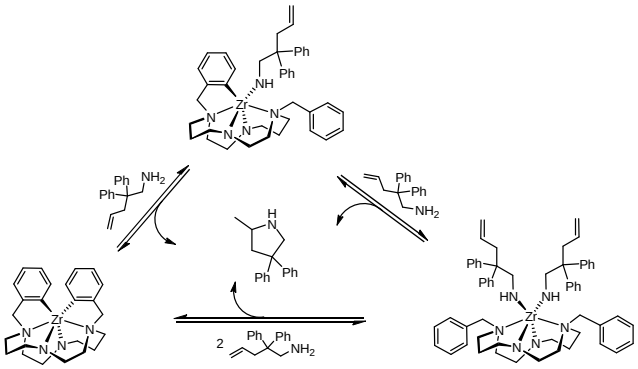
The reactivity of *trans*-disubstituted cyclam-based diamido-diamine zirconium complexes revealed particular features that are intimately related to the nature of the macrocyclic frame. Complexes of the type (R_2Cyclam)$ZrCl_2$ (where R = CH_2=C(H)CH_2 (All), CH_2=C(Me)CH_2 (^{Me}All) and PhCH_2 (Bn)) react with suitable Grignard reagents to produce the corresponding alkyl derivatives (R_2Cyclam)R'_2 (R' = Me, CH_2Ph).[1] Thermally induced double metalation of the pending arms of the cyclam ligand led to the formation of (($C_6H_4CH_2)_2$Cyclam)Zr or (($CH=C(R)CH_2)_2$Cyclam)Zr (R = H, Me) complexes (**Scheme 1**).[1] This reaction proceeds with R'H elimination converting the original dianionic tetracoordinated cyclam in a tetraanionic hexacoordinated ligand where two new Zr-C bonds complete the metal sphere.



Scheme 1

The afore mentioned complexes are the unique macrocyclic-based hydroamination catalysts reported to date.[2] NMR and DFT studies of the reaction mechanism disclosed the central role of the cyclam ligand in the catalytic process that involves C-H activation of the pending arms (**Scheme 2**).[1a] In this communication we will discuss the catalytic intramolecular hydroamination of aminoalkenes that involves a cooperative metal-ligand mechanism.



Scheme 2

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (UID/QUI/00100/2013, SFRH/BPD/86815/2012 and SFRH/BD/87679/2012).

References:

1. a) Alves L. G.; Madeira F.; Veiros L. F.; Martins A. M. *unpublished results*. b) Munhá, R. F.; Antunes M. A.; Alves, L. G.; Veiros L. F.; Fryzuk M. D.; Martins A. M. Organometallics **2010**, *29*, 3753.
2. Antunes M. A.; Munhá R. F.; Alves L. G.; Schafer L. L.; Martins A. M. *J. Organomet. Chem.* **2011**, *696*, 2.

An Azoaromatic Ligand as Electroprotic Reservoir: Exclusively Ligand-Mediated Catalytic Dehydrogenation of Alcohols

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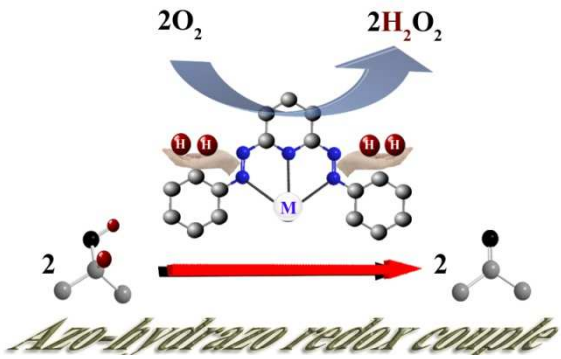
Hydrogen production from renewable sources now promises potential sources of clean energy.[1] With the help of fuel cells, molecular hydrogen can be converted efficiently to produce electricity. However, storage of hydrogen is a challenging task. Recent developments on the dehydrogenation catalysts are focused on transition metal complexes of redox non-innocent ligands because of their ability to store the hydrogen using metal-ligand cooperation.[2] Such systems are well utilized for hydrogen production from liquid organic hydrogen carriers.

We have been interested in coordination chemistry of redox active azo-aromatics and exploration of their application possibilities. In this present work, we describe redox chemistry of a nickel complex of bis-(arylazo)pyridine ligand.[3] This complex has been turned out to be an efficient catalyst for dehydrogenation reaction for both primary and secondary alcohols using azo/hydrazo redox couple. Isolation and characterization of reactive intermediates, kinetic studies, isotope labeling experiments have revealed that a hydrogen atom transfer pathway is operative which involves exclusively ligand redox keeping the metal as spectator.[3]



Scheme 1: Ligand-mediated catalytic alcohol dehydrogenation.

Acknowledgments: We thank Dr. Ayan Datta and Mr. Rameswar Bhattacharjee for theoretical calculations

References:

1. Rodriguez-Lugo, R. E.; Trincado, M.; Vogt, M.; Tewes, F.; Santiso-Quinones, G.; Gruetzmacher, H. *Nat. Chem.* **2013**, *5*, 342-347.
2. Gunanathan, C.; Ben-David, Y.; Milstein, D. *Science* **2007**, *317*, 790-792.
3. Sengupta, D.; Bhattacharjee, R.; Pramanick, R.; Rath, S. P.; SahaChowdhury, N.; Datta, A. *Inorg. Chem*. **2016**, *55*, 9602-9610.

An Optimized Catalytic Route to Dibenzodiazepines using *Ortho*-ChlorophenylTosyl-imine Substrates

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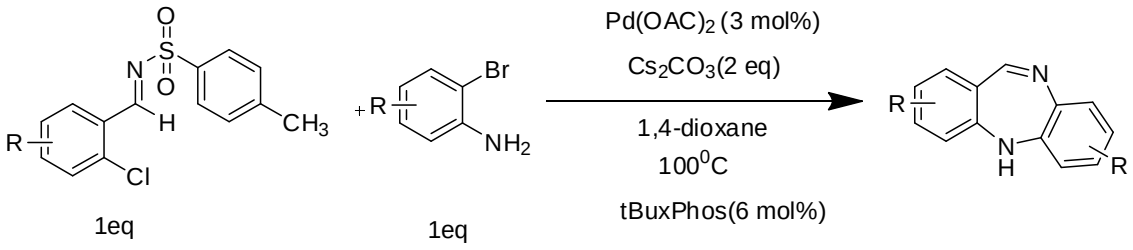
Dibenzodiazepine derivatives (DBDAs) are medicinally important hetero aromatic systems, with many applications in alcohol dependence, seizures, anxiety disorders, panic, agitation and insomnia medicine. Many methods are available for the synthesis of DBDAs, but we have developed a novel method that involves a one-pot Buchwald-Hartwig/C-N coupling process involving Pdcatalysts.[1,2] Recently, we have shown that this reaction is now successfully accomplished using *ortho-chlorophenyltosyl-imines* derived from cheaper *o-chloro benzaldehydes*. The reaction conditions were optimized (solvent, base, ligand and catalyst) and best results were obtained with 1,4-dioxane,Cs_2CO_3,*t*BuxPhos, $Pd(OAc)_2$.This method provides the products in high yields with easy reaction workup.



Scheme or Figure 1: Synthetic Route to obtain DBDAs.

Acknowledgements: We thank the ERASMUS-Mundus Leader program for support to SM and theFundação para a Ciência e a Tecnologia (FCT) through grantUID/QUI/0619/2016(contributed to CQE-UE) for supporting this work.

References:

1. D. Peixoto, A.Locati, C.S. Marques, A.Goth, J.P.P. Ramalho, A.J. Burke, RSC Advances, 2015, 5,99990-99999.

2. D. Peixoto, AJ Burke, WO2016/207790 A1.

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Efficient and Innovative Method for the Enantioselective Synthesis of Rivastigmine using *Cinchona*-alkaloids Organocatalysts

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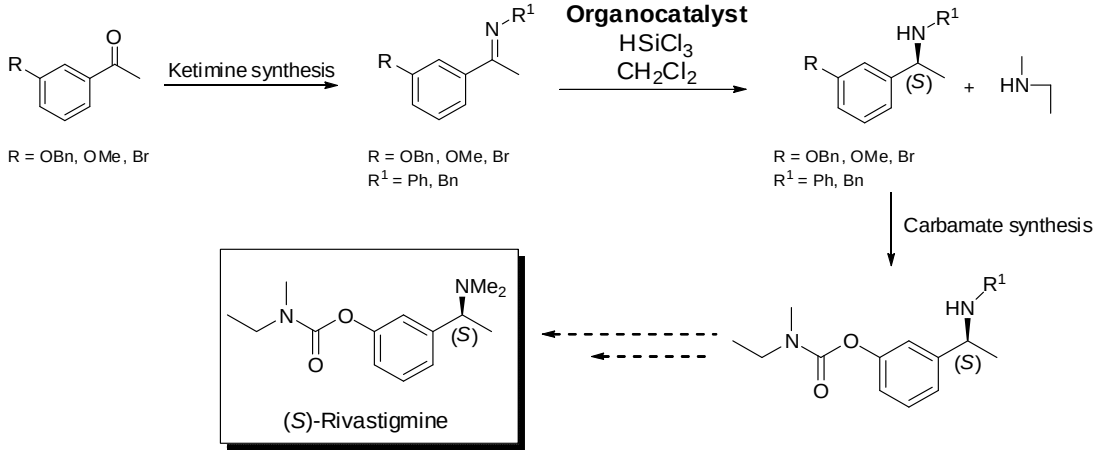
At this time, Alzheimer's disease (AD) is becoming one of the most serious public health problems. One of the best drugs for the symptomatic treatment of Alzheimer's disease is (*S*)-Rivastigmine[1] (**Scheme 1**), a dual cholinesterase inhibitor (acetylcholinesterase and butylcholinesterase). Currently, the only successful synthetic route for this compound is via symmetric catalytic hydrogenation of ketimines that usually relies on the use of very expensive and harmful catalysts. We have successfully applied Cinchonidine and Quinine-derived Picolinamides as organocatalysts for the hydrosilylation of ketimines[2] – the key step on our new and highly efficient synthetic pathway for the synthesis of (*S*)-Rivastigmine (**Scheme 1**). These organocatalysts have shown to be very efficient in the enantioselective reduction of ketimines.[3] Overall, these Cinchonidine-derived organocatalysts showed the best results in terms of enantioselectivity with excellent yields.[2] However, the results differ considerably depending on the starting structure of the ketimine substrate, with the phenyl-derived ketimines giving the best overall results.



Scheme 1: Proposed synthetic pathway for (*S*)-Rivastigmine synthesis.

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References:

1. a) Plinsky R.J. *Clinical Therapeutics* **1998**, *20*, 634-647. b) Bhanja, C.; Jena S. *J.Chem. Pharm. Res.* **2012**, *4,* 3171-3183.
2. a) Fernandes S.D.; Porta R.; Barrulas P.C.; Puglisi A.; Burke A.J; Benaglia M. *Molecules* **2016**, *21*, 1182. b) Brenna D.; Benaglia M.; Porta R.; Fernandes S.; Burke A.J. *Eur. J. Org. Chem*. **2017**, *1*, 39-44.
3. a) Barulas P.C.; Genoni A.; Benaglia M.; Burke A.J. *Eur. J. Org. Chem*. **2014**, 7339-7342. b) Novel Picolinamide-Cinchona Organocatalysts and derivatives, P.C. Barrulas, A.J. Burke, WO2015052656.

Oxindoles as Privileged Structure Scaffolds for Drug Design

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In 1988, Evans[1] and co-workers underlined the term 'privileged structures', describing them as simple structural subunits present in the molecules of several drugs, with distinctive therapeutic uses, or affinities to several different receptors. The oxindole framework, bearing a tetrasubstituted quaternary carbon stereocenter in the 3-position is a so-called privilege structure, found in numerous natural products and active pharmaceutical ingredients (APIs) (**Figure 1**). Despite many advances over the last years by synthetic chemists concerning the easy access of libraries containing thousands of oxindole type compounds, the ability to make critical discoveries pertinent to disease remains a slow, serendipitous and debatable process. Our group has a particular interest in library design of 3-substituted oxindoles, exploring new synthetic paths using transition-metal catalysts with the aim to test their biological activities mostly for cancer and neurodegenerative disiases.[2] We wish to report our recent efforts concerning new catalytic synthetic routes to 3-substituted oxindole derivatives and some preliminary results concerning bio-assays.

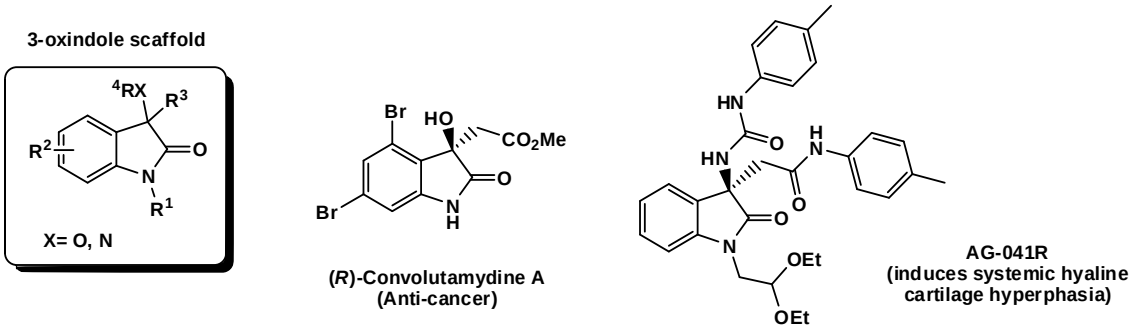

Figure 1: 3-Oxindole framework and examples of natural products and APIs.

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References:

1. Evans, B. E.; Rittle, K. E.; Bock, M. G.; DiPardo, R. M.; Fredinger, R. M.; Whitter, W. L.; Lundell, G. F.; Veber, D. F.; Anderson, P. S.; Chang, R.S. L.; Lotti, V. J.; Cerino, D.J.; Chen, T. B.; Kling, P. J.; Kunkel, K. A.; Springer, J. P.; Hirshfield, J. *J. Med. Chem.* **1988**, 31, 2235.
2. a) Marques, C. S.; Burke, A. J. *Eur. J. Org. Chem.* **2016**, 806; b) Bacalhau, P.; San Juan, A. A.; Marques, C. S.; Peixoto, D.; Goth, A.; Guarda, C.; Silva, M.; Arantes, S.; Caldeira, A. T:; Martins, R.; Burke, A. J. *Bioorg. Chem.* **2016**, 67, 1; c) Totobenazara, J.; Bacalhau, P.; San Juan, A. A.; Marques, C. S.; Fernandes, L.; Goth, A.; Caldeira, A. T.; Martins, R.; Burke, A. J. *Chem. Select* **2016**, 1, 3580; d) Marques, C. S.; Burke, A.J. *ChemCatChem*, **2016**, 8, 3518.

Chiral Molecules from Renewable Resources - Chemists Supporting Chemists

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ChiraTecnics is a custom research organisation (CRO) based in Portugal, with lab facilities in the Science and Technology Park of Évora. The company was founded in 2009 as a spin-out from the University of Évora with the aim to commerciallise chiral speciality chemicals for asymmetric syntheses. A selection of chiral building blocks and ligands from the ChiraTecnics compound catalogue is shown in Figure 1. Some of these compounds originate from the Burke research group[1] and find use in natural product syntheses or reactions such as asymmetric hydrosilylations, hydrogenations, arylations, Mannich reactions.

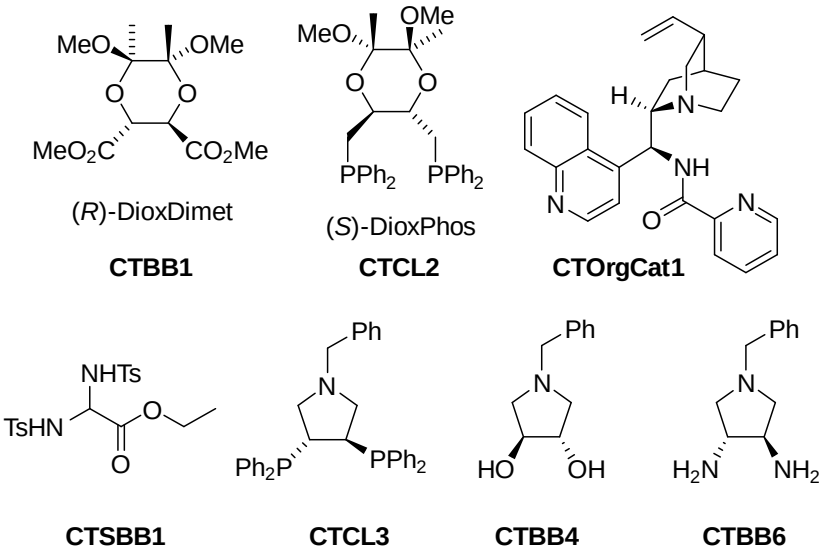

Figure 1: Selection of chiral building blocks and ligands from the ChiraTecnics compound catalogue.

In addition ChiraTecnics offers contract research services on an FTE basis to support medicinal chemistry and drug discovery programmes for pharmaceutical and biotech companies. With extensive knowledge and experience ChiraTecnics prides itself with responding rapidly to customer's needs and operating up to high standards at affordable costs.

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References:

1. a). C. S. Marques, A. J. Burke, *Tetrahedron* 69, 10091-10097 (2013); b) C. S. Marques, A. J. Burke, *Tetrahedron: Asymmetry* 18(15) 1804-1808 (2007); c) C. S. Marques, A. J. Burke, *Synth. Commun.* 38(23), 4207-4214 (2008); d) C. S. Marques, A. J. Burke, *Eur. J. Org. Chem.* 9, 1639-1643 (2010); e) C. S. Marques, A. J. Burke, *Eur. J. Org. Chem.* 22, 4232-4239 (2012); f) A. J. Burke, P. M. Cambeiro Barrulas, WO2015052656 (2015).

One-Pot Four-Component Synthesis of 1,2,3-Triazole-Dihydropyrimidinone Hybrids by a Click-Biginelli Reaction

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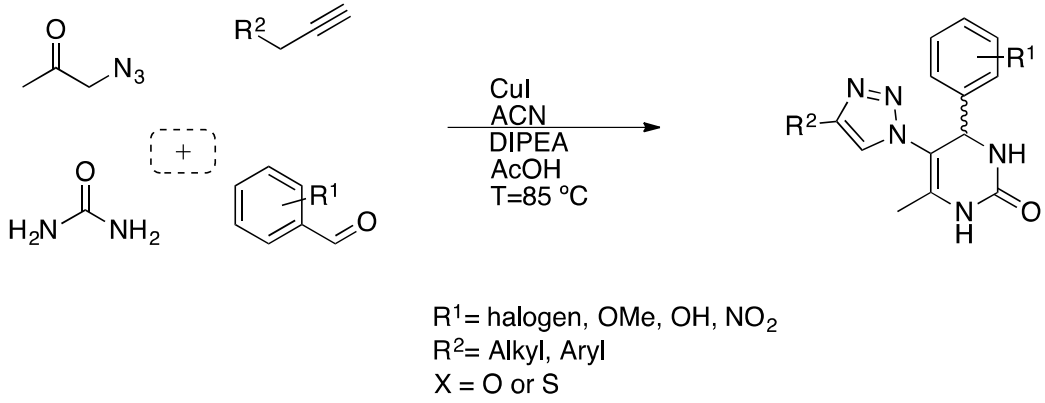
We have developed an efficient one-pot four-component synthesis of a new family of 1,2,3-triazole-dihydropyrimidinone hybrids using the combination of the copper (I)-catalysed azide-alkyne cycloaddition (CuAAC) reaction – which is a standard click reaction – followed by Biginelli reactions using aromatic aldehydes, propargyl derivatives, urea or thiourea, and a 1-azidopropan-2-one compound with CuI as catalyst, with DIPEA and acetic acid under mild reaction conditions (**Scheme 1**). Some one-pot syntheses of 1,2,3-triazole-dihydropyrimidinones have been desbribed in the literature, but they used *O*-propargylbenzaldehydes, whereas in our work we used a 1-azidopropan-2-one precursor, and a triazole linked in the C5-position to a dihydropyrimidinone unit.[1] Both triazole and dyhydropyrimidinone heterocycles have a large spectrum of biological applications[2], and thus these molecules were designed for antiproliferative activity in certain cancer cell lines. Our latest results are described in this communication.



Scheme 1: Schematic representation of one-pot synthesis of 1,2,3-triazole-dihydropyrimidinone hybrids.

Acknowledgements: EPC thanks the Fundação para a Ciência e Tecnolgia for financial support for a post-doctoral research fellowship (SFRH/BPD/72182/2010). We are grateful also for funding from FCT via the Strategic Project UID/QUI/0619/2016 (contributed to CQE-UE). We are grateful to project LADECA (ALENT-07-0262-FEDER-001878) for financing the acquisition of our Bruker Avance III NMR spectrometer.

References:

1. a) Salehi P., Dabiri M., Koohshari M. et al. *Mol Divers* **2011**, *15*, 833. b) González-Olvera R.; Román-Rodríguez V.; E. Negrón-Silva G. E.; Espinoza-Vázquez A.; Rodríguez-Gómez F. J.; Santillan R. *Molecules* **2016**, *21*, 250.
2. a) Agalave, Sandip G.; Maujan, Suleman R.; Pore Vandana S. *Chem. Asian J.* **2011**, *6*, 2696; b) De Fátima, A.; Braga, T.C.; Neto, L.S.; Terra, B.S.; Oliveira, B.G.F.; da Silva, D.L.; Modolo, L.V. *J. Adv. Res.* **2015**, *6*, 363.

Synthesis and Characterization of Silver Sulfide Nanoparticles for Catalytic Activity

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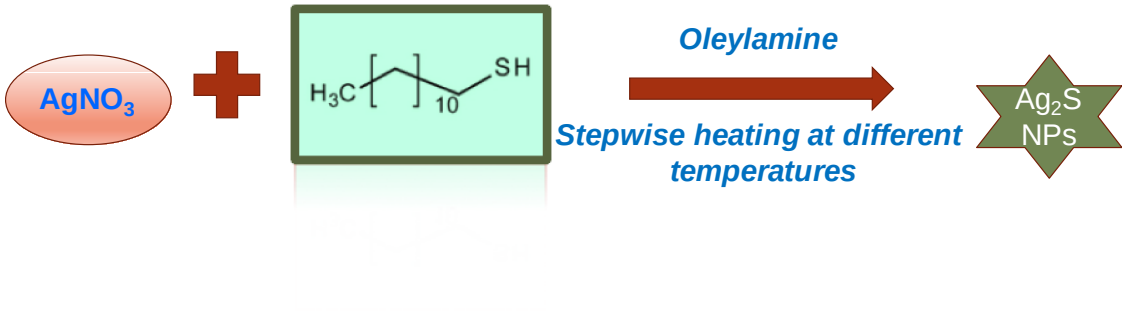
Increase in energy demand during recent time is encouraging researchers to find an alternative robust green energy source like hydrogen fuel. Different metal chalcogenides have attracted great deal of attention due to their highly thermal and chemical stability along with their good catalytic activity in electrochemical and photochemical hydrogen evolution reactions by water splitting or alcohol oxidation. Here in this present study, we have successfully synthesized noble metal sulfide eg, Silver sulfide (Ag2S) by a novel wet-chemical technique using different temperatures at different steps (Scheme 1). After synthesis, different characterization tools like; X-Ray Diffraction, FEGTEM, Cyclic Voltammetry and Raman spectroscopy have been employed and after that we have confirmed about the nanostructure of this new type of material. In our future plan, we would like to use this material as potential electrocatalyst for hydrogen evolution reaction using water or alcohol as the source of hydrogen.



Scheme 1: Synthesis of Ag2S nanoparticles.

Acknowledgements: We thank Department of Science and Technology (DST), India and Indian Association for the cultivation of Science for financial support and infrastructural facilities.

References:

1. Li D. J.; Maiti U. N.; Lim J.; Choi D. S.; Lee W. J.; Oh Y.; Lee G. Y. and Kim S. O. Nano Lett. **2014**, 14, 1228-1233
2. Dinda D.; Ahmed M. E.; Mandal S.; Mondal B. and Saha S. K. S. J. Mater. Chem. A, **2016**, 4, 15486-15493

Kinetics of Product Formation between Nitrobenzenethiol and Benzoquinone Derivatives

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Allergic contact dermatitis is a global health problem caused by a wide range of chemicals after repeated contact with the skin [1]. Among these chemicals benzoquinone and its derivatives are categorized as extreme skin sensitizers [2]. There is, therefore, a need to fully study the reaction of benzoquinone derivatives (BQD) with nitrobenzenethiol (NBT) as a surrogate for protein haptenation. The BQD investigated included: 1,4-benzoquinone (BQ), 2,5-dimethylbenzoquinone (2,5DBQ) and 2,6-dimethylbenzoquinone (2,6DBQ). The reaction of NBT with BQD led to the formation of 2-(4-nitrophenylthio) hydroquinone (NPTH), 3-(4-nitrophenylthio)-2,5-dimethylbenzene-1,4-diol (NPTBT), and 2-(4-nitrophenylthio)-3,5dimethylbenzene-1,4-diol (NPTDMBD). The formation of these products was verified by a number of spectroscopic techniques. The kinetics of the reaction between BQD and NBT were studied under pseudo first-order conditions at different pH and initial reactant concentrations by UV-spectrophotometry and stopped-flow techniques. The reaction stoichiometry was ratio 1:1 NBT to BQD. The reaction is faster at the lower pH. The kinetic results showed the reactivity of the BQD towards NBT followed the order: BQ > 2,6DBQ > 2,5DBQ due to inductive electron-donating effect of methyl group.

References:

1. A.-T. Karlberg, M. A. Bergström, A. Börje, K. Luthman and J. L. G. Nilsson, *Chemical Research in Toxicology*, 2007, **21**, 53-69.
2. I. Kimber, D. Basketter, M. Butler, A. Gamer, J.-L. Garrigue, G. Gerberick, C. Newsome, W. Steiling and H.-W. Vohr, *Food and Chemical toxicology*, 2003, **41**, 1799-1809.

One-Pot and One-Step Microwave-Assisted Synthesis of Tryptanthrin – a Relevant Natural Product in Medicinal Chemistry

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Tryptanthrin is a weakly basic indoloquinazolinone alkaloid isolated from several natural sources, including indigo plants, which are commonly used in Tradicional Chinese Medicine. Tryptanthrin and its derivatives present diverse biological activities, such as antipathogenic, anticancer, antioxidant and anti-inflammatory [1,2].

Due to its relevance, several synthetic methodologies were developed in order to obtain tryptanthrin, including the reaction between isatin and isatoic anhydride, in the presence of and organic or an inorganic base, under conventional heating or using microwave-assisted organic synthesis (MAOS). In addition, the two described reactants are also oxidation products of another very relevant natural product – indigo. This dye can be oxidized to tryptanthrin in the presence of ozone and methanol at 0ºC [3,4].

In this work, we describe a new one-pot and one-step synthesis of tryptanthrin from indigo under microwave irradiation (**Figure 1**), the respective structure elucidation and some preliminary results of its spectral and photophysical properties.

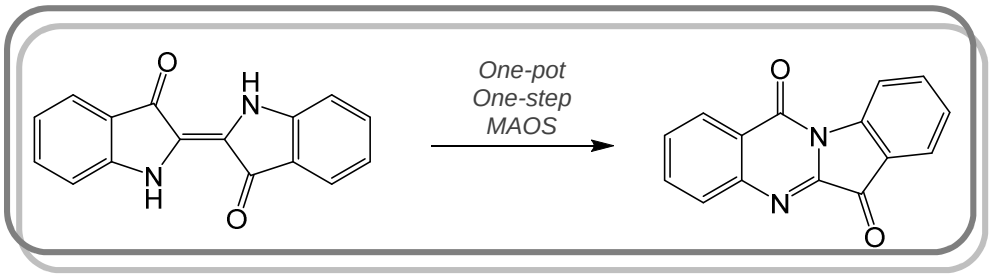

Figure 1: Synthesis of Tryptanthrin from indigo using MAOS.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (Pedro Brandão - PD/BD/128490/2017 – CATSUS FCT-PhD Program and Daniela Pinheiro - SFRH/BD/74351/2010).

References:

1. Jahng, Y. (2013), *Progress in the studies on tryptanthrin, an alkaloid of history*, Arch. Pharm. Res, 36, pp. 517–535.
2. Tucker, A. M., Grundt, P. (2012), The chemistry of tryptanthrin and its derivatives, Reviews and Accounts, 1, pp. 546-569.
3. Li, H-Y., Chen, C-Y., Cheng, H-T., Chu, Y-H. (2016), *Exploiting 1,2,3-triazolium ionic liquids for synthesis of tryptanthrin and chemoselective extraction of copper (II) ions and histidine-containing peptides*, Molecules, 21 (10), pp. 1355.
4. Matsui, M., Morita., M., Shibata, K., Takase, Y. (1982), *Ozonolysis of Indigo*, Nippon Kagaku Kaishi, 7, pp. 1268-1269.

Oxindole Hybrids: the Quest for New Molecules with Drug-Like Properties (preliminary studies)

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The hybridization method is a topic with great interest for chemists since the beginning of this century, since it allows to expand the known chemical space of molecules with drug-like properties. The association of two or more scaffolds with known biological/pharmacological properties in one molecule can result in an improvement of the clinical results of a drug. The oxindole scaffold is present in several commercialized drugs or in different stages of clinical trials and it is widely known for presenting several bioactivities. Among the different oxindoles, isatin (1H-indole-2,3-dione) is a very important scaffold in Medicinal Chemistry, since several derivatives have shown wide biological activities, namely in the treatment of cancer, neurodegenerative disorders and other central nervous system pathologies[1-3]. In our work, we plan to develop libraries of new chiral oxindole hybrids, by using green methods and asymmetric catalysis (**Figure 1**). In this communication, we report some preliminary results regarding the isatin scaffold. Isatin presents a highly reactive C-3 carbonyl group, which many times can be converted into a chiral center. However, in order to expand the pool of compounds with drug-like properties, the C-3 carbonyl group needs to be protected prior to molecular modification in other positions. One of the typical methodologies applied to achieve this goal is the protection with ethyleneglycol[4,5]. In this work, we explore different methods to obtain this molecule, comparing the conventional methodology with greener approaches. Even though the best result so far was still obtained under conventional conditions, in the future we will continue to explore different reactional conditions to promote a greener route for this important synthetic building block.

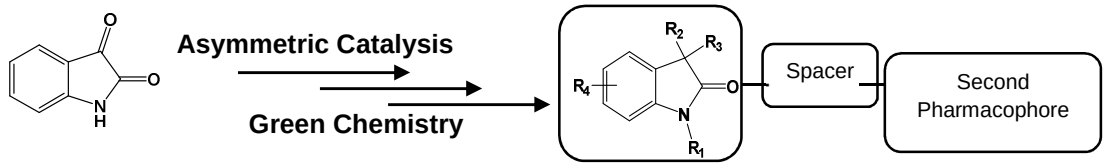

Figure 1: Drug design of new oxindole hybrids.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia (FCT) for financial support (Pedro Brandão - PD/BD/128490/2017 – CATSUS FCT-PhD Program) and for the strategic project UID/QUI/0619/2016 attributed to CQE-UE.

References:

1. Phogat, P., Singh, P. (2015), *A mini review on central nervous system potential of isatin derivatives,* Central Nervous System Agents in Medicinal Chemistry, 15(1), pp. 28-31.
2. Totobenazara, J., Bacalhau, P., San Juan, A. A., Marques, C. S., Fernandes, L., Goth, A., Caldeira, A. T., Martins, R., Burke, A. J. (2016), *Design, Synthesis and Bioassays of 3-Substituted-3-Hydroxyoxindoles for Cholinesterase Inhibition*, Chemistry Select, 1 (13), pp. 3580-3588.
3. Vine, K. L., Matesic, L., Locke, J. M., Ranson, M., Skropeta, D. (2009), *Cytotoxic and Anticancer Activities of Isatin and Its Derivatives: A Comprehensive Review from 2000-2008*, Anti-Cancer Agents in Medicinal Chemistry, 9 (4), pp. 397-414.
4. Singh, G. S., Desta, Z. Y (2013), *Applications of Isatin Chemistry in Organic Synthesis and Medicinal Chemistry* in *Chemistry and Pharmacology of Naturally Occurring Bioactive Compounds*, by G. Brahmachari, Chapter 4, pp. 73-115, CRC Press.
5. Ribeiro, N. M., Pinto, A. C., da Silva, B. V., Violante, F. A., Dias, M. O. (2007), *A fast, efficient and eco-friendly procedure to prepare isatin ketals*, Catalysis Communications, 8 (12), pp. 2130-2136.

Asymmetric Grignard Synthesis of Tertiary Alcohols

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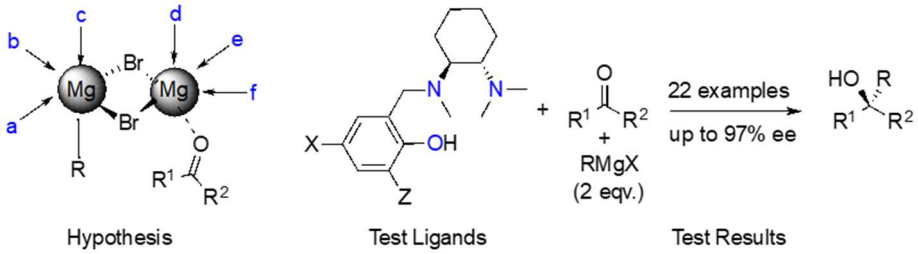
Chiral tertiary alcohols constitute an important class of biologically active molecules.[1] However their asymmetric synthesis remains problematic. An efficient and general enantioselective direct 1,2-addition of organomagnesium reagents to ketones would be extremely desirable but is very challenging. To the best of our knowledge, only two cases have been reported to date where high enantioselectivity was obtained in the absence of metals other than magnesium.[2] The challenges lie in: low enantioface discrimination between the prochiral sides of a ketone, competitive non-stereoselective reaction, enolization/reduction side reactions, competitive radical processes and, most significantly, dynamic processes originating from Schlenk and aggregation equilibria.[3]



Scheme 1: Proposed reactive dimeric intermediate towards the formation of chiral tertiary alcohols utilizing novel tridentate ligands

We recently used a rational design process based on a mechanistic hypothesis to propose that tridentate ligands should lead to better stereoselection. The hypothesis was tested with the salan ligands shown**.** Their use in the asymmetric 1,2-addition of Grignard reagents to ketones allowed generation of chiral tertiary alcohols in high yields and enantioselectivites, with full recovery of the ligand in the work-up.[4] These results will be presented, as will further research with other tridentate ligand types, mechanistic studies and preliminary investigation of the reaction in flow synthesis.

Acknowledgements: This work has been supported by Science Foundation Ireland. Grant number: 12/RC/2275

References:

1. M. Shibasaki, M. Kanai, *Chem. Rev.* **2008***, 108,* 2853-2873.
2. B. Weber, D. Seebach, *Angew. Chem. Int. Ed.***1992**, *31*, 84-86, K. Osakama, M. Nakajima, *Org. Lett.* **2016**, *18*, 236–239.
3. D. Seyferth, *Organometallics* **2009**, *28*, 1598; H. G. Richey, *Grignard Reagents: New Developments*, Wiley, **1999**.
4. B. Bieszczad, D.G. Gilheany, *Angew. Chem. Int. Ed.***2017**, *56*, 4272-4276.

Synthesis of Dimeric Porphyrin as a Model for Oxygen Carrier Inartificial Blood

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The availability of blood for medical treatments always has been a problem. For transfuses caused by extensive blood loss or as therapy for chronic anaemia, massive amounts of blood are dailyneeded. In this contest, the search for artificial blood substitutes in order to fabricate artificial blood has been increased in last two decades [1; 2] Two distinct approaches are being explored in development of red blood cell substitute (RCS) [1]. Hemoglobin-based and perfluorocarbon-based oxygen carriers. Hemoglobin-based carriers are based on human or animal hemoglobins, optimized for O_2 delivery and longer intravascular circulation. On theother hand, PFBOCs are aqueous emulsions of perfluorocarbon derivatives that dissolve large amounts of O_2. However, these structures still have some problems. The most notable being the insolubility in water, and biocontamination due to the use of natural hemoglobin. Due this fact, is necessary to proceed with the studies and development of structures to replace natural blood, for efficient O_2 transport. Monofunctionalisation of meso-tetrakis-porphyrin through introduction of carboxylic group in one of the meso positions confers the possibility to anchor a stable amide to a functionalized support and create dimeric structures similar to heme proteins. His the case of the iron complexes of the flexible dimeric structure, bis-(meso-tetrakis-5,10,15-triphenyl-20-(p-carboxyphenyl)-porphyrinyl)-1,6-hexanediamide, where is possible protect the iron cations and thereby replace same of the functions of natural hemoglobin. This dimeric systems are therefore very good candidates for artificial blood[3]. In this communication we describe the synthesis and characterization of the functionalized flexible dimeric porphyrin, bis-(meso-tetrakis-5,10,15-triphenyl-20-(p-carboxyphenyl)-porphyrinyl)-1,6hexanediamide and also new computational studies on the iron-O_2 bonds that will be used to evaluate the nature of the stable structures based in dimeric porphyrins for O_2 coordination and transport [4].

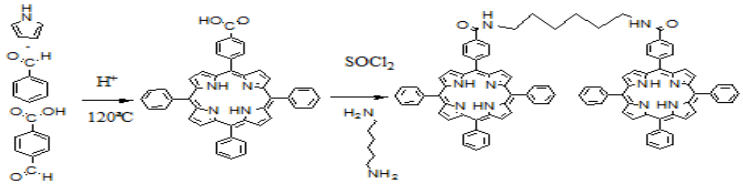

Figure 1: Synthesis of dimeric porphyrin, bis-(meso-tetrakis-5,10,15-triphenyl-20-(p-carboxyphenyl)-porphyrinyl)-1,6-hexanediamide

Acknowledgements: This work was supported by Fundo Europeu de Desenvolvimento Regional- QREN, COMPETE through projects PTDC/AAC-CLI/098308/2008 and project PTDC/AACCLI/118092/2010 of Fundação para a Ciência e Tecnologia (FCT) Cláudia T. Arranja acknowledges funding from FCT (Ph.D grant: SFRH/BD/61637/2009). All authors thanks Centro de Química da Universidade de Coimbra.

References:

[1] Hae Won Kim, A. Gerson Greenburg,*Artif Organs***2004***, Vol. 28,*813.
[2] Lowe K. C., *Blood Reviews* **1999,** *3*, 171.
[3] Michel Momenteau, Christopher A. Reed,*Chem. Rev.* **1994**, *94,* 659.
[4]Abilio J. F. N. Sobral, Susana M. Melo, M. Luísa Ramos, Raquel Teixeira, Susana M. Andrade and Silvia M. B. Costa, *Tetrahedron Letters,***2007**,*48*, 3145.

Oxidative Debenzylation of *O*-Benzyl Ethers Catalyzed by $VO(acac)_2$ and a Triazole based Ligand

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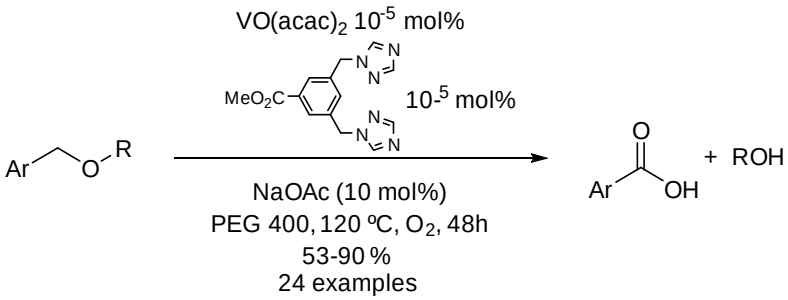
The easy preparation of benzyl ethers and their stability towards a number of reaction conditions make benzyl ether a commonly used protecting group for alcohols.[1] Conventional methods of debenzylation, like reductive cleavages and Lewis or Brönsted acid-promoted processes, are not compatible with labile or reduction susceptible functional groups so that dealing with multifunctional substrates can be problematic. Oxidative cleavage is an advantageous strategy to carry out debenzylation in this situation, although limitations regarding the type of substrates that can be deprotected have appeared.[2] Interestingly, although a number of metal catalyzed aerobic oxidative processes have been reported,[3] the aerobic cleavage of ethers has been scarcely explored to date.[2e] Herein, we wish to report a convenient methodology for the aerobic oxidative debenzylation of ethers. Infinitesimal amounts of a catalyst system based on $VO(acac)_2$ and a 1,2,4-trialoze type ligand in the presence of oxygen as sole oxidant allows the selective oxidative cleavage of a number of *O*-benzyl ethers and other benzyl-based protecting groups (PMB, MMB, PFB, and NAP, *inter alia*) at atmospheric pressure in a sustainable media (**Scheme 1**). The presence of several groups like trifluoromethyl, halogen, alkoxy, alkyl, alkene or alkyne is tolerated in the substrates. Chirality is also preserved under reaction conditions.[4]



Scheme 1: Vanadium-catalyzed aerobic cleavage of benzyl ethers.

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References:

1. Wuts, P. G. M.; Greene, T. W. in *Greene's Protective Groups in Organic Synthesis*, 4th ed.; Wiley-Interscience, New York, **2007.**
2. See for example: a) Bull, S. D.; Davies, S. G.; Fenton, G.; Mulvaney, A. W.; Prasad, R. S.; Smith, A. D. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3765−3774. b) Madsen, J.; Bols, M.; *Angew. Chem., Int. Ed.* **1998**, *37*, 3177−3178; c) Madsen, J.; Viuf, C.; Bols, M. *Chem. Eur. J.* **2000**, *6*, 1140−1146. d) Grayson, E. J.; Davis, B. G. *Org. Lett*. **2005**, *7*, 2361−2364; e) Shen, Z.; Sheng, L.; Zhang, X.; Mo, W.; Baoxiang, S.; Hu, X. *Tetrahedron Lett.* **2013**, *54*, 1579-1583; f) Moriyama, K.; Nakamura, Y. Togo, H. *Org. Lett.*, **2014**, *16*, 3812-3815.
3. a) Sheldon, R. A. *Catal. Today* **2015**, *247*, 4–13; b) Sawama, Y.; Asai, S.; Monguchi, Y.; Sajiki, H. *Chem. Record* **2016**, *16*, 261-272.
4. Urgoitia, G.; SanMartin, R.; Herrero, M.T.; Dominguez, E. *Adv. Synth. Catal*. **2016**, *358*, 3307-3312.

Synthesis of a Novel Potent Radiosensitizer

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Cancer, one of the main causes of death in highly developed countries, is a disease extremely hard to defeat. Three most commonly used methods to overcome it are surgery, chemotherapy and radiotherapy. However, it is worth noting that hypoxia occurring in solid tumors decreases efficacy of radiotherapy. Indeed, studies have shown that the hypoxic cells are up to three fold less radiosensitive than the normoxic ones.

Radiotherapy relies on interactions between cellular DNA and the products of water radiolysis (•OH radicals and solvated electrons are the most abundant among them). However, hydrated electrons are not able to damage native DNA. In order to make them as effective as •OH radicals, one has to employ sensitizing molecules.[1]

One of the group of such radiosensitizers are nucleosides modified on a nucleobase with an electrophilic substituent. Two most comprehensively studied examples of nucleosides with electrophilic substituents are 5-bromo-2′-deoxyuridine (5-BrdU) and 5-iodo-2′-deoxyuridine (5-IdU).[2] These derivatives possess high electron affinity and undergo dissociative electron attachment (DEA) which ultimately produces reactive radicals inside DNA.[3] Based on those premises our research group proposed a series of radiosensitizing 5-substituted uridine derivatives.

The main aim of the current study was to synthetize one of those nucleosides which have especially favorable characteristics: the free enthalpy of DEA equal to -127 kcal/mol (at the B3LYP/6-31++G(d,p) level) and no activation barrier for -tf abstraction. 5-OtfdU (5-trifluoromethanosulfonate-2'-deoxyuridine) has been synthesized according to the procedure depicted in **Figure 1** in moderate yield (24%). To obtain 5-OHdU (5-hydroxy-2'-deoxyuridine) we used the protocol described in the literature.[4] The obtained 5-OHdU was reacted with *N*-Phenyl-bis(trifluoromethanesulfonimide) to form the desired product. Finally, 5-OtfdU was characterized by ^{1}H NMR and mass spectrometry to confirm its structure.

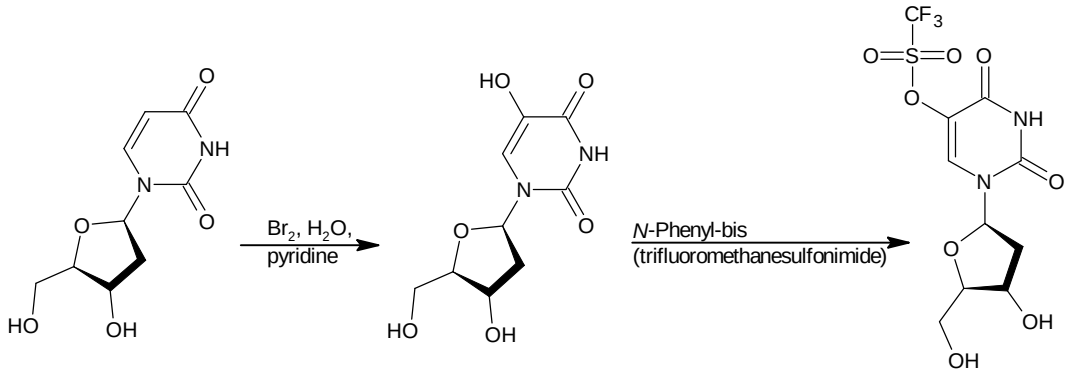

Figure 1: Synthetic route for 5-OtfdU

Acknowledgements: We thank the Polish National Science Centre for financial support (Grant Number: 2014/14/A/ST4/00405).

References:

1. Rak J., Chomicz L., Wiczk J., Westphal K., Zdrowowicz M., Wityk P., Żyndul M., Makurat S., Golon Ł. *J. Phys. Chem. B,* **2015**, 119, 8227-8238.
2. Makurat S., Chomicz-Manka L., Rak J. *ChemPhysChem*, **2016**, 17, 2572-2578.
3. Shewach D. S., Lawrence T. S. Nucleoside Radiosensitizers. In *Deoxynucleoside Analogs in Cancer Therapy*; Godefridus J. P., Ed.; Humana Press Inc.: Totowa, NJ, **2006**.
4. Song C., Kim Y. H., Jin C. H., Kim S. K., Rhee M. H., Byung O. S., Moon J. *BMB Rep*, **2009**, 42, 373-379.

Synthesis of 3,3-Dimethylchroman-4-ones and 3,3-Dimethylchroman-4-ols: Palladium-Catalyzed Intramolecular Addition of Aryl bromides to Aldehydes

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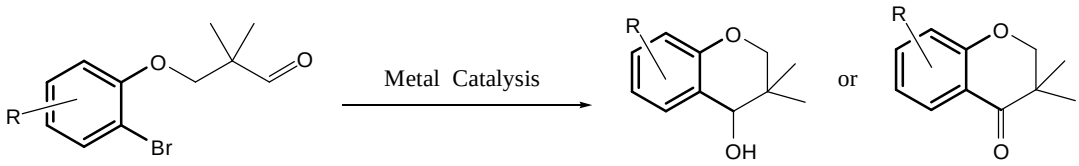
The quest for new molecules with potent biological activities is currently of great importance, particularly as regards to diseases such as cancer and neurodegenerative diseases like Alzheimer's and Parkinson's diseases, which are reaching alarming rates in the world population.

For many years, pyran containing molecules such as chroman-4-ones and chroman-4-ols have demonstrated important biological activities.[1] From a medicinal chemistry point-of-view both 3,3-dimethylchroman-4-one and 3,3-dimethylchroman-4-ols, are quite fascinating, and relatively unexplored.

Using a novel catalytic protocol similar to Solé's group[2], we successfully synthesized these compounds using palladium catalysts, via a metal-catalyzed cyclization[3], starting from appropriate aldehyde precursors (Scheme 1). This approach will be discussed in this communication.



Scheme 1: Our synthetic pathway.

Acknowledgements: We are grateful also for funding from FCT via the strategic project UID/QUI/0619/2016 (contributed to CQE-UE).

References:

1. a) González S. D.-; Marion N.; Nolan S. P. *Chem. Rev.* **2009**, *109*, 3621. b) Hahn F. E. *Angew. Chem. Int. Ed.* **2006**, *45*, 1348.
2. Solé, D.; Mariani, F.; Fernández, I. Adv. Synth. Catal. **2014**, 356, 3237.

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