Durham University

ESOR 2017

European Symposium on Organic Reactivity

3-8 September 2017, Durham UK

Conference Information and Book of Abstracts

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IMPORTANT INFORMATION

Main Scientific Programme Venue:

Chemistry Café Area and lecture theatre CG93
Department of Chemistry
Lower Mountjoy Science Site
Durham University
DH1 3QX

Poster Presentation Venue:

Durham Cathedral Cloister (see map)
The Cloister **must be entered from the south side** via North/South Bailey to avoid disturbing the evensong cathedral service, which runs 5:15-6:15 pm. Evensong will be finished by the end of the poster session so we will be able to exit via the cathedral. Presenters will be able to hang their posters from 5:30 pm onwards.

Conference Dinner Venue:

Durham Castle

Conference Secretariat:

Daryl Dowding will be at the conference registration desk at key times throughout the meeting. She will also be reading email: Daryl.dowding@durham.ac.uk
Event Durham +44 (0)191 334 2887 (staffed 8:15 am to 5:45 pm Monday to Friday)

Internet Access:

Via TheCloud@Durham (see https://www.dur.ac.uk/cis/wireless/thecloud/ for details)

1. Switch on your smartphone, tablet or other Wi-Fi device and check that Wi-Fi is enabled.
2. Select 'TheCloud@Durham' from the available network list
3. Open your Internet browser - 'TheCloud' landing page below will appear. Click 'Get Online'.
4. You will then see the service selection screen. Select 'The Cloud Wi-Fi'.
5. Once this is done you can either login with an existing 'TheCloud' account, or click on the 'Create Account' button to register for a free account.
6. Once you have logged in or registered you will be able to access the Internet using 'TheCloud@Durham'.

Eduroam

Durham University subscribes to Eduroam

Conference Website:

www.dur.ac.uk/esor.2017/

WELCOME

We are delighted to host you in Durham for the 2017 European Symposium on Organic Reactivity.

The ESOR series is now in its sixteenth rendition, and the current meeting represents ESOR's second 'visit' to the UK. The ESOR series has a long and proud history, with meetings being held in Paris (1987), Padova, Italy (1989), Göteborg, Sweden (1991), Newcastle, UK (1993), Santiago de Compostela, Spain (1995), Louvain la Neuve, Belgium (1997), Ulm, Germany (1999), Cavtat (Dubrovnik), Croatia (2001), Oslo, Norway (2003), Rome, Italy (2005), Faro, Portugal (2007), Haifa, Israel, (2009), Tartu, Estonia (2011), Prague, Czech Republic (2013) and Kiel, Germany (2015).

We are grateful to all of you for coming to ESOR and sharing your diverse range of fundamental organic chemistry research. We are also indebted to plenary and invited speakers for making commitments to ESOR so far in advance of the meeting. We hope you enjoy the meeting and we encourage you to discuss ideas freely across the science and social programmes.

With very best wishes from your local organisers,

AnnMarie C. O'Donoghue
Department of Chemistry
Durham University

David R. W. Hodgson
Department of Chemistry
Durham University

Daryl Dowding
Event Durham
Durham University

ESOR 2017 3 - 8 September 2017, Durham UK

Schedule

Time	Sunday 3 September	Monday 4 September	Tuesday 5 September	Wednesday 6 September	Thursday 7 September	Friday 8 September
09:00		Plenary Sijbren Otto 09:00 - 09:40	Plenary Franziska Schoenebeck 09:00 - 09:40	Plenary John Richard 09:00 - 09:40	Plenary Albrecht Berkessel 09:00 - 09:40	Plenary Guy Lloyd-Jones 09:00 - 09:40
09:10						
09:20						
09:30						
09:40		Invited Rainer Herges 09:40 - 10:10	Invited Peter Schreiner 09:40 - 10:10	Invited Nick Williams 09:40 - 10:10	Invited John Murphy 09:40 - 10:10	Invited Michael Page 09:40 - 10:10
09:50						
10:00		Dave Carbery 10:10 -10:30	Markus Griesser 10:10 -10:30	Heidi Korhonen 10:10 -10:30	Craig Butts 10:10 -10:30	Robert Cox 10:10 -10:30
10:10						
10:20						
10:30		coffee break 10:30-11:00	coffee break 10:30-11:00	coffee break 10:30-11:00	coffee break 10:30-11:00	coffee break 10:30-11:00
10:40						
10:50						
11:00		Invited Anke Kruger 11:00 - 11:30	Invited Manube Abe 11:00 - 11:30	Invited Lynn Kamerlin 11:00 - 11:30	Invited María Paz Muñoz 11:00 - 11:30	Invited Maria Cristiano 11:00 - 11:30
11:10						
11:20						
11:30		Leo Frkanec 11:30 - 11:50	Victor Chechik 11:30 - 11:50	Ian Fairlamb 11:30 - 11:50	Adam Islip 11:30 - 11:50	Chuks Isanbor 11:30 - 11:50
11:40						
11:50		Kirill Nikitin 11:50 - 12:10	Götz Bucher 11:50 - 12:10	Moisés Canle 11:50 - 12:10	James Walton 11:50 - 12:10	N. Konstandaras 11:50 - 12:10
12:00		Ian Ashworth 12:10 - 12:30	Christof Jäger 12:10 - 12:30	Jiří Váňa 12:10 - 12:30	Rebecca Hawker 12:10 - 12:30	Closing Remarks 12:10 - 12:30
12:10						
12:20						
12:30		lunch break 12:30 - 14:00 Grey College	lunch break 12:30 - 14:00 Grey College	packed lunch served from Chemistry Café	lunch break 12:30 - 14:00 Grey College	packed lunch served from Chemistry Café
12:40						
12:50						
13:00				Excursions (optional)		
13:10						
13:20						
13:30						
13:40						
13:50						
14:00	registration and University accommodation check-in at Grey College 14:00 - 20:30	Plenary Michael Ward RSC Award for Supramolecular Chemistry 14:00 - 15:00	Plenary Ivan Huc 14:00 - 14:40		Olah Symposium Introduction & Surya Prakash 14:00 - 15:00	
14:10						
14:20						
14:30						
14:40			Invited Ian Williams 14:40 - 15:10			
14:50						
15:00		Invited Jason Harper 15:00 - 15:30	Simon Webb 15:10 - 15:30		Invited H.-U. Siehl 15:00 - 15:30	
15:10						
15:20						
15:30		coffee break 15:30-16:00	Paul McGonigal 15:30 - 15:50		Graham Sandford 15:30 - 15:50	
15:40						
15:50			coffee break 15:50-16:20		coffee break 15:50-16:20	
16:00		Siying Zhong 16:00 - 16:20				
16:10						
16:20		Ivana Biljan 16:20 - 16:40	Fernanda Duarte 16:20 - 16:40		Armin Ofial 16:20 - 16:40	
16:30						
16:40		Fujio Yagihashi 16:40 - 17:00	Anna Vetter 16:40 - 17:00		Kazuhide Nakata 16:40 - 17:00	
16:50						
17:00	Introduction & Opening Lecture: Chris Hunter 17:00 - 18:00		Ivan Kodrin 17:00 - 17:20		Hrvoj Vancik 17:00 - 17:20	
17:10						
17:20			Peter Byrne 17:20 - 17:40			
17:30		Poster presenters to hang posters 17:30 - 18:00				
17:40						
17:50						
18:00	Welcome Party 18:00 - 20:30	Posters: Durham Cathedral Cloister 18:00 - 20:00				
18:10						
18:20						
18:30						
18:40						
18:50						
19:00					Conference Dinner (optional) 19:00 onwards	
19:10						
19:20						
19:30						

SCIENTIFIC PROGRAMME

Sunday 3 September, 2017 (in Grey College)		
Starting at 14:00	University accommodation check-in and conference registration at Grey College Reception	
17:00	Conference opening in Holgate House, Grey College	
17:00 – 17:10	AnnMarie O'Donoghue Durham	Conference Chair's welcome and introduction
17:10 – 18:00	Chris Hunter Cambridge	Opening plenary lecture (in Holgate House): Chemical Information Processing
18:00 – 20:30	Welcome Party and Registration in Grey College Dining Hall	
Monday 4 September, 2017 (room CG93, Chemistry Department)		
Morning Sessions Chair: David Hodgson, Durham		
09:00 - 09:40	Sijbren Otto Groningen	Can We Make Life in the Lab? Emergence and Evolution of Self-Replicating Molecules in Dynamic Molecular Networks
09:40 – 10:10	Rainer Herges Kiel	Molecular Spin Switching
10:10 – 10:30	Dave Carbery Bath	Helicene Amphiphiles: From organocatalysis to liquid crystal topological quasiparticles via fractals
10:30 – 11:00	coffee break	
11:00 - 11:30	Anke Krueger Wuerzburg	Surface-dependent reactivity of nanodiamond and related materials
11:30 – 11:50	Leo Frkanec Ruđer Bošković Institute	Photo and gamma ray induced polymerisation of the bis(aminoacid) fumaramide self-assemblies
11:50 – 12:10	Kirill Nikitin UCD Dublin	Reaction Bifurcation, Electronic Effects and Stereochemical Inversion at the Phosphonium Centre
12:10 – 12:30	Ian Ashworth AZ Macclesfield	Strong Acid Catalyzed Deprotection Reactions: Application of Acidity Functions to Support Reaction Optimisation
12:30 – 14:00	lunch break (Grey College)	
Afternoon Sessions Chair: Nick Williams, Sheffield		
14:00 – 15:00	Mike Ward Warwick RSC Award	Guest binding and catalysed reactions in the cavity of a coordination cage
15:00 – 15:30	Jason Harper UNSW Sydney	Ionic liquids to control reaction outcome. The importance of understanding microscopic interactions

15:30 – 16:00	coffee break	
16:00 – 16:20	Siying Zhong Bristol	Synergy of Computation, NMR and Synthesis Reveals to Elucidate the Correct Structure of Baulamycins
16:20 – 16:40	Ivana Biljan Zagreb	Dimerization of aromatic C-nitroso compounds as a route to new supramolecular architectures
16:40 – 17:00	Fujio Yagihashi Tsukuba	Structural Study on Cyclic Silsesquioxane Oligomers for the Elucidation of Polymer Forming Polycondensation Process
17:30 – 18:00	Poster presenters to proceed to Durham Cathedral Cloister to hang posters	
18:00 – 20:00	Poster Session in Durham Cathedral Cloister	

Tuesday 5 September, 2017

Morning Sessions Chair: Maria L. S. Cristiano, Algarve

09:00 - 09:40	Franziska Schoenebeck Aachen	Adventures in Catalysis: from Mechanisms to Applications
09:40 – 10:10	Peter Schreiner Giessen	Tunneling Control of Chemical Reactions
10:10 – 10:30	Markus Griesser Ottawa	Nitroxides as Catalytic Radical Trapping Antioxidants: Insight into their Different Reaction Mechanisms
10:30 – 11:00	coffee break	
11:00 - 11:30	Manabu Abe Hiroshima	Chameleonic Character of Singlet 1,2-Diazacyclopentane-3,5-diyl Diradicals
11:30 – 11:50	Victor Chechik York	A New Type of Radical Trap with a Nitroxide Leaving Group, Designed for Detection by Mass Spectrometry
11:50 – 12:10	Götz Bucher Glasgow	New Mechanistic Aspects in Diels-Alder Reactions Catalysed by Tris-(4-bromophenyl)aminium Radical Cation Salts
12:10 – 12:30	Christof Jäger Nottingham	Towards Engineering Radical Enzymes - Thermodynamic Reaction Profiling and Mechanistic Insights into QueE
12:30 – 14:00	lunch break (Grey College)	

Afternoon Session Chair: Lynn Kamerlin, Uppsala

14:00 – 14:40	Ivan Huc LMU Munich	Foldamers: Expanding the Chemical Space
14:40 – 15:10	Ian Williams Bath	Environmental Influences on Isotope Effects
15:10 – 15:30	Simon Webb Manchester	Foldamers as Devices for the Transmission of Binding Information
15:30 – 15:50	Paul McGonigal Durham	Excited-State Aromatic Interactions in Fluorescent Molecular Rotors
15:50 – 16:20	coffee break	

16:20 – 16:40	Fernanda Duarte Edinburgh	Chiral ion-pairs: dissociation, dynamics and asymmetric catalysis
16:40 – 17:00	Anna Vetter UCD Dublin	A Classical Case of Umpolung at Phosphorus
17:00 – 17:20	Ivan Kodrin Zagreb	Ferrocene derivatives as flexible model systems to study the effect of chirality on hydrogen-bonding patterns
17:20 – 17:40	Peter Byrne UCC Cork	Quantifying Lewis Basicity Using the Benzhydrylium Methodology

Wednesday 6 September, 2017

Morning Sessions Chair: Mike Page, Huddersfield

09:00 - 09:40	John Richard Buffalo	Probes for the Enzyme Mechanisms: Studies on Enzyme Activation by Dianions
09:40 – 10:10	Nick Williams Sheffield	Exploring Efficient and Promiscuous Biocatalysis
10:10 – 10:30	Heidi Korhonen Turku	Novel DNA-templated Chemical Ligation
10:30 – 11:00	coffee break	
11:00 - 11:30	Lynn Kamerlin Uppsala	Dynamics, Cooperativity and the Evolution of Enzyme Function
11:30 – 11:50	Ian Fairlamb York	Aerobic C-H bond activation-functionalisation catalysis involving 'Pd-NO_x'
11:50 – 12:10	Moisés Canle A Coruña	Stability of Cu(II) complexes with potential use in PET
12:10 – 12:30	Jiří Váňa Pardubice	Palladium Acetate/Trifluoroacetic Acid Catalytic System: Ligand Exchange and Catalytic Behaviour
12:30 – 12:45	packed lunch served outside lecture theatre	
13:00 -	excursions	

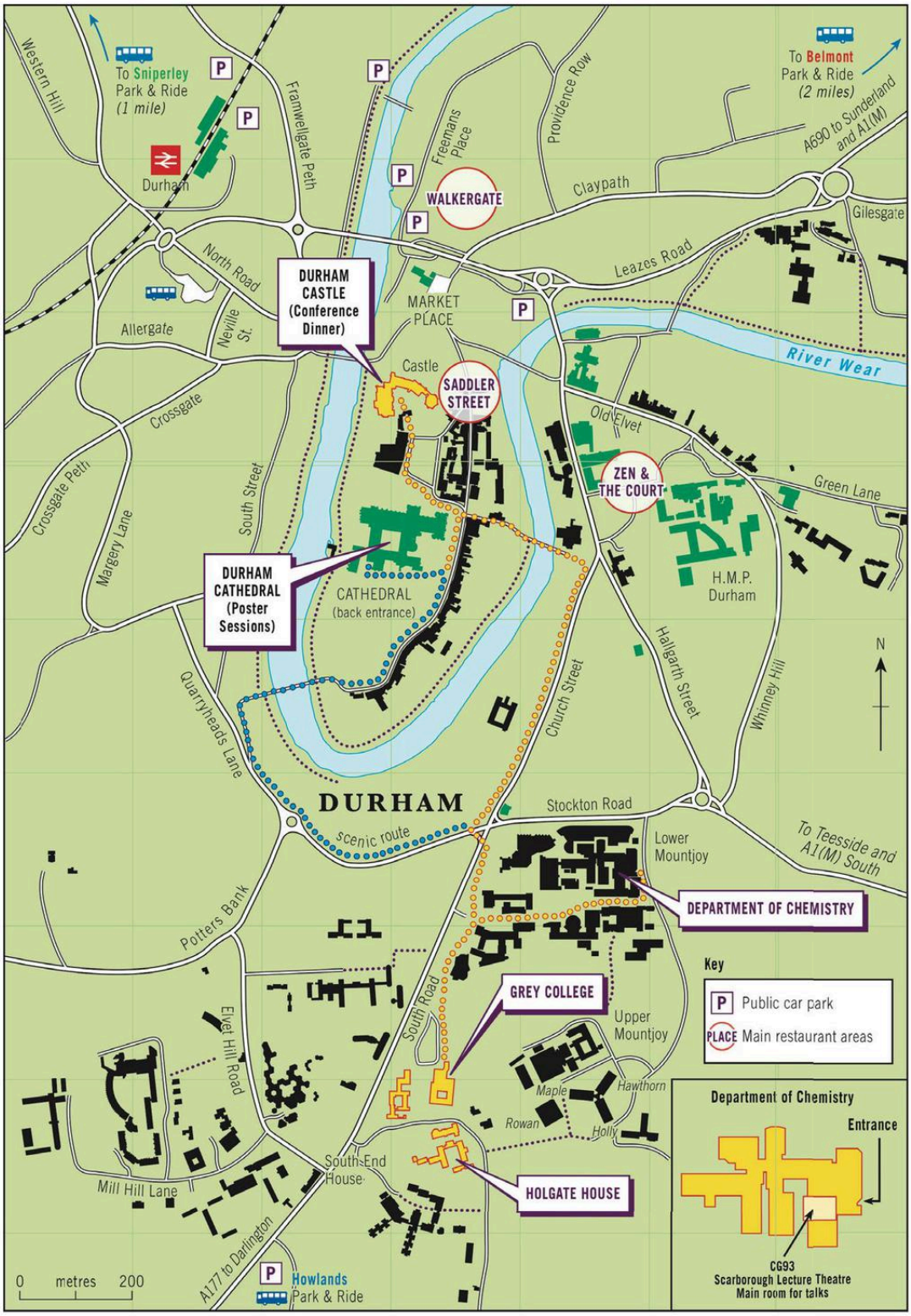
Thursday 5 September, 2017

Morning Sessions Chair: Moisés Canle, A Coruña

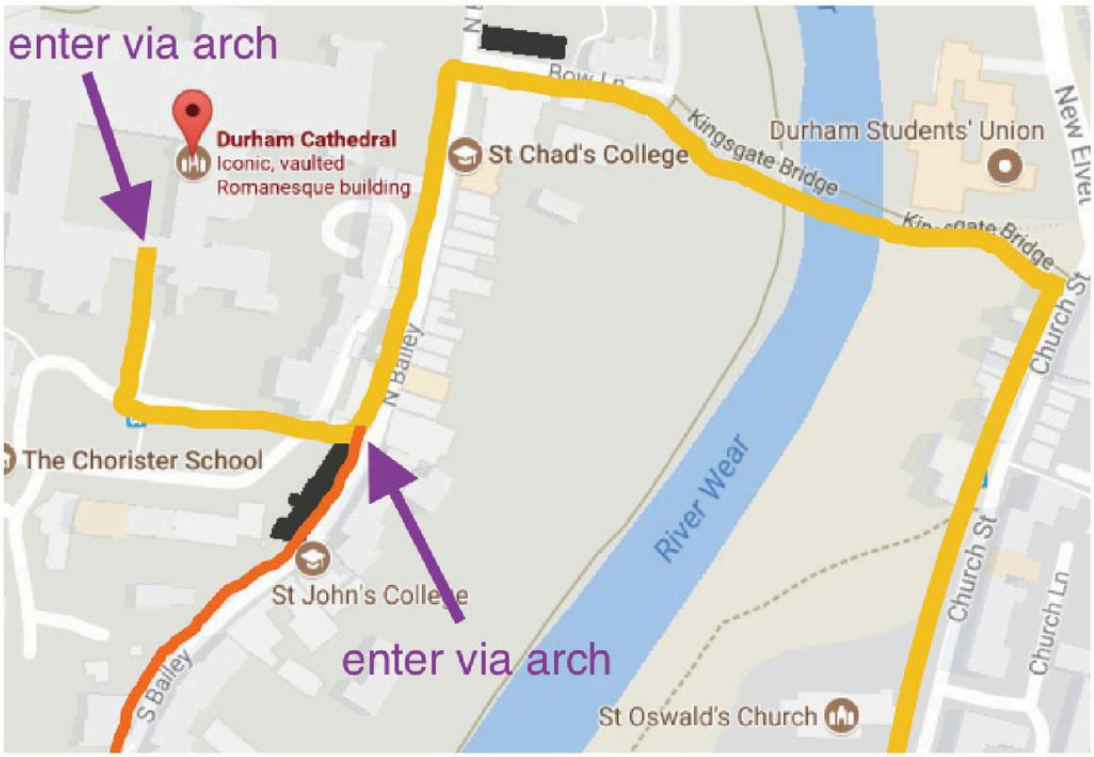
09:00 - 09:40	Albrecht Berkessel Cologne	Carbene Catalysis and the Breslow Intermediate
09:40 – 10:10	John Murphy Strathclyde	Potassium tert-Butoxide in SET Reactions?
10:10 – 10:30	Craig Butts Bristol	2D NMR Spectra in <10 seconds for Reaction Monitoring
10:30 – 11:00	coffee break	
11:00 - 11:30	María Paz Muñoz UEA Norwich	Twists and Turns of Platinum-Allene Chemistry
11:30 – 11:50	Adam Islip York	Lithiation-Trapping of N-Boc Heterocycles: How Fast is Each Step?

11:50 – 12:10	James Walton Durham	Catalytic Reaction of Organometallic Ruthenium Complexes
12:10 – 12:30	Rebecca Hawker UNSW Sydney	Using ionic liquids as solvents for organic processes: Which one do you choose?
12:30 – 14:00	lunch break (Grey College)	
Afternoon Sessions Chairs: Ulli Siehl, Ulm		
14:00 – 15:00	Olah Symposium Introduction & Surya Prakash	Beyond Oil and Gas: The Methanol Economy
15:00 – 15:30	Ulli Siehl Ulm	The Conundrum of the $C_4H_7^+$ Cation
15:30 – 15:50	Graham Sandford Durham	Selective Fluorination Strategies
15:50 – 16:20	coffee break	
16:20 – 16:40	Armin Ofial LMU Munich	Counter-Intuitive Nucleophilicities of Peroxide Anions
16:40 – 17:00	Kazuhide Nakata Hosei	Computational Study of Substituent Effects on Gas-Phase Stabilities of Phenylaminomethyl Cations
17:00 – 17:20	Hrvoj Vancik Zagreb	Aromatic C-Nitroso Compounds and their Dimers: A Model for Physical Organic Chemistry of Reactions in Crystalline Molecular Solids
Friday 6 September, 2017		
Morning Session Chair: AnnMarie O'Donoghue, Durham		
09:00 - 09:40	Guy Lloyd-Jones Edinburgh	Kinetics and Mechanism of Catalyst and Reagent Activation in Synthesis
09:40 – 10:10	Michael Page Sheffield	The kinetics and mechanism of the organoiridium-catalysed enantioselective reduction of imines
10:10 – 10:30	Robert Cox AZ Macclesfield	Catalyst choice aided by mechanistic understanding on AZD9496 Heck stage
10:30 – 11:00	coffee break	
11:00 - 11:30	Maria L. S. Cristiano Algarve	Saccharinate-based Ligands; Structure, Reactivity and Properties
11:30 – 11:50	Chuks Isanbor Lagos	Towards the Design of New Anti-Parasitic Drug Candidates: Some Studies of the Reaction of Aromatic Nitro-Compounds with Anionic and Amino Nucleophiles.
11:50 – 12:10	Nicholas Konstandaras UNSW Sydney	The Effects of Electronics and Strain on the Acidity and Reactivity of a Range of Systems
12:10 – 12:30	closing remarks	
12:30 – 12:45	packed lunch served outside lecture theatre	
13:00 -	depart	

DURHAM CITY AND VENUES MAP



Entry Routes to the Cloister (Poster Session)



CONFERENCE VENUES

University accommodation, initial registration desk, Conference Opening, Welcome Party and several conference lunches are to be based in Grey College.

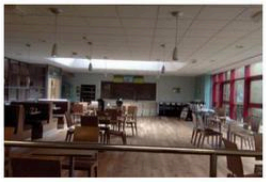
Grey College Reception

Grey College Dining Hall

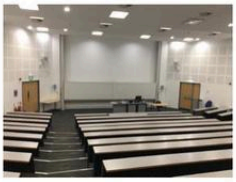
Holgate House, Grey College

The majority of the science programme will take place in the Department of Chemistry in and around lecture theatre CG93. If you need directions to the venue, ask for the Science Site Security Office or the 'red' greenhouse. If you are arriving after the start of the meeting, taxis drivers will be able to drop you directly outside the Security Office. The registration and conference secretariat will be based in this area for the remainder of the meeting

Science Site Security Office (the 'red' greenhouse)

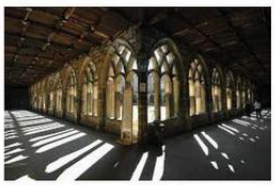


Chemistry Café area



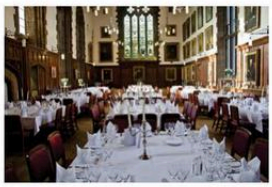
Lecture theatre CG93

The poster Session will take place in the Cloister of Durham Cathedral, which sits at the heart of the UNESCO World Heritage Site. **The Cloister sits on the South side of the Cathedral and must be accessed via North/South Bailey (see maps) to avoid disturbing the Evensong cathedral service.** The conference banquet will take place in Durham Castle.



Durham Cathedral Cloister

Durham Castle



Castle Great Hall

INTERNATIONAL STANDING COMMITTEE OF ESOR CONFERENCES

Moises Canle Lopez (a Coruna)

Mirjana Eckert-Maksic (Zagreb)

Rainer Herges (Kiel)

Maria de Lurdes Cristiano (Faro)

AnnMarie O'Donoghue (Durham)

Michael Page (Huddersfield)

Jana Roithová (Prague)

Alan Rowan (Rabboud)

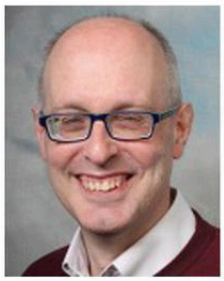
Hans-Ullrich Siehl (Ulm)

Maurizio Speranza ("La Sapienza")

Amnon Stanger (Haifa)

Einar Uggerud (Oslo)

RSC Supramolecular Chemistry Award: Professor Michael Ward



Mike Ward did his BA at Cambridge, studying Natural Sciences (1983-1986). He remained in Cambridge for his PhD (1986-1989) with Ed Constable, studying some of the first examples of helicate complexes of transition-metal ions with polydentate ligands. After a post-doctoral year with Jean-Pierre Sauvage in Strasbourg playing with catenates, he started his independent academic career as a lecturer at Bristol in 1990 where he developed a long and productive collaboration with Jon McCleverty. He was promoted to Reader in 1998 and to a Chair in 2001, and then moved to Sheffield in 2003 where he was in his second term as Head of Department until this summer. In August 2017, Mike moved to the University of Warwick where he is also Head of Department.

Mike's interests are all based around the coordination chemistry of transition metal and lanthanide ions and their multinuclear assemblies; in particular, current emphases in his research are on (i) self-assembly and host-guest chemistry of hollow metal/ligand cage complexes, and (ii) photophysical properties of polynuclear complexes and supramolecular assemblies, including applications in imaging and sensing. Previous awards for his research include the RSC Corday Morgan medal for 1999, Sir Edward Frankland Fellowship for 2000-2001, and the 'Chemistry of the Transition Metals' award for 2005.

Outside his home departments, Mike has been involved with the RSC in various capacities including two stints on Dalton Council and one on the editorial board of ***Dalton Transactions***; he is currently Chair of the Editorial Board of ***RSC Advances***.

Professor Ward's webpage:
http://www2.warwick.ac.uk/fac/sci/chemistry/research/ward

Social Programme

We hope that participants will enjoy the opportunities to network during the morning and afternoon breaks, outside the lecture venue, and during lunch breaks in Grey College Dining Hall. In addition, there will be receptions, excursions and a conference dinner, which are detailed below:

Sunday 3 September—Welcome Reception

After Professor Hunter's opening plenary presentation, drinks and a buffet supper will be served in Grey College Dining Hall.

Monday 4 September—Poster Presentations

The poster session will be held in the cloister of Durham Cathedral. Drinks and canapes will be served throughout the poster session.

Wednesday 5 September—Excursion/Tour

Hadrian's Wall

Registrants who have booked this excursion should assemble outside **Grey College Reception at 1.15pm** to depart for Northumberland. The bus journey will take approximately 1 h 15 min. The bus will go to Houseteads Roman Fort. There are many walking opportunities in this area, which pass across beautiful landscape with the backdrop of the Hadrian's Wall UNESCO World Heritage Site.

The return coach will **leave at 6.30 pm** to travel back to Durham.

We strongly advise participants to wear comfortable walking shoes/boots, waterproof clothing, and to bring some cash to buy refreshments.

Durham City Walking Tour

Registrants who have booked this excursion should assemble outside Grey College Reception at **2pm at Grey College Reception**. The tour runs for approximately two hours.

The guided tour includes the World Heritage Site area (Durham Cathedral and Durham Castle from outside only); the historic Market Place; the riverbank area and Saddler Street. The guide will also give information on the history and architecture of the city.

We advise participants to wear comfortable shoes and to bring waterproofs and/or an umbrella

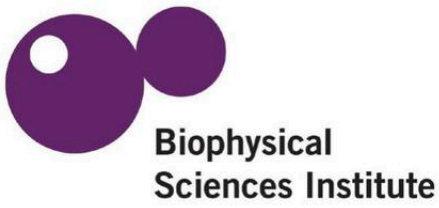
If you have not booked a place on the excursion or walking tour, more ideas are available at: http://www.thisisdurham.com/things-to-do/durham-attractions

Thursday 6 September—Conference Banquet in Durham Castle

The conference banquet will take place in the Great Hall of University College (='The Castle'). Drinks will be served from 7 pm with dinner beginning at 7:30 pm. A shuttle bus service will run from 6:30 pm between Grey College Reception and the Castle.

SPONSORS, DONORS AND EXHIBITORS

We are grateful for support from the following organisations:

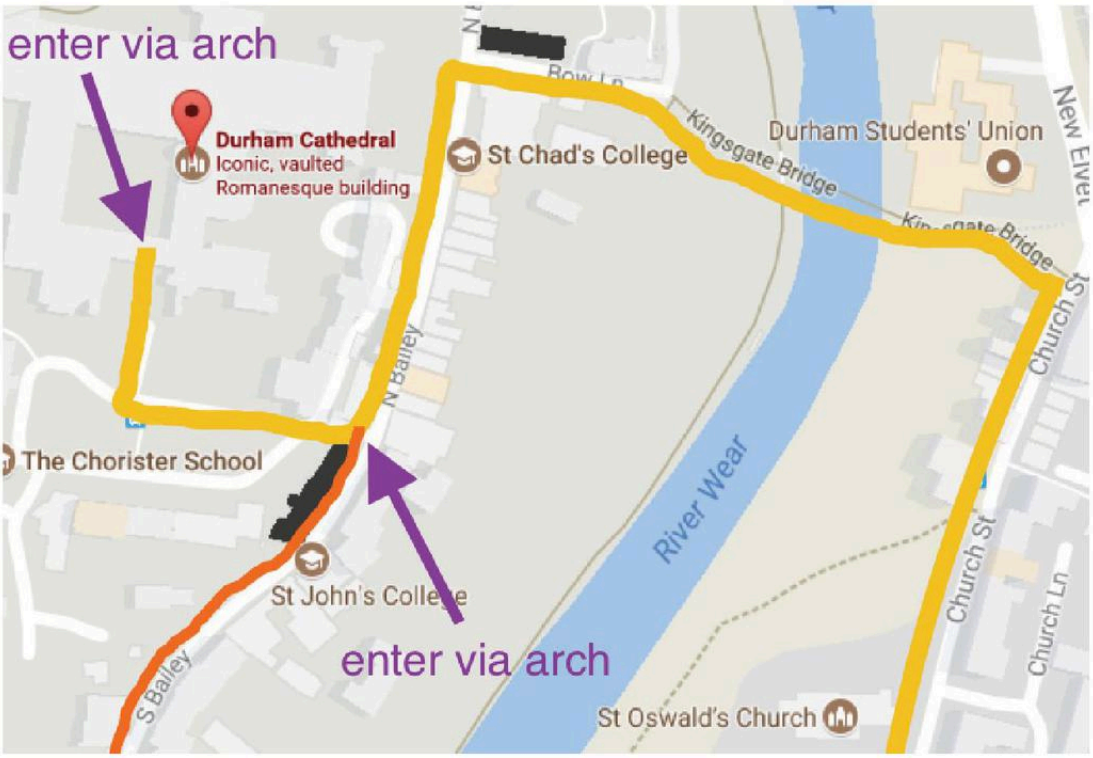


TECHNICAL GUIDELINES FOR ORAL AND POSTER PRESENTATIONS

Apart from the opening lecture, all oral presentations will take place in the large Chemistry lecture theatre (room number CG93). The room has capacity for 260 people and it is equipped with a full range of AV facilities including a microphone.

Oral presenters are very welcome to use their own laptops. The data projector is equipped with a VGA connector. The room has an in-built Windows PC running Office 2016. We will also provide our own Mac laptop, which is running Office 2016.

Poster presentations will take place in the Cloister of Durham Cathedral. The posters are to be presented on floor-standing 1830mm tall x 940mm wide panels**. It is therefore essential to prepare A0 posters in portrait format**. Poster presenters should hang their posters from 5:30 pm onwards. The Cloister is part of the cathedral and the Evensong service runs 5:15 pm-6:15 pm. **Please do not enter the Cloister via the Cathedral**. Please enter the Cloister from the south side as indicated on the map below:



ABSTRACTS

ORAL CONTRIBUTIONS

PLENARY SPEAKERS

in order of presentation during ESOR meeting

P1 Chris Hunter
(Cambridge)

P2 Sijbren Otto
(Groningen)

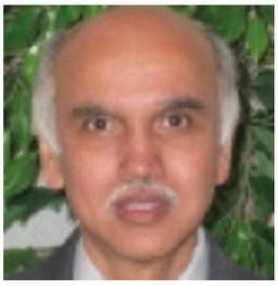
P3 Mike Ward
(Warwick)

P4 Franziska Schoenebeck
(RWTH Aachen)

P5 Ivan Huc
(LMU Munich)

P6 John Richard
(Buffalo)

P7 Albrecht Berkessel
(Cologne)



P8 Surya Prakash (Southern
California)

P9 Guy Lloyd-Jones
(Edinburgh)

List of Plenary Presentations

P1 ***"Chemical Information Processing"***
Chris Hunter
University of Cambridge, UK

P2 ***"Can We Make Life in the Lab? Emergence and Evolution of Self-Replicating Molecules in Dynamic Molecular Networks"***
Sijbren Otto
University of Groningen, the Netherlands

P3 ***"Guest binding and catalysed reactions in the cavity of a coordination cage"***
Mike Ward
University of Warwick, UK

P4 ***"Adventures in Catalysis: from Mechanisms to Applications"***
Franziska Schoenebeck
RWTH Aachen University, Germany

P5 ***"Foldamers: Expanding the Chemical Space"***
Ivan Huc
Ludwig-Maximilians-Universität, Germany

P6 ***"Probes for the Enzyme Mechanisms: Studies on Enzyme Activation by Dianions"***
John Richard
University at Buffalo, USA

P7 ***"Carbene Catalysis and the Breslow Intermediate"***
Albrecht Berkessel
University of Cologne, Germany

P8 ***"Beyond Oil and Gas: The Methanol Economy"***
Surya Prakash
University of Southern California, Los Angeles, USA

P9 ***"Kinetics and Mechanism of Catalyst and Reagent Activation in Synthesis"***
Guy Lloyd-Jones
University of Edinburgh, UK

Chemical Information Processing

Christopher A Hunter

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW (UK)
(herchelsmith.orgchem@ch.cam.ac.uk)

This presentation will describe two different projects dealing with communication of chemical information in molecular systems: synthetic information molecules and transmembrane signal transduction.

Transmission and amplification of chemical signals across lipid bilayer membranes is of profound significance in many biological processes, from the development of multi-cellular organisms to information processing in the nervous system. The ability to reproduce such processes in artificial systems has potential applications in sensing, controlled drug delivery and communication between compartments in tissue-like constructs of synthetic vesicles. We have developed a new mechanism for transmitting chemical information across membranes based on controlled translocation of a synthetic molecular transducer from one side of a lipid bilayer membrane to the other.[1]

The encoded recognition properties of nucleic acids are currently unrivalled in any other material. High fidelity sequence selective duplex formation is the molecular basis for replication of the genetic information encoded by DNA and is finding widespread applications in the programmed assembly of complex nucleic acid nanostructures. We have been investigating the sequence-selective duplex formation properties of synthetic recognition-encoded oligomers that bear no resemblance to the natural system.[2]

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Plenary Presentation 2

Can We Make Life in the Lab? Emergence and Evolution of Self-Replicating Molecules in Dynamic Molecular Networks

Sijbren Otto[a]

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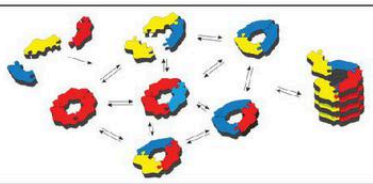
How the immense complexity of living organisms has arisen is one of the most intriguing questions in contemporary science. We have started to explore experimentally how organization and function can emerge from complex molecular networks in aqueous solution. We focus on networks of molecules that can interconvert, to give mixtures that can change their composition in response to external or internal stimuli. Molecular recognition between molecules in such mixtures leads to their mutual stabilization, which drives the synthesis of more of the privileged structures (see Figure). Intriguingly, in this process the assembling molecules are replicating themselves, where replication is driven by self-recognition of these molecules in the dynamic network.[1] We have observed that factors such as mechanical energy[1] and the presence of cosolvents[2] can determine which replicator wins the competition for building blocks. We have also witnessed spontaneous differentiation (a process akin to speciation as it occurs in biology) in a system made from a mixture of two building blocks.[3] When such systems are operated under far-from-equilibrium flow conditions adaptation of the replicators to a changing environment can occur. Thus, the prospect of Darwinian evolution of purely synthetic molecules is tantalizingly close and the prospect of synthesizing life de-novo is becoming increasingly realistic.



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Guest binding and catalysed reactions in the cavity of a coordination cage

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Simple bis-bidentate bridging ligands based on two chelating pyrazolyl-pyridine termini combine with transition metal dications to give a range of polyhedral coordination cages, varying from M_4L_6 tetrahedra to $M_{16}L_{24}$ truncated capped tetrahedra, with a metal ion at each vertex and a bridging ligand spanning every edge. Amongst these a set of M_8L_{12} cubic cages have well-developed host-guest chemistry, able to accommodate a wide range of small molecules in the central cavity, with binding constants of up to 10^8 M^{-1} in water. Guest binding leads to a wide range of interesting types of behaviour, including (i) reversible uptake and release of drug molecules triggered by changes in pH; (ii) luminescence signaling of binding of chemical warfare agent simulants; and (iii) substantial catalytic acceleration with multiple turnovers of a range of reactions of bound guests.

Plenary Presentation 4

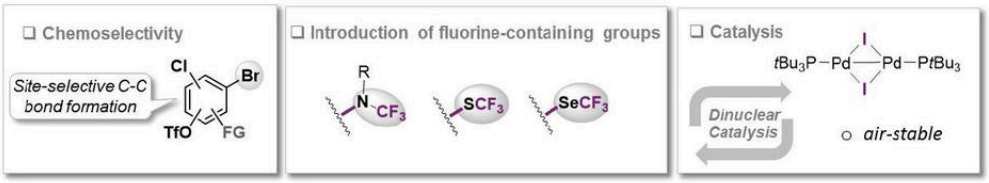
Adventures in Catalysis: from Mechanisms to Applications

Franziska Schoenebeck

RWTH Aachen University, Institute of Organic Chemistry, Landoltweg 1, 52074 Aachen, Germany

(franziska.schoenebeck@rwth-aachen.de)

Detailed understanding of catalytic transformations is key to designing better catalysts. This talk will give insights on case studies and reactivity designs recently undertaken in our laboratory. The focus will be on our recent activities in exploring catalysis at dinuclear $Pd^{(I)}$ sites. Parallels to Ni-catalysis will be drawn also, and direct applications of these concepts to the late-stage introduction of fluorine-containing groups and chemoselective C-C bond formations for the creation of richly functionalized (hetero)aryl motifs will be presented.[1] Experimental and computational tools were applied in these studies.[2]



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Foldamers: Expanding the Chemical Space

Ivan Huc

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Aromatic amide oligomers constitute a new, distinct, and promising class of synthetic foldamers – oligomers that adopt stable folded conformations. Single helical structures are predictable, show unprecedented conformational stability, and constitute convenient building blocks to elaborate synthetic, very large (protein-sized) folded architectures (Fig. 1). They possess a high propensity to assemble into double, triple and quadruple helices, or to fold into sheet-like structures. Cavities can be designed within such synthetic molecules that enable them to act as artificial receptors and molecular motors. Water soluble analogues of these foldamers show promise in nucleic acid and protein recognition. This lecture will give an overview of the design principles of these functional molecular architectures.

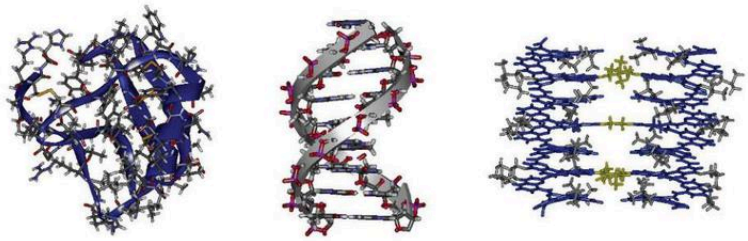

Fig. 1. Crystal structures shown at the same scale of an 8 kDa protein (left), B-DNA (center) and an aromatic foldamer helix bundle (right)

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Plenary Presentation 6

Probes for the Enzyme Mechanisms: Studies on Enzyme Activation by Dianions

John P. Richard and Tina L. Amyes

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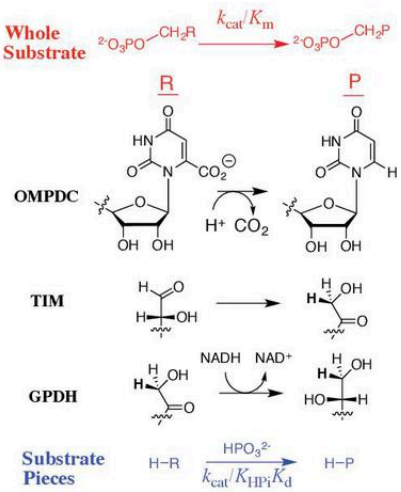
It is not widely appreciated that snapshots of ground-state protein structures from X-ray crystallographic analyses provide little insight into the origin of enzymatic rate accelerations. The examination of numerous X-ray crystals structures failed to reveal that orotidine 5'-monophosphate decarboxylase (OMPDC), triosephosphate isomerase (TIM) and glycerol phosphate dehydrogenase (GPDH) show 6 - 8 kcal/mol stronger binding interactions with the substrate phosphodianion, or with the phosphite dianion piece (Scheme) at their respective reaction transition states, compared with their ground states.[1] This specificity in transition state binding is enabled by interactions between overlapping, but functionally distinct, catalytic sites and dianion activation sites. A general mechanism for enzyme activation by dianions will be presented and evidence for this mechanism will be discussed for each enzyme from the Scheme. The architecture of the different dianion activation sites at these enzymes will be compared, and the roles of side chain cations at each site will be discussed. The substrate pieces bind fast and reversibly to GPDH, so that the chemical hydride transfer step is rate determining for dianion activated reduction of glcolaldehyde by NADH. This allows for the determination of intrinsic primary kinetic isotope effects on these dianion activated reactions, which will be reported and discussed. The relevance of these primary kinetic isotope effects to the role of quantum mechanical tunneling in enzyme-catalyzed hydride transfer will be discussed.

Scheme



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Carbene Catalysis and the Breslow Intermediate

Albrecht Berkessel, M. Paul, D. Kootz, W. Harnying, V. R. Yatham, S. Elfert,
A. Wessels, P. Sudkaov, M. Breugst

Cologne University, Department of Chemistry, Organic Chemistry,
Greinstraße 4, 50939 Cologne, Germany
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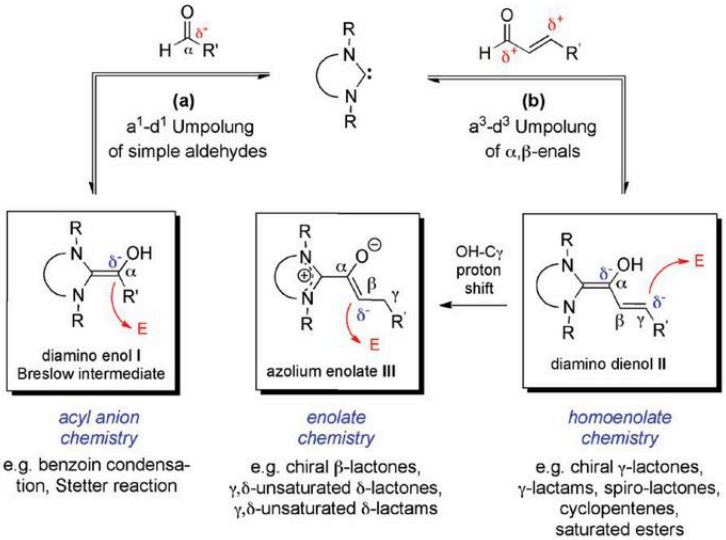
Both in B_1-enzymes and in organocatalytic Umpolung, catalysis by N-heterocyclic carbenes hinges on the formation of the so-called Breslow-intermediates [(di)amino enols] **I** (Scheme, reaction a), in which the innate polarity of *e.g.* an aldehyde substrate is inverted from electrophilic to nucleophilic. In the related a^3-d^3 Umpolung ("conjugate Umpolung"; Scheme, reaction b), the diamino dienol **II**, a homoenolate equivalent, is assumed to be pivotal. OH-Cγ proton shift in the diamino dienol **II** leads to the azolium enolate **III**, an enolate equivalent. The lecture will present (i) the first generation and study of Breslow intermediates,[1,2] (ii) the mechanism-based design of a new generation of carbene organocatalysts,[3] and (iii) the application of the latter in hitherto impossible catalytic transformations involving diamino dienols **II** and azolium enolates **III**.[3]



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Plenary Presentation 8

Beyond Oil and Gas: The Methanol Economy[R]

G. K. Surya Prakash

Donald P. and Katherine B. Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, CA 90089-1661, USA

(gprakash@usc.edu)

Methanol, a liquid at ambient temperature, is preferable to low volumetric energy density hydrogen for energy storage and transportation. It is also an excellent drop in fuel for internal combustion (gasoline) and auto-ignition (diesel) engines. It is an excellent fuel for direct oxidation fuel cells. Dimethyl ether (DME) derived from methanol is a high cetane diesel substitute and also could replace liquefied natural gas (LNG) and liquefied petroleum gas (LPG). Methanol is a convenient feedstock to produce ethylene and propylene that can be converted to synthetic petrochemical products. Chemical recycling of excess carbon dioxide formed from human activities, natural and industrial sources, or even from the air can be converted to methanol via capture followed by reductive conversion with hydrogen. Any available energy source (preferably alternative energies such as solar, wind, geothermal, atomic, etc.) can provide the needed energy for generating hydrogen. Direct electrochemical reduction of CO_2 is also possible. Methanol, presently produced from fossil fuel based syngas (mixture of CO and H_2), can also be made by direct oxidative conversion of natural gas or other methane sources. Even coal and biomass can be converted to methanol through syngas. The Methanol Economy concept that was jointly developed with the late Nobel Laureate colleague, George A. Olah is expected to solve the energy and material problems of the world in the long run and at the same time address the issue of global warming due to increased CO_2 emissions by excessive fossil fuel use.

Kinetics and Mechanism of Catalyst and Reagent Activation in Synthesis

Guy Lloyd-Jones[a]

[a] School of Chemistry, EaStChem, Joseph Black Building, David Brewster Road, Edinburgh, EH9 2JY (guy.lloyd-jones@ed.ac.uk)

A selection of data from our recent mechanistic investigations into the in situ liberation / activation of catalysts (Au, Rh, Pd) and reagents ($RSiX_3$ and RBX_2) in coupling, addition, and substitution reactions will be presented. For example, general mechanistic understanding of direct aqueous protodeboronation has previously been limited to simple phenylboronic acids. The study of the mechanism of release of aromatic boronic acids from MIDA reservoirs[1] has allowed study of the pH-dependence of the intrinsic rates of aqueous protodeboronation of (hetero)aromaticboronic acids.[2] In turn this has facilitated pH-rate profile simulations using a general model, allowing a range of new mechanisms and side processes to be identified. The kinetics of nucleophile-initiated trifluoromethylaytion by TMS-CF_3 demonstrates the importance of acquiring data under a broad range of conditions in order to understand the mechanism of action - and to elucidate some surprising inhibition effects. We have also explored how Rh(I) precatalysts are activated in situ for nitrile-silane substitution reactions, and how the co-product from reaction impacts strongly on the activation and inhibition of the catalyst system. Analogously, our recently-discovered gold-catalysed arylation of arenes using aryl silanes displays unusual kinetic behaviour that, when carefully interpreted, facilitates the design of new processes and applications in synthesis.[3] These studies have involved collection of large sets of kinetic data, requiring redesign of analytic methods to allow this to be achieved in a time-efficient and material-efficient manner on standard instruments.

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3. Au-catalyzed Biaryl Coupling to Generate 5- to 9-membered Rings: Turnover-Limiting Reductive Elimination versus π-complexation, Corrie, T. J. A.; Ball, L. T.; Russell, C. J.; Lloyd-Jones, G. C. *J. Am. Chem. Soc.*, **2017**,*139*, 245–254

INVITED SPEAKERS

I1 Rainer Herges
(Kiel)

I2 Anke Krueger
(Wuerzburg)

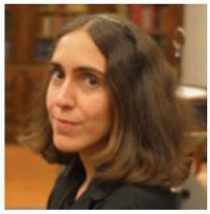
I3 Jason Harper
(UNSW)

I4 Peter Schreiner
(Giessen)

I5 Manabu Abe
(Hiroshima)

I6 Ian Williams
(Bath)

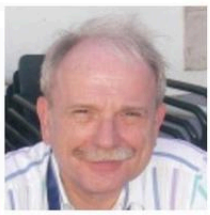
I7 Nick Williams
(Sheffield)



I8 Lynn Kamerlin
(Uppsala)

I9 John Murphy
(Strathclyde)

I11 Maria Paz Muñoz
(East Anglia)



I11 Ulli Siehl
(Ulm)

I12 Mike Page
(Huddersfield)

I13 Maria L. S. Cristiano
(Algarve)

List of Invited Presentations

I1 ***"Molecular Spin Switching"***
Rainer Herges
University of Kiel, Germany

I2 ***"Surface-dependent reactivity of nanodiamond and related materials"***
Anke Krueger
Julius-Maximilians University Würzburg, Germany

I3 ***"Ionic liquids to control reaction outcome. The importance of understanding microscopic interactions"***
Jason Harper
University of New South Wales, Australia

I4 ***"Tunneling Control of Chemical Reactions"***
Peter Schreiner
Justus-Liebig University, Giessen, Germany

I5 ***"Chameleonic Character of Singlet 1,2-Diazacyclopentane-3,5-diyl Diradicals"***
Manabu Abe
Hiroshima University, Japan

I6 ***"Environmental Influences on Isotope Effects"***
Ian Williams
University of Bath, UK

I7 ***"Exploring Efficient and Promiscuous Biocatalysis "***
Nick Williams
University of Sheffield, UK

I8 ***"Dynamics, Cooperativity and the Evolution of Enzyme Function"***
S. C. L. Kamerlin
Uppsala University, Sweden

I9 ***"Potassium tert-Butoxide in SET Reactions?"***
John Murphy
University of Strathclyde, UK

I10 ***"Twists and Turns of Platinum-Allene Chemistry"***
M. Paz Muñoz
University of East Anglia, UK

I11 ***"The Conundrum of the C4H7+ Cation"***
Hans-Ullrich Siehl
University of Ulm, Germany

I12 ***"The kinetics and mechanism of the organoiridium-catalysed enantioselective reduction of imines"***
Michael Page
University of Huddersfield, UK

I13 ***"Saccharinate-based Ligands; Structure, Reactivity and Properties"***
Maria de Lurdes dos Santos Cristiano
University of Algarve, Portugal

Molecular Spin Switching

Rainer Herges

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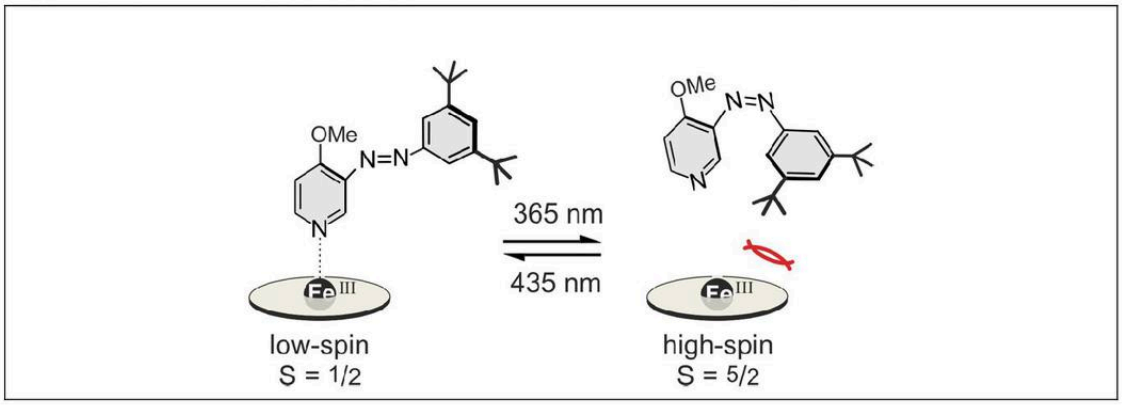
Controlled switching of the spin state of transition metal ions, particularly of Fe^{2+} and Fe^{3+} is essential to achieve selectivity and catalysis in a number of metalloenzymes. We report on an iron(III) porphyrin with a photochromic axial ligand which, upon irradiation with two different wavelengths reversibly switches its spin state between low-spin ($S=^1/_2$) and high-spin ($S=^5/_2$). Conversion is almost quantitative in both directions at room temperature. The system is neither oxygen nor water sensitive, and no fatigue was observed after more than 1000 switching cycles. Concomitant with the spin-flip is a change in redox potential by 60 mV. Besides serving as a simple model for the first step of the cytochrome P450 catalytic cycle, the spin switch can be used as a switchable paramagnetic NMR or MRI relaxation agent. The spin-lattice relaxation time T_1 of the water protons in a 2 mM solution reversibly changes between 0.56 s (low-spin) and 0.04 s (high-spin) upon irradiation with UV and visible light.



Surface-dependent reactivity of nanodiamond and related materials

Benjamin Kiendl[a], Amélie Vénerosy,[b] Sneha Choudhoury,[c] Mailis Lounasvuori,[d] Emina Hadzifejzovic,[d] Hugues Girard,[b] Jean-Charles Arnault,[b] Tristan Petit,[c] Emad Aziz[c] John Foord,[d] and Anke Krueger[a],

[a] Institute for Organic Chemistry, Julius-Maximilians University Würzburg, Würzburg, Germany, [b] CEA, LIST, Diamond Sensors Laboratory, Gif-sur-Yvette, France, [c] Institute of Methods for Material Development, Helmholtz Zentrum Berlin für Materialien und Energie GmbH, Berlin, Germany, [d] Dept. of Chemistry, Chemistry Research Laboratory, University of Oxford, Oxford, UK
(anke.krueger@uni-wuerzburg.de)

The reactivity of carbon materials strongly depends not only on the type of hybridization (sp^2 vs. sp^3) but also on the size of the carbon nanoobject and the actual orientation and morphology of its surface. Additionally, the surface termination in case of unsaturated binding sites plays a major role in the surface chemistry that is subsequently accessible for the respective carbon nanomaterial.

Here we discuss the production of differently terminated nanodiamond materials and their physicochemical properties. Furthermore, the functionalization of different types of nanodiamond will be presented. These include the immobilization of transition-metal catalysts and sensitizers as well as the grafting of organic moieties for improved dispersibility of the nanoparticles. Such efforts aim at the synthesis of tailored functional materials for applications such as (photo)catalysis, energy transformation and storage as well as biomedical applications.

This project has received funding from the European Union´s Horizon 2020 Program under Grant Agreement no. 665085 (DIACAT).

Ionic liquids to control reaction outcome. The importance of understanding microscopic interactions

Jason B. Harper[a]

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Whilst touted as having the potential to reduce the environmental impact of a process, the application of ionic liquids has been limited by a lack of understanding as to how they affect reaction outcomes.[1] Our group has been developing a series of predictive principles for such solvent effects, particularly focussing on identifying the key microscopic interactions responsible for the changes in reaction outcome.[2] A key result of understanding these interactions is the possibility of specifically *designing* ionic solvents to maximise the interactions and hence the observed solvent effects.

The work described will discuss the interactions responsible for the effects of ionic liquids on each of a range of processes (*e.g.* Figure 1).[3] The utility of this information is illustrated through control of reaction outcome using different ionic solvents and the preparation of novel ionic liquids specifically to affect a given process.[4] Methods for assessing solvent structure[5] and interactions in solution,[6] in order to predict the effectiveness of an ionic liquid solvent will also be introduced.

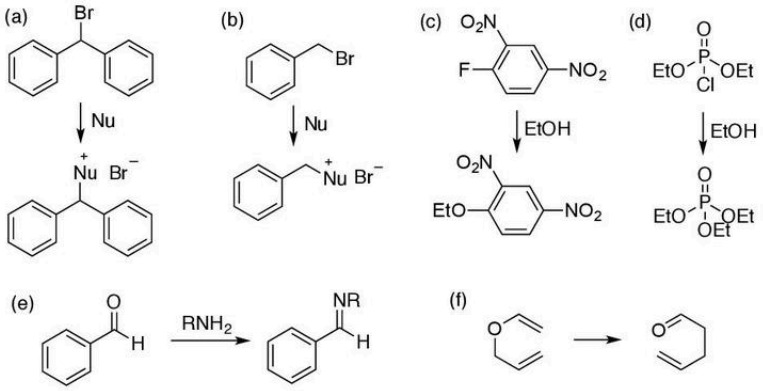

Figure 1. Representative processes for which the microscopic origins of the solvent effects of ionic liquids will be discussed: (a) S_N1, (b) S_N2, (c) S_NAr, (d) $S_N2@P$, (e) condensation and (f) pericyclic.

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Tunneling Control of Chemical Reactions[1]

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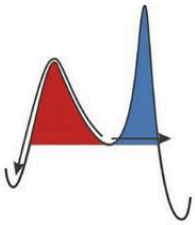

Chemical reactivity is traditionally understood[2] in terms of kinetic versus thermodynamic control,[3] wherein the driving force is the lowest activation barrier among the possible reaction paths or the lowest free energy of the final products, respectively. Here we expose quantum mechanical tunneling as a third driving force that can overwrite traditional kinetic control and govern reactivity based on nonclassical penetration of the potential energy barriers connecting the reactants and products. These findings are exemplified with the first experimental isolation and full spectroscopic and theoretical characterization of the elusive hydroxycarbenes (R–C–OH)[4] that undergo facile [1,2] hydrogen tunneling to the corresponding aldehydes under barriers of nearly 30.0 kcal mol^{-1} with half-lives of around 1–2 h even at 10 K, despite of the presence of paths with substantially lower barriers. We will demonstrate that this is a general phenomenon,[5] as exemplified by other OH-tunneling examples such as the rotational isomerization of a variety of carbocylic acids.[6] Such tunneling processes do not merely represent corrections to the reaction rate, they *are* the reaction rate, i.e., the completely *control* the reaction outome.[1a] They can also override common notions such as the Curtin-Hammett principle.[7] Finally, we will–for the first time–introduce a *tunneling product*, i.e., a product of a chemical reaction that can, from a given starting material, only form through a tunneling process as it is otherwise inaccessible kinetically *or* thermodynamically.

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Chameleonic Character of Singlet 1,2-Diazacyclopentane-3,5-diyl Diradicals

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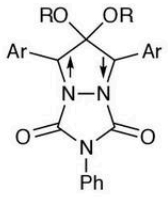
Localized singlet diradicals are key intermediates in bond homolyses. Their ultra-short-lived character have retarded the experimental investigation on the reaction intermediates. In the last decade, we have developed long-lived singlet diradicals to investigate singlet diradical chemistry.[1] In this presentation, we would like to talk about the generation of singlet 1,2-diazacyclopentane-3,5-diyl diradicals **1** and their chameleonic reactivity.[2]



1

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Environmental Influences on Isotope Effects

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Quantum-mechanical calculations are useful for interpretation and rationalization of experimental kinetic (KIE) and equilibrium (EIE) isotope effects, but often neglect the influence of the chemical environment for reactions in solution or catalyzed by enzymes. Our recent studies for methyl transfer have indicated (i) that EIEs for transfer of CH_3^+ from vacuum to a dielectric continuum varies very significantly for $2 < \varepsilon < 10$ (often considered as the range of values of the dielectric constant in an enzyme active site) and (ii) that non-covalent interactions with this group in the TS may affect KIEs significantly.[2] We now show that S_N1 heterolyses of alkyl and glycosyl substrates in water to form cationic intermediates in non-polar media are sensitive to the dielectric environment. Variations in EIEs for substitution of H (for D or T) at the anomeric centres of glycosides may be understood by consideration of the dielectric-environmental influence at the site of isotopic substitution alone ("atomic hessian analysis"). We also report computational results for 2° α-D and 1° ^{14}C KIEs at the anomeric centre in S_N1 hydrolyses of tetrahydropyranosyl and methylthioadenosyl acetals and in S_N2 methyl transfer.

It is conceivable that a reaction involving charge redistribution, separation or neutralization within an enzyme active site could manifest variations in KIEs, as between a wild-type and a mutant form of the enzyme, that originate from changes in the local dielectric within the protein environment, or from changes in non-covalent interactions in the TS; if so, there would be important implications for the interpretation of experimental KIEs in mechanistic enzymology.

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Exploring Efficient and Promiscuous Biocatalysis

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Phosphoryl transfer is ubiquitous in biology, but is extremely slow under physiological conditions.[1] These data mean that the enzymes that catalyse these reactions are among the most proficient known and that these enzymes have (and need) particularly high discrimination between the ground state and transition state. That is not obviously consistent with the observation that some of these enzymes exhibit catalytic promiscuity: they catalyse chemically distinct reactions, often with comparable efficiency – despite the differences in the changes that occur during the process.[2]

This talk will consider the chemical features involved in achieving efficient catalysis and whether the transition state (or mechanism) for phosphoryl and related transfer reactions are changed in the active site of a metallo protein – a frequent, but sometimes controversial, proposal that may have implications for how enzyme functionality evolves – based on our studies with model compounds, artificial catalysts and a metallophosphatase enzyme.[3]

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Dynamics, Cooperativity and the Evolution of Enzyme Function

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Recent years have seen an explosion of interest in both experimental and computational studies of the evolution of enzyme function.[1,2] In particular, it has been argued that conformational selection plays a major role in allowing old enzymes to acquire new activities.[3] My group and I have performed detailed computational studies of a broad range of catalytically promiscuous enzymes, in order to probe the molecular origins of both their multifunctionality and its implications for their functional evolution.[4-7] These include alkaline phosphatases,[4] organophosphate hydrolases,[5,6] aldolases[7] and Kemp eliminases, to name a few examples. Based on this work, we present a molecular model for enzyme evolution, highlighting the critical importance of a fine-tuned interplay between enzyme dynamics, electrostatic cooperativity and conformational selection in allowing for the acquisition of new activities, as well as the ability to select more than one possible reaction from a pool of given substrates.

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Potassium *tert*-Butoxide in SET Reactions?

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Florimond Cumine,[a] Giuseppe Nocera,[a] Matt P. John[b],
Leonard E. A. Berlouis,[a] Thomas McGuire,[c] Tell Tuttle [a]

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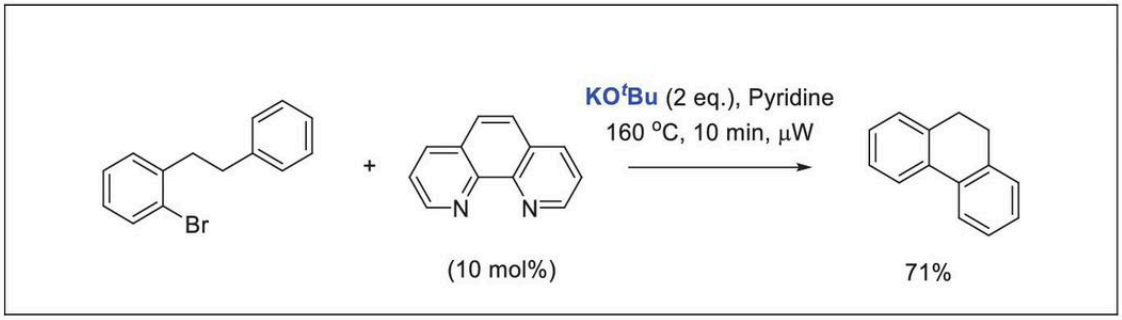
Many recent papers have proposed[1] that KO*t*Bu or a derived complex, acts as a single electron donor. This presentation reports some of the available data from our work[2] and that of others to examine this proposal.



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Twists and Turns of Platinum-Allene Chemistry

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Although platinum exhibits similar reactivity to gold in general, there are increasing examples where under similar conditions, these two metals get involved in different reaction pathways and give different products.[1] For example, we have reported the Pt-catalysed dihydroalkoxylation and bisindolylation of allenes,[2] which give acetals or bisindolyl alkanes with double addition of the nucleophile to the terminal or less substituted double bond of the allene, and complete saturation of the second double bond, instead of the most common allyl derivatives obtained under gold catalysis.[3] To explain the different reactivity of the two metals, different mechanisms and metallic intermediates have to be proposed for the two processes. The mode of coordination in metal-allene complexes is crucial for the understanding of the reactivity of these important systems. Although a lot of attention has been paid to Au-allene complexes,[4] studies on Pt-allene complexes are still rare.

We are very interested in revealing the secrets behind the divergent reactivity in Pt-allene systems using a POC approach. In this talk our efforts towards this understanding, including the development of a new NMR method (SSTD NMR) to study the fluxional behavior of platinum-allene complexes in solution[5] and examples of the divergent reactivity in Pt-allene chemistry recently discovered in our group will be discussed.[2,6]

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The Conundrum of the $C_4H_7^+$ Cation

Dedicated to George A. Olah
at the Olah memorial session of the European Symposium of Physical Organic Chemistry ESOR 2017
at Durham

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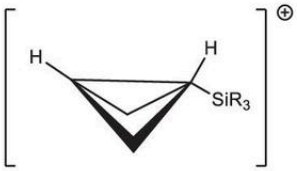
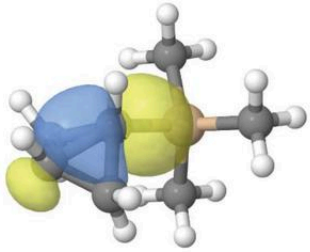
Nobel Laureate George A. Olah passed away March 8 2017 at the age of 89. George Olah was a true legend in the field of chemistry. His pioneering research created an entire new field of chemistry of considerable theoretical and practical importance. The work on carbocations fundamentally redefined the field of physical organic chemistry.and revolutionized the understanding of organic chemistry, leading to new discoveries, new fields of research and countless applications.

This contribution will mainly review some retrospective and recent results from our group focused on experimental and computational NMR Spectroscopy of highly reactive carbocations such as the Bicycobutonium $C_4H_7^+$ and related cations.





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M. Holzschuh, C. Freudenberger, H.-U. Siehl, submitted.

The kinetics and mechanism of the organoiridium-catalysed enantioselective reduction of imines

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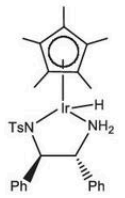
The iridium complex of pentamethylcyclopentadiene and (S,S)-1,2-diphenyl-N'-tosylethane-1,2-diamine (I) is an effective catalyst for the asymmetric transfer hydrogenation of imine substrates (2) under acidic conditions, a 5 : 2 ratio of formic acid : triethylamine in either acetonitrile or dichloromethane. However, the reaction shows unusual enantiomeric excess (*ee*) profiles for the product amines. The reactions initially give predominantly the (R) enantiomer of the chiral amine products with >90% *ee* but which then decreases significantly during the reaction. This is because the rate of formation of the (R)-enantiomer follows first-order kinetics whereas that for the (S)-enantiomer is zero-order. This difference in reaction order explains the change in selectivity as the reaction proceeds – the rate formation of the (R)-enantiomer decreases exponentially with time while that for the (S)-enantiomer remains constant.



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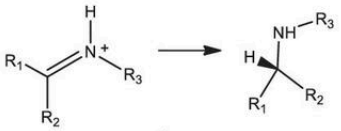

2

These reactions have been studied by investigating the effect of substituents in the cyclopentadiene ring and the imine as well as replacing the metal ion by ruthenium.

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Saccharinate-based Ligands; Structure, Reactivity and Properties

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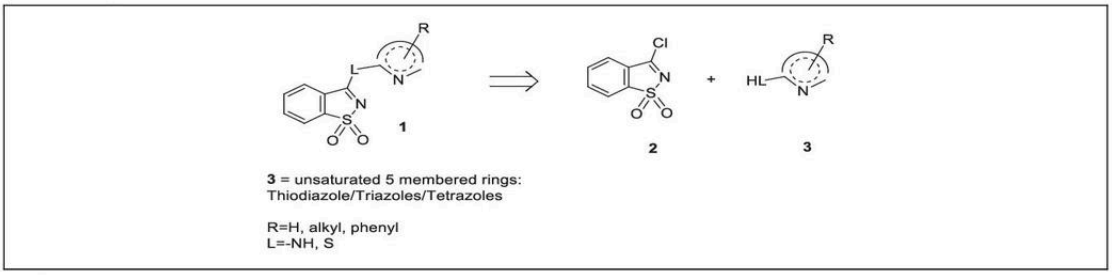
Saccharin (3-oxo-1,2-benzisothiazole 1,1-dioxide) and saccharinates have important applications in coordination chemistry, as ligands.[1] However, conjugates that combine the saccharyl system with other heterocycles have been scarcely explored hitherto, in spite of their expectable capabilities as bridging ligands. We have designed and prepared a representative library of saccharinate-based ligands **1** from tailored building blocks (**2**, **3**),[2] in view of exploring their potential as chelants. The structure, photoreactivity and chelating capacity of selected conjugates towards divalent cations of transition metals were scrutinised.[3] The properties and applications of ligands and of corresponding complexes were evaluated and revealed to be promising. Results will be presented and discussed.



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We acknowledge Fundação para a Ciência e a Tecnologia (FCT)-Portugal and COMPETE (projects UID/Multi/04326/2013, UI0313/QUI/2013, PTDC/QEQ-QFI/3284/2014, PTDC/MAR-BIO/4132/2014).

LIST OF SUBMITTED ORAL PRESENTATIONS

S1 ***"Helicene Amphiphiles: From organocatalysis to liquid crystal topological quasiparticles via fractals"***
Dave Carbery
University of Bath, UK

S2 ***"Photo and gamma rays induced polymerisation of the bis(aminoacid) fumaramide self-assemblies"***
Leo Frkanec
Ruđer Bošković Institute, Croatia

S3 ***"Reaction Bifurcation, Electronic Effects and Stereochemical Inversion at the Phosphonium Centre"***
Kirill Nikitin
University College Dublin, Ireland

S4 ***"Strong Acid Catalyzed Deprotection Reactions: Application of Acidity Functions to Support Reaction Optimisation"***
Ian Ashworth
Astra Zeneca, UK

S5 ***"Synergy of Computation, NMR and Synthesis Reveals to Elucidate the Correct Structure of Baulamycins"***
Siyong Zhong
University of Bristol, UK

S6 ***"Dimerization of aromatic C-nitroso compounds as a route to new supramolecular architectures"***
Ivan Biljan
University of Zagreb, Croatia

S7 ***"Structural Study on Cyclic Silsesquioxane Oligomers for the Elucidation of Polymer Forming Polycondensation Process"***
Fujio Yagihashi
Advanced Industrial Science and Technology, Tsukuba, Japan

S8 ***"Nitroxides as Catalytic Radical Trapping Antioxidants: Insight into their Different Reaction Mechanisms"***
Markus Griesser
University of Ottawa, Canada

S9 ***"A New Type of Radical Traps with a Nitroxide Leaving Group, Designed for Detection by Mass Spectrometry"***
Victor Chechik
University of York, UK

S10 ***"New Mechanistic Aspects in Diels-Alder Reactions Catalysed by Tris-(4-bromophenyl)aminium Radical Cation Salts"***
Götz Bucher
University of Glasgow, UK

S11 ***"Towards Engineering Radical Enzymes - Thermodynamic Reaction Profiling and Mechanistic Insights into QueE"***
Christof Jäger
University of Nottingham, UK

S12 ***"Foldamers as Devices for the Transmission of Binding Information"***
Simon Webb
University of Manchester, UK

S13 ***"Excited-State Aromatic Interactions in Fluorescent Molecular Rotors"***
Paul McGonigal
Durham University, UK

S14 ***"Chiral ion-pairs: dissociation, dynamics and asymmetric catalysis"***
Fernanda Duarte
University of Edinburgh, UK

S15 ***"A Classical Case of Umpolung at Phosphorus"***
Anna-Christina Vetter
University College Dublin, Ireland

S16 ***"Ferrocene derivatives as flexible model systems to study the effect of chirality on hydrogen-bonding patterns"***
Ivan Kodrin
University of Zagreb, Croatia

S17 ***"Quantifying Lewis Basicity Using the Benzhydrylium Methodology"***
Peter Byrne
University College Cork, Ireland

S18 ***"Novel DNA-templated Chemical Ligation"***
Heidi Korhonen
University of Turku, Finland

S19 ***"Aerobic C-H bond activation-functionalisation catalysis involving 'Pd-NOx'"***
Ian Fairlamb
University of York, UK

S20 ***"Stability of Cu(II) complexes with potential use in PET"***
Moisés Canle
University of A Coruña, Spain

S21 ***"Palladium Acetate/Trifluoroacetic Acid Catalytic System: Ligand Exchange and Catalytic Behaviour"***
Jiří Váňa
University of Pardubice, Czech Republic

S22 ***"2D NMR Spectra in <10 seconds for Reaction Monitoring"***
Craig Butts
University of Bristol, UK

S23 ***"Lithiation-Trapping of N-Boc Heterocycles: How Fast is Each Step?"***
Adam Islip
University of York, UK

S24 ***"Catalytic Reaction of Organometallic Ruthenium Complexes"***
James Walton
Durham University, UK

S25 ***"Using ionic liquids as solvents for organic processes: Which one do you choose?"***
Rebecca Hawker
University of New South Wales, Australia

S26 ***"Selective Fluorination Strategies"***
Graham Sandford
Durham University, UK

S27 ***"Counter-Intuitive Nucleophilicities of Peroxide Anions"***
Armin Ofial
Ludwig-Maximilians Universität München, Germany

S28 ***"Computational Study of Substituent Effects on Gas-Phase Stabilities of Phenylaminomethyl Cations"***
Kazuhide Nakata
Hosei University, Japan

S29 ***"Aromatic C-Nitroso Compounds and their Dimers: A Model for Physical Organic Chemistry of Reactions in Crystalline Molecular Solids"***
Hrvoj Vančik
University of Zagreb, Croatia

S30 ***"Catalyst choice aided by mechanistic understanding on AZD9496 Heck stage"***
Robert Cox
Astra Zeneca, UK

S31 ***"Towards the Design of New Anti-Parasitic Drug Candidates: Some Studies of the Reaction of Aromatic Nitro-Compounds with Anionic and Amino Nucleophiles."***
Chukwumeka Isanbor
University of Lagos, Nigeria

S32 ***"The Effects of Electronics and Strain on the Acidity and Reactivity of a Range of Systems"***
Nicholas Konstandaras
University of New South Wales, Australia

Helicene Amphiphiles: From organocatalysis to liquid crystal topological quasiparticles *via* fractals

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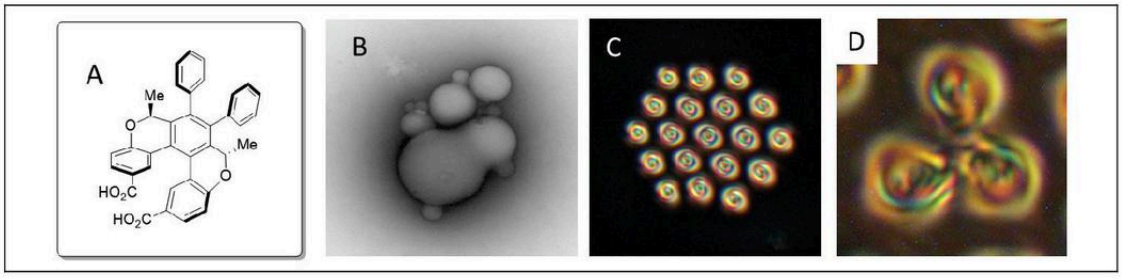
This presentation will cover the progress we have made with the design, synthesis of helical amphiphiles, initially designed for asymmetric catalysis, serendipity uncovered their self-assembly properties and ultimately their use as chiral dopants in chiral nematic liquid crystal phases.

Helicenes featuring pyridine and percarboxylic acid functionality were designed to desymmetrise the popular DMAP organocatalyst (*Org. Lett*, **2011**, *13*, 1250)' and *m*-CPBA reagent (*J. Org. Chem*. **2009**, *74*, 5320) for asymmetric catalysis. The carboxylic diacid in particular (Fig A) displays a rich self-assembly profile, capable of forming H-bonding dimers with a chiral figure-of-eight shape, and in aqueous media assembling *via* spherical vesicles to fractal structures (Fig B). The pH-sensitive nature of the carboxylic acids means that circular dichroism and particle size is reversibly controlled, meaning these helicenes act as a topographical *and* large magnitude chiroptical based switch ($\Delta\Delta\varepsilon$=170 $M^{-1}cm^{-1}$).

These helicenes offer themselves as chiral dopants for nematic liquid crystals where both interfacial and chirality considerations are crucial at microscale spatial dimensions, such as aqueous-dispersed and glass-adhered droplets. We have observed the formation of liquid crystal topological quasiparticles, hexagonally-packed Skyrmions (Fig C). Furthermore, these entities have shown examples which display intricate trefoil-like shapes (Fig D).



Submitted Presentation 2

Photo and gamma rays induced polymerisation of the bis(aminoacid) fumaramide self-assemblies

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and Janja Makarević

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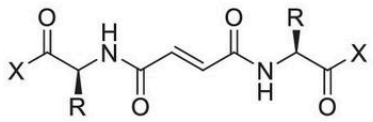
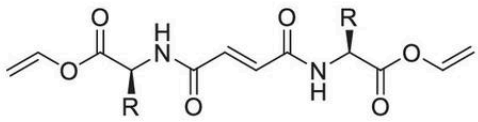
Recent study in a field of supramolecular gels resulted in the development of recognizable areas in materials chemistry with an emphasis on the self-organizing soft materials.[1] They have a great opportunity for specific applications in various fields, such as pharmaceutical, food and cosmetic industry or in tissue engineering and regenerative medicine. Polymerization can improve the mechanical properties of supramolecular gels, or prepared the specific polymer materials. In order to achieve "solid-state" reaction within the gel network is necessary to meet the special requirements of self-organization of organogelators. This especially refers to the distance of the atoms entering the reaction and position of functional groups. Our attention was focused on the synthesis and investigations of the properties of new gelators.[2] The Leu, Val, Phe and Phg fumaramides derivatives were synthesized and characterized. Their advanced self-organization into gels and their polymerization (covalent crosslinking) induced by photo and gamma radiation were tested. We have shown that small changes in the structure of compound cause specific self-organization through non-covalent interactions which effects on the reactivity of crosslinked moleculs. Gelators with two polymerized functional groups experienced a successful "solid-state" reactions without compromising the morphology of the initial gel network.



a) R = *i*Bu, *i*Pr, Bzl or Ph, X = OH, OMe, NH_2



b) R = *i*Bu, *i*Pr, Bzl or Ph

1. E. Busseron, Y. Ruff, E. Moulin, and N. Giuseppone, *Nanoscale*, **5** (2013) 7098.
2. a) L. Frkanec, M. Jokić, J. Makarević, K. Wolsperger, and M. Žinić, *J. Am. Chem. Soc.*, **124** (2002) 9716.; b) L. Frkanec and M. Žinić, *Chem. Commun.*, **46** (2010) 522.

Reaction Bifurcation, Electronic Effects and Stereochemical Inversion at the Phosphonium Centre

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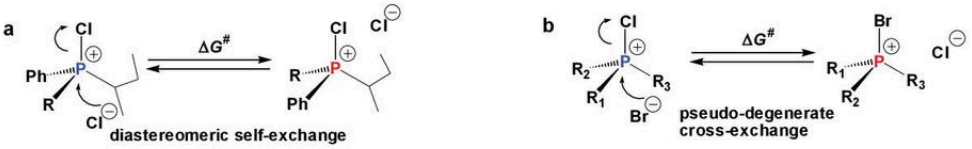
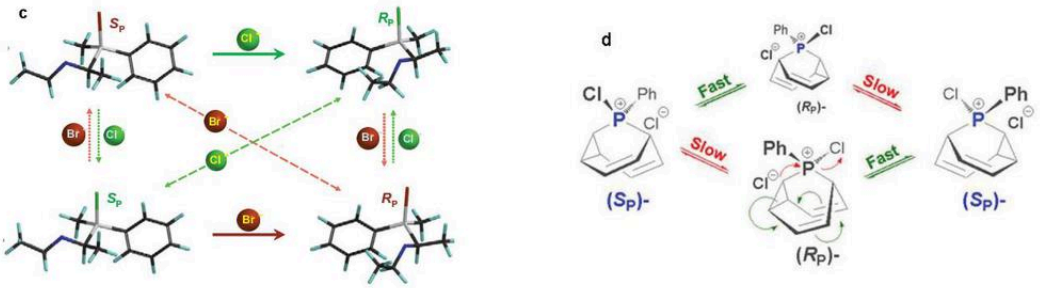
We extend our dynamic NMR study of diastereomeric[1] (a) tetrahedral halophosphonium salts (XPS) to the cross-exchange series (b)[2] to probe key reaction pathways and their stereochemical outcome.



In particular, we constructed[2] a unified reactivity scale of phosphonium structures. For example, XPS containing compact Ar and Alk groups have exchange barriers ca. 10-12 kcal/mol, rising rapidly with increased steric bulk in agreement with our findings on diastereomeric exchange.[1] Secondly, we have, for the first time, completed millisecond-range exchange experiments to build a LFER plot showing strong acceleration (ρ = 1.46) by electron-withdrawing substituents. Finally, an analysis of unprecedented multi-exchange system (c) was, for the first time, used to unambiguously show *exclusive inversion* of the *P*-configuration in a dynamic nucleophilic process in agreement with our earlier computational predictions.[1]



Further to that, we designed a cyclic phosphonium system[3] (d) integrating *two independent stereomutation mechanisms* at the same asymmetric centre: a Walden nucleophilic inversion and a Cope rearrangement. This extraordinary phenomenon provides important insights into reaction pathway bifurcation, microscopic reversibility, and dynamic stereochemistry.

1. Jennings, E.; Nikitin, K.; Ortin, Y.; Gilheany, D.G. *J. Am. Chem. Soc.,* **2014**, 136, 16217-16226. 2. Nikitin, K.; Gilheany, D.G. *MS in prep.* **2017**. 3. Gillick-Healy, M., Jennings, E.; Nikitin, K.; Ortin, Y.; Gilheany, D.G. *Chem. Eur. J.* **2017**, 23, 2332-2339.

Submitted Presentation 4

Strong Acid Catalyzed Deprotection Reactions: Application of Acidity Functions to Support Reaction Optimisation

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and Robert Cox[a]

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Many protecting groups are designed to be removed under acidic conditions.[1] In a small scale synthetic environment deprotections are often achieved with large volumes of acids such as trifluoroacetic acid. However, such conditions are not ideal for large scale production and weaker acids are often replaced during process development with strong acids such as HCl. While effective, the use of acids such as HCl can lead to deprotection reactions that exhibit a non-linear dependence upon the concentration of the acid catalyst at high concentrations, due to their non-ideality.

This type of non-linear behavior was observed in the deprotection of a MEM protected phenol using 2.0 M HCl. As expected for an acid catalyzed acetal hydrolysis the deprotection reaction exhibits pseudo first order kinetics,[2] with the observed first order rate constants showing a non-linear dependence upon $[H^+]$. A good linear correlation was obtained between log k_{obs} and the Hammett acidity function,[3] H_0 implying a specific acid catalyzed process analogous to the hydrolysis of methylal.[4] The identification of a chlorinated impurity resulting from the use of HCl in the MEM deprotection necessitated a change in the catalytic acid very late in development. Using the existing understanding of the HCl catalyzed process a new process using H_2SO_4 was rapidly developed and implemented in time for validation of the commercial API manufacturing process.

A more complex situation has been found to exist in the HCl catalyzed deprotection of a N-Boc protected hydrazine. In this case it was determined that the pseudo-first order deprotection kinetics are coupled with the extraction of the starting protected hydrazine from toluene into the aqueous reaction phase.

1. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis,* 3rd Edn. Wiley, 1999.
2. Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, Cornell University press, 1953, 334.
3. Paul, M. A.; Long. F. A. *Chem. Rev.*, **1957**, *57*, 1.
4. McIntyre, D.; Long, F. A. *J. Am. Chem. Soc.*, **1954**, *76*, 3240.

Synergy of Computation, NMR and Synthesis Reveals to Elucidate the Correct Structure of Baulamycins

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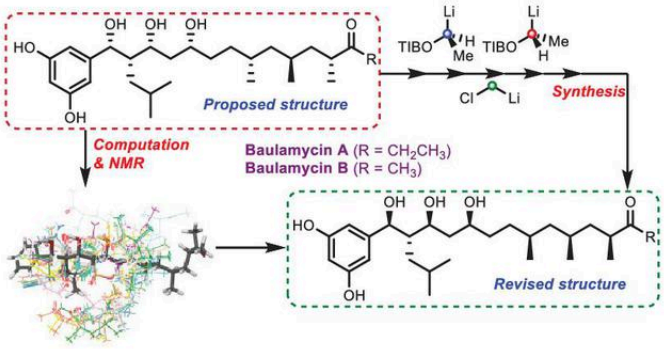
Structural elucidation of acyclic natural products, in particular the determination of relative configuration, still remains a challenge[1] because the observed time-averaged NMR parameters, such as scalar coupling constants, are strongly influenced by the molecules' complex dynamic conformation(s) in solution state.[2]

The configuration of a recently isolated polyketide Baulamycin A,[3] which exhibits potent antibacterial activity, was reassigned using a combination of Density Functional Theory (DFT) calculations and synthesis. In this work, DFT calculations were employed to predict Boltzmann-averaged NMR parameters. Comparison between the computed NMR parameters with the experimentally determined values eliminated 120 out of the possible 128 diastereomeric candidates. Finally, synthesis[4] allowed the relative and absolute configurations of Baulamycin A to be positively identified.



Our work demonstrates the power of using a combination of computation and NMR in structural elucidation of acyclic natural products. Further developments in accurate conformational analysis by computation are required to enable us to confidently and reliably determine the structures of flexible open chain-molecules exclusively *in silico*.

References: (1) G. Bifulco, P. Dambruoso, L. Gomez-Paloma and R. Riccio, *Chem. Rev.* **2007**, *107*, 3744; (2) G. J. Sharman and I. C. Jones, *Magn. Reson. Chem.* **2001**, *39*, 549; (3) D. H. Sherman and co-workers, *J. Am. Chem. Soc.*, **2014**, *136*, 1579. (correction: **2014**, 10541) (4) V. K. Aggarwal and co-workers, *Nature*, **2012**, *489*, 278.

Submitted Presentation 6

Dimerization of aromatic C-nitroso compounds as a route to new supramolecular architectures

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Aromatic C-nitroso compounds can exist as monomers and azodioxide dimers.[1] In solution at room temperature, the dominant species are monomers whereas lowering of temperature or crystallization favors dimerization. The efficacy of solid-state dimerization is influenced by the topochemistry *i.e.* the vicinity of the reacting nitroso groups.

In our recent studies, we investigated dimerization of aromatic C-nitroso compounds on 2D gold surface.[2] We prepared nitrosoarenes with one and two nitroso groups functionalized with sulfur headgroups for adsorption on an Au(111) surface. Self-assembled layers of nitrosoarenes were studied by scanning tunneling microscopy (STM), atomic force microscopy (AFM), ellipsometry and reflection-absorption IR spectroscopy. It was found that in addition to self-assembly into ordered monolayers, nitroso derivatives can dimerize on an Au(111) surface through reaction of exposed nitroso groups with those free in solution and form bilayers.

Recently, we prepared a series of bis(4-nitrosophenyl) derivatives with different spacers between two aromatic rings and investigated kinetics of their dimerization in solid state at different temperatures. Starting monomers, obtained by cryogenic photodissociation of the corresponding azodioxides, redimerize upon heating. Dimerization of methane derivative at 200 K proceeds in parallel reactions producing *Z*- and *E*-forms of which the latter isomerizes to *Z*-form through monomer intermediate at 270 K. On the other hand, ethane, methanone and biphenyl derivatives redimerize to *E*-isomers. Activation energies for solid-state dimerization, estimated by using Arrhenius plots, are in the range of 4-12 $kJmol^{-1}$.

1. Vančik, H. *Aromatic C-Nitroso Compounds*; Springer: New York, 2013.
2. Biljan, I.; Kralj, M.; Mišić Radić, T.; Svetličić, V.; Vančik, H. *J. Phys. Chem. C* **2011**, *115*, 20267-20273.

This work was supported by the Croatian Science Foundation, grant no. 7444.

Structural Study on Cyclic Silsesquioxane Oligomers for the Elucidation of Polymer Forming Polycondensation Process

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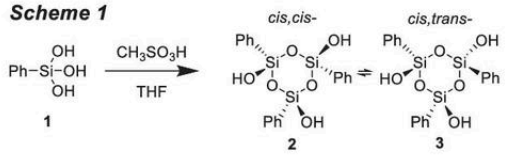
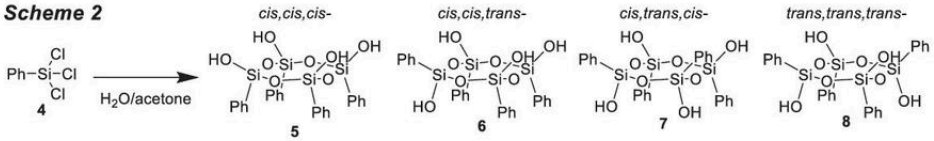
Organosilicon materials consisting of siloxane bonds (Si-O-Si) are widely used in modern industry. In order to produce high-performance organosilicon materials, precise understandings of the detailed structure of both final products and their intermediates and also elucidation of the reaction mechanism are essential. In spite of a long history of research on the field, a lot of uncertainties still remain because of the difficulties of their structural analysis and uncontrollable reactivity of silanols in the intermediates.

We have investigated initial stages of the acid-catalyzed condensation reaction of $PhSi(OH)_3$ and have successfully clarified the formation of cyclotrisiloxanes (Scheme 1)[1]. The hydrolytic condensation reaction of $PhSiCl_3$ in aqueous solution forming cyclotetrasiloxanes was also studied in detail (Scheme 2)[2]. Their reaction mechanisms and our recent research on methyl-substituted cyclotetrasiloxanes will also be discussed.

Scheme 1



Scheme 2



1. F. Yagihashi et al. Organometallics, **2014**, *33*, 6278-6281.
2. F. Yagihashi et al. Eur. J. Inorg. Chem., **2016**, 2882-2886.

This work was supported by the "Development of Innovative Catalytic Processes for Organosilicon Functional Materials" project (PL: K. Sato) from the New Energy and Industrial Technology Development Organization (NEDO).

Submitted Presentation 8

Nitroxides as Catalytic Radical Trapping Antioxidants: Insight into their Different Reaction Mechanisms

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Omkar Zilka, and Derek. A. Pratt*

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Ottawa, ON K1N 6N5, Canada (markus.griesser@uottawa.ca)

Diarylamines and hindered amines are known to be highly effective inhibitors of hydrocarbon autoxidation. Nitroxides have been proposed to play a central role in their mechanism of action, giving them the ability to catalytically trap peroxyl radicals. The two main mechanisms are a) H-atom transfer from a protonated nitroxide trapping a peroxyl radical followed by electron transfer to the oxoammonium ion to regenerate the nitroxide[1] and b) direct reaction of nitroxide with an alkyl radical followed by a retro-carbonyl ene reaction to give an amine from which the nitroxide can be formed again via reactions with peroxyl radicals.[2] Both mechanisms have different requirements, such as presence of acid for a) and elevated temperatures for the bond cleavage of b).

Recently, we have found two instances where nitroxides can also catalytically trap peroxyl radicals in the absence of either acid or elevated temperatures. The first is in water, and the second is when the substrates undergoing autoxidation contain an unsaturation (e.g. styrene, hexadecane and cyclooctene). Autoxidations of saturated substrates (e.g. ethylbenzene, dioxane, cumene) are not inhibited.

The results can be explained by the intervention of a hithertofore undescribed propagation pathway in hydrocarbon autoxidation – one wherein hydroperoxyl is produced. The hydroperoxyl radicals reduce nitroxides to give hydroxylamines – potent peroxyl radical-trapping antioxidants. We will describe the results of mechanistic studies and computations that have enabled us to characterize this pathway, which operates only for the autoxidation of unsaturated hydroperoxides.

(1) Haidasz, E. A.; Meng, D.; Amorati, R.; Baschieri, A.; Ingold, K. U.; Valgimigli, L.; Pratt, D. A. *J. Am. Chem. Soc.* **2016**, 138, 5290. (2) Haidasz, E. A.; Shah R.; Pratt, D. A. *J. Am. Chem. Soc.* **2014**, 136, 16643.

A New Type of Radical Trap with a Nitroxide Leaving Group, Designed for Detection by Mass Spectrometry

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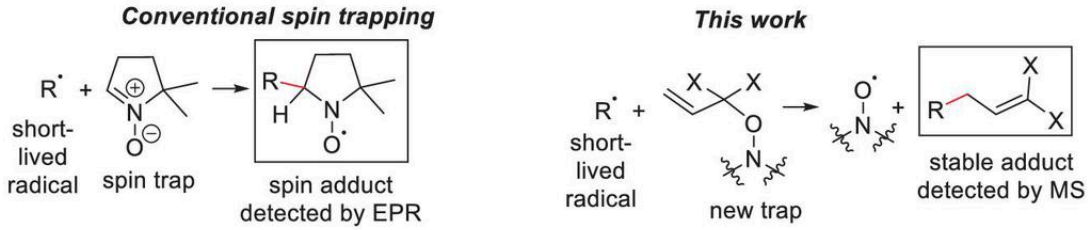
Spin traps have been used for detection of short lived free radical intermediates by EPR since 1960s. There are however some disadvantages to using spin traps, e.g., they provide limited structural information about the trapped radical, they are prone to artefacts, the detection limit of EPR is relatively low etc. To overcome some of these disadvantages, several research groups recently explored detection of spin adducts by mass spectrometry (MS).[1] However, conventional spin traps are not designed for MS detection.

In this work, we develop a new type of radical traps which eliminate a stable nitroxide upon reaction with short-lived free radicals. The stable adducts are detected by MS. We applied this technique to the radical detection in the gas phase. We were able to simultaneously detect a large number of radical intermediates in complex mixtures at concentrations relevant to atmospheric chemistry. The new method also enables quantification of the radical concentrations.



- *Unstable adducts (lifetime seconds to minutes)*
- *Limited sensitivity (M adduct concentration)*
- *Prone to artefacts (via nucleophilic additions)*
- *Limited structural information*
- *Difficult to resolve several adducts*

- *Stable non-radical adducts*
- *Very high sensitivity (<nM adduct concentration)*
- *Inert to nucleophilic attacks*
- *Accurate mass yields elemental composition*
- *Simultaneous detection of many adducts*

1. Y. Wang, M. Liu, Y. Zhu, K. Cheng, D. Wu, B. Liu, F. Li, *Talanta* **2016**, *160*, 106; B. Tuccio, R. Lauricella, L. Charles, *Int. J. Mass Spectrom*. **2006**, *252*, 47.

Submitted Presentation 10

New Mechanistic Aspects in Diels-Alder Reactions Catalysed by Tris-(4-bromophenyl)aminium Radical Cation Salts

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Cycloaddition reactions can be catalysed by stable radical cations. Weitz' salt, tris-(4-bromophenyl)aminium hexachloroantimonate, a stable radical cation salt of a triarylamine, has been particular popular for the catalysis of Diels-Alder reactions and related cycloadditions. The commonly accepted reaction mechanism involves electron transfer from the diene component to the triarylamine radical cation, followed by a very rapid Diels-Alder reaction of the diene radical cation. The catalytic cycle is then closed by reverse electron transfer from the neutral triarylamine catalyst to the cyclohexene radical cation formed.

In this contribution, I will present new data suggesting that the reaction, at least at low temperatures, preferentially proceeds via a previously-discounted associative mechanism involving a ternary complex between triarylamine radical cation, diene, and ene component. Mechanistic implications will be discussed.

Towards Engineering Radical Enzymes - Thermodynamic Reaction Profiling and Mechanistic Insights into QueE

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Radical S-adenosylmethionine (SAM) dependent enzymes[1] are a class of enzymes dealing with radical intermediates during catalysis. The enzymes harness these intermediates that are hard control in classical synthesis, in a very controlled way for a wide range of challenging chemical processes leading to products of potential use in anti-viral, anti-cancer and antibiotic treatments.

A thorough knowledge of the reaction mechanisms involved in the biocatalysis of these enzymes can lay the foundation for rational enzyme engineering. On the other hand this also shows one of the bottlenecks for a more rapid access to rational enzyme design. At best, all factors influencing the enzyme kinetics from substrate binding, the catalytic mechanism to effects by flexible protein dynamics are known in detail. Still, individual steps of the catalysis can be addressed by quicker methods, in order to get a first qualitative picture of how these steps can be influenced and can feed into the enzyme design process.

Radical stabilization energies (RSEs)[2] for example, offer an attractive possibility to assess the overall thermodynamics of radical rearrangements as central steps in radical SAM enzyme catalysis. Through the example of the bacterial 7-carboxy-7-deazaguanine (CDG) synthase (QueE),[3] we will highlight key features and details of the biocatalytic radical rearrangement mechanism involved[4] and will discuss the potential of using radical stabilization energies for of thermodynamic reaction profiling directly from enzyme substrate complexes. Further, we will provide insights into other challenges of radical SAM enzymes addressed in the context of enzyme engineering.

1) Broderick, J. B. et al., *Chem. Rev.*, **2014**, *114*, 4229-4317.

2) Hioe, J.; Zipse, H.,.*Faraday Discussions*, **2010**. *145*, 301-313.

3) Dowling, D. P. et al., *Nat. Chem. Biol.,* **2014**, *10*, 106-112.

4) Jäger, C. M.; Croft, A. K., *Chem. Eur. J.*, **2017**, *23*, 953-962.

Submitted Presentation 12

Foldamers as Devices for the Transmission of Binding Information

F. G. A. Lister,[a,b] B. A. F. Le Bailly,[c] R. A. Brown,[a] J. R. D. Brown,[b] V. Diemer,[a,b] J. Clayden[c] and S. J. Webb[a,b]

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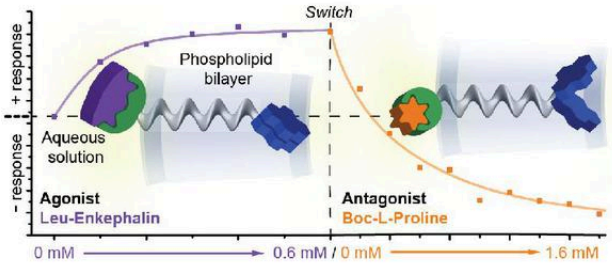
Molecular devices that can reversibly bind messenger ligands and relay this information into compartments will be a key part of programmed manufacturing at the nanoscale. Such devices can be found in nature, for example the G protein-coupled receptors, where they are used to transmit external signals to the cell interior.

Foldamers (folded oligomers) comprising α-aminoisobutyric acid (Aib) have promise as information transfer devices. These oligomers, which fold into 3_{10} helices, have a conformation that is very sensitive to binding events at their N-terminus. Initial studies showed ligand binding in solution could trigger a conformational switch that is relayed several nanometres along the foldamer to a reporter group at the far end.[1] Then light-switchable Aib foldamers were shown to relay photochemical information over similar distances within phospholipid bilayers.[2] Recently we combined both features, creating a foldamer that transmits binding information several nanometres into a bilayer.[3] We now hope to develop this prototype into a synthetic device for molecular communication between the exterior and interior of artificial vesicles.



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Excited-State Aromatic Interactions in Fluorescent Molecular Rotors

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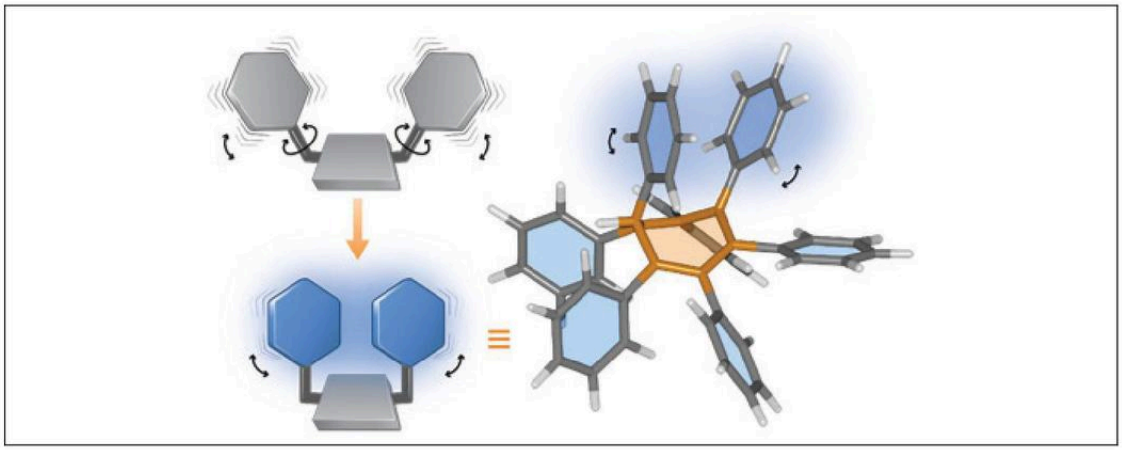
Small, apolar aromatic groups, such as phenyl rings, are commonly included in the structures of fluorophores in order to impart hindered intramolecular rotations, leading to desirable solid-state luminescence properties. However, they are not normally considered to take part in through-space interactions that influence the fluorescent output. This presentation describes the photoluminescence properties of a series of phenyl-ring molecular rotors bearing three, five, six, and seven phenyl groups. The fluorescent emissions from two of the rotors are found to originate, not from the localised excited state as one might expect, but from unanticipated through-space aromatic dimer states. We demonstrate that these relaxed dimer states can form as a result of intra- or intermolecular interactions across a range of environments in solution and solid samples, including conditions that promote aggregation-induced emission. Computational modelling also suggests that the formation of aromatic-dimer excited states may account for the photophysical properties of a previously reported luminogen. These results imply, therefore, that this is a general phenomenon that should be taken into account when designing and interpreting the fluorescent outputs of luminescent probes and optoelectronic devices based on fluorescent molecular rotors.



Submitted Presentation 14

Chiral ion-pairs: dissociation, dynamics and asymmetric catalysis

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Ion-pairing with a charged, chiral catalyst has emerged as a versatile strategy in asymmetric catalysis[1]. However, theoretical work on the stereoselectivities of these transformations remains a challenging task. This is due to the difficulties in identifying the most stable configurations in a given environment, where the predominantly electrostatic nature of these interactions make then less directional and more solvent dependent than e.g. hydrogen-bonding or dispersion interactions.

Here we investigate the structures, dynamics and stabilities of the chiral ion-pairs in the condensed phase for the landmark anionic asymmetric PTC ring-opening reaction of *meso*-aziridinium and episulfonium cations[2]. We find that the stability of chiral ion-pairs, a pre-requisite for asymmetric catalysis, is dominated by electrostatic interactions at long-range and by CH--O interactions at short-range. The decisive role of solvent upon ion-pair formation and of non-bonding interactions upon enantioselectivity are quantified by complementary computational approaches. Our computational results rationalize the stereoselectivity for several experimental results and demonstrate a combined classical/quantum approach to perform realistic-modelling of chiral counterion catalysis in solution[3].

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A Classical Case of Umpolung at Phosphorus

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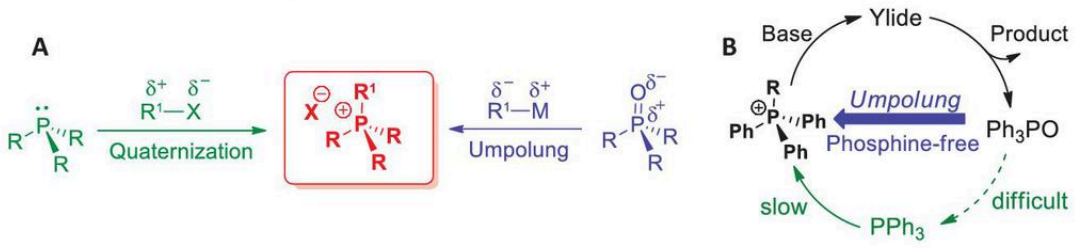
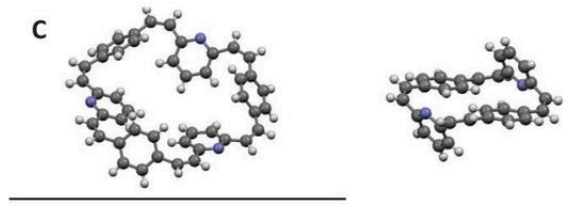
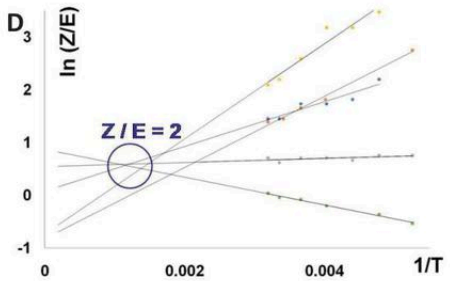
Wider applications of the Wittig reaction are inhibited by the production of its phosphine oxide by-product. Furthermore, the preparation of the required phosphonium salts via phosphine quaternization often requires forcing conditions. To counter this, we have implemented a classical Umpolung approach[1] where the organometallic nucleophile attacks the positively-polarised phosphorus (**A**). The new "inverse" quaternization is very fast and high-yielding (95% yield after 45 minutes i.e. 10^6-times faster than direct quaternization of phosphine). In a neat example of a shortcoming becoming an opportunity, the phosphine oxide problem is eliminated as Wittig reactions can now be run phosphine-free (**B**). Moreover, this route allows access to entirely new phosphonium salts and phosphine oxide structures.



In our earlier mechanistic studies of the Wittig reaction, we have found high *Z*-selectivity by introduction of *o*-heteroatom substituents in ylide and aldehyde fragments.[2] For the first time, we present an in-depth temperature study, which suggests an intriguing convergence of *Z*/*E* product ratio for different combinations of ylide and aldehyde (**D**). To exclude steric factors, we probed the sterically-innocent pyridine ring. Owing to highly increased *Z*-selectivity, we succeeded in creating an entirely novel class of rigid *all-Z* nitrogen macrocycles (**C**).





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Submitted Presentation 16

Ferrocene derivatives as flexible model systems to study the effect of chirality on hydrogen-bonding patterns

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Ferrocene-based peptidomimetics have already proven as flexible and efficient templates to study intramolecular hydrogen bonds formed within or between small peptide chains attached to cyclopentadienyl rings of a ferrocene unit. These compounds also show a great potential to mimic secondary structures of proteins acting as turn inducers and some of them even exhibit self-assembly and gelation properties. An opposite chirality of a single amino acid can promote different hydrogen-bonding patterns. Favorable intermolecular interactions found in the crystal structure can trigger conformational changes of single molecules from the most stable conformer they adopt in solution to energetically less favorable form observed in the solid state.[1]

If we want to predict the structural properties of ferrocene-based peptidomimetics, firstly we need to fully understand the conformational preferences of small modeling compounds. Recently, we prepared ferrocene derivatives like FcCO–Pro–Ala–NHFc to test the effect of heterochiral *vs*. homochiral amino acid sequence on different hydrogen-bonding patterns. These compounds are dinuclear derivatives and exhibit different chiro-optical properties in comparison with the previously synthesized derivatives bearing only one ferrocene unit. We performed a detailed conformational study by means of computational chemistry methods (DFT, QTAIM) to get a deeper insight into their structural preferences and fine-tuning properties. In addition, results were compared with those obtained by experimental techniques (IR, NMR, CD).

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This work was partially supported by the Croatian Science Foundation under the project HRZZ-IP-11-2013-7444.

Quantifying Lewis Basicity Using the Benzhydrylium Methodology

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Understanding the "direction" of spontaneous change in a chemical reaction is one of the most important fundamental goals in chemistry – i.e. is the left or right hand side of the following reversible reaction favoured at equilibrium?

$$R—X^{m+1} + Y^{n} \rightleftharpoons X^{m} + R—Y^{n+1} \qquad (1)$$

Here, R is an alkyl group, and X^m and Y^n are Lewis bases. The position of the equilibrium in this reaction is dictated by the relative Lewis basicities of X^m and Y^n towards carbon. Up to now, organic chemists have typically relied on related Brønsted basicity data to give a qualitative indication of which product(s) should be favoured at equilibrium, with the implicit assumption that if Y^n is a stronger Brønsted base than X^m (i.e. with R = H in equation 1), then it must also be a stronger Lewis base towards carbon. This qualitative indicator is useful when comparing within a series of closely related Lewis bases, but does not apply in general, especially if there is no structural relationship between the compounds under comparison.

Recently, the following relationship has been shown to apply for reactions of strong Lewis bases with benzhydrylium ions (Ar_2CH^+) in MeCN and CH_2Cl_2:

$$\log_{10} K = LA + LB \qquad (2)$$

where *K* is the equilibrium constant for the reaction (determined photometrically), *LA* is the Lewis acidity of the benzhydrylium ion, and *LB* is the Lewis basicity of the Lewis base.[1] Herein will be described a general NMR spectroscopic method that allows extension of the Lewis basicity scales beyond the frontiers accessible using the photometric technique, with emphasis on weak Lewis bases. Included in this range are phosphine oxides, *N*-oxides, amides, various anions (e.g. Br^-, I^-, TsO^-) and various aromatic heterocycles. Calculation of equilibrium constants for reactions of these weakly Lewis basic species is now possible using equation 2.

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Submitted Presentation 18

Novel DNA-templated Chemical Ligation

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Nucleic acid based diagnosis, drug discovery, therapeutics and study of biological systems are under intense research and development. Our aim is to develop kinetically rapid, enzyme-free method for ligation of DNA fragments in aqueous solution with the introduction of a previously unpublished DNA backbone (Figure 1. **B**). Ligation will be templated through Watson-Crick base-pairing, which offers selectivity and hastens the chemical reactions by bringing the reactive groups into close proximity.

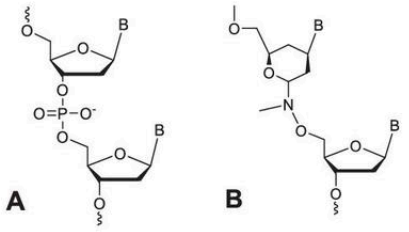

Figure 1. **A**. Native DNA with a phosphodiester group. **B**. Modified DNA with charge-free backbone.

The ligation method utilizes a glycosylation reaction where *N,O*-substituted hydroxylamines react with reducing sugars[1,2] (Figure 2.). The choice of sugar and pH contribute significantly to the reaction rate.

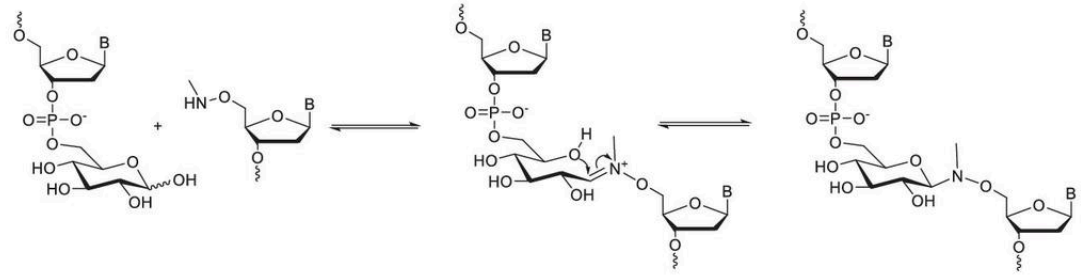

Figure 2. Enzyme-free chemical ligation.

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Aerobic C-H bond activation-functionalisation catalysis involving 'Pd-NO_x'

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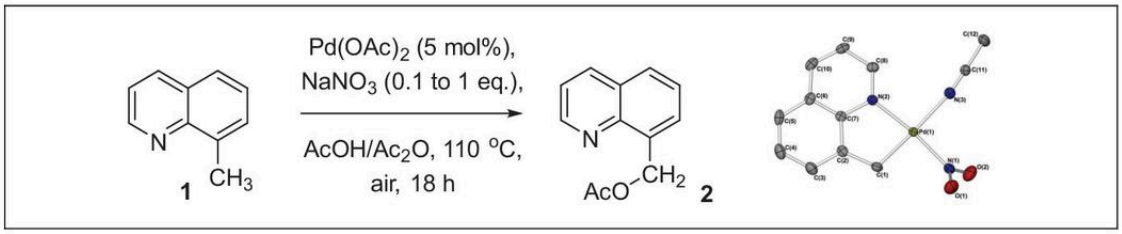
Over the past 15 years we have been interested in the reaction mechanisms[1] of Pd-mediated cross-coupling processes. The motivation for understanding a reaction mechanism is to gain key information that aids catalyst design, improves catalyst efficacy and expands substrate scope and process robustness. Historically, MNO_x salts have been used in Pd-mediated acetoxylation and nitration.[2] Tangentially, NO_2–linkage isomerisation is known in cyclopalladated complexes.[3] Of particular note is the finding that $NaNO_x$, in the presence of air (O_2), assists Pd-catalysed sp^3-C-H bond acetoxylation of suitable substrates. In this presentation I will explain the role played by 'NO_x' anions in aerobic C-H bond activation,[4] with evidence showing NO_x anion interactions at Pd^{II} during productive catalysis. Palladacyclic-NO_x complexes are competent catalysts for acetoxylation of 8-methylquinoline (**1**→**2**; see single crystal X-ray structure for exemplar Pd-NO_2 palladacycle).



The investigation shows that NO_x anions act as participating ligands at Pd^{II} in aerobic sp^3-C-H bond acetoxylation processes, in addition to redox processes. We believe that our findings may help inform other recent synthetic chemistry-catalysis developments,[5] including catalyst-controlled Wacker oxidation.[5a]

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Submitted Presentation 20

Stability of Cu(II) complexes with potential use in PET

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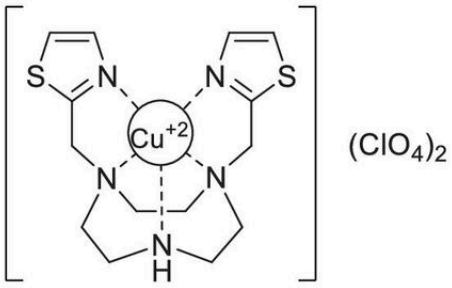
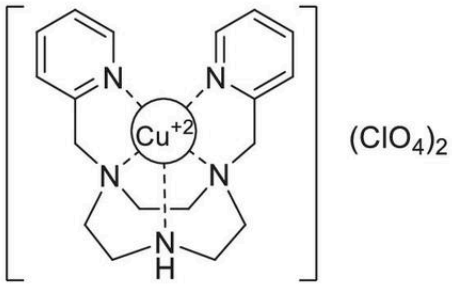
Copper (II) complexes derived from triazacyclononane (TACN), with potential use in molecular imaging techniques (PET) were prepared and characterized. A comparative kinetic study was performed of different copper release pathways in the organism: i) acid catalyzed dissociation, ii) transmetalation, or iii) bioreduction. Two structurally related systems: **Cuno2th** and **Cuno2py** (see below), were used in order to analyze how the physicochemical properties of each system may affect the values of the obtained rate constants and thus evaluate their kinetic inertness.



Cuno2th



Cuno2py

Both complexes showed to be very inert toward demetallation in acidic medium. Their protonation is not only conditioned by the basicity of the functional groups in the pendant arms, but also by the anions present in the medium.

The presence of ligands with affinity for copper(II) can lead to dissociation through a transmetallation reaction. For both complexes this takes place in two steps: spontaneous release of Cu(II) by partial dissociation, followed by coordination of free Cu(II) by the chelating agent.

Bioreductor agents with a suitable reduction potential can lead to labile Cu(I) complexes which undergo fast dissociation in physiological conditions.

Palladium Acetate/Trifluoroacetic Acid Catalytic System: Ligand Exchange and Catalytic Behaviour

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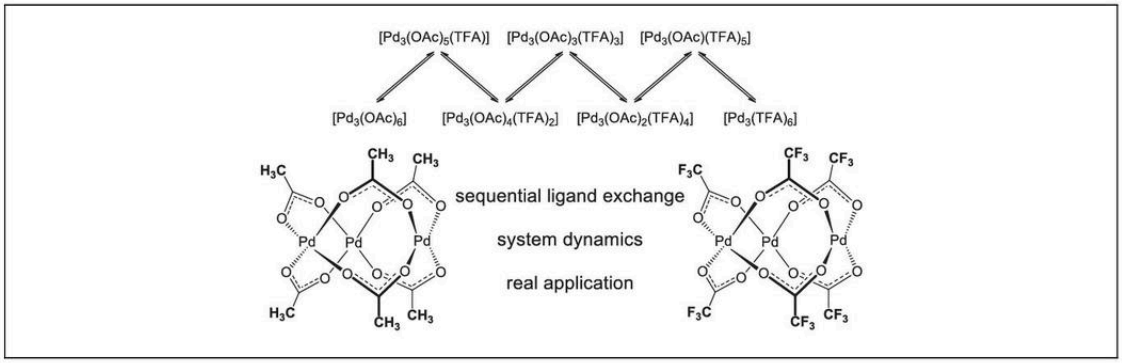
One of the very common catalytic systems for C–H functionalization of aromatic compounds is based on combination of palladium(II) acetate and trifluoroacetic acid.[1] The aim of our presentation is to show which species are formed in the catalytic mixture and describe their role in real reaction.
The palladium(II) acetate is known to dominantly occurs in trimeric cyclic form. Influence of additional trifluoroacetic acid to its dichloromethane solution was in detail studied by NMR techniques. The analysis of spectra shows sequential exchange of the acetate ligands for trifluoroacetate ones while the trimeric cyclic motive remains preserved. Furthermore, with the knowledge of structure of the precatalytic system, the mechanism of C–H activation of acetanilides was studied in detail.[2] We have shown that trinuclear species are involved in the reaction pathway.



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Submitted Presentation 22

2D NMR Spectra in <10 seconds for Reaction Monitoring

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Combining ASAP[1], EXACT (EXtended ACquisition Time)[2] and NUS (non-uniform sampling)[3] provides 2D NMR spectra in only a few seconds for reaction monitoring. The short (~30ms) 'ASAP' mixing period in EXACT ASAP HSQC[4] (Figure 1, left) replaces a long (~1s) relaxation delay, thus reducing experiment time from ~5 minutes to ~30 seconds, *but also introduces damaging NMR power demands* which are circumvented by EXACT 'burst-sampling' of the FID so that high power ^{13}C decoupling is switched off during Δ gaps in the FID. Iterative Soft Thresholding[5] reconstructs the missing datapoints in the spectrum (Figure 1, centre). The experiments can be further accelerated with NUS in the indirect ^{13}C dimension to access full 2D datasets in <10 seconds (Figure 1, right)

Volume integration of peaks in EXACT ASAP-HSQC spectra provide comparable quantitative information to those obtained by ^{1}H NMR spectroscopy (Figure 2).

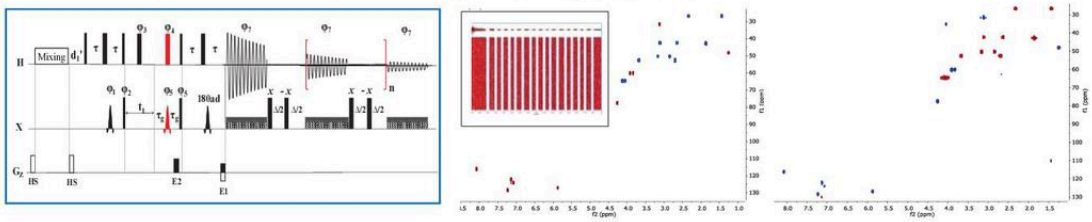

Figure 1 (left) EXACT ASAP HSQC sequence; (centre) EXACT ASAP HSQC spectrum (inset: FID) acquired in 36 seconds (right) 12.5% NUS EXACT ASAP HSQC spectrum acquired in 6 seconds

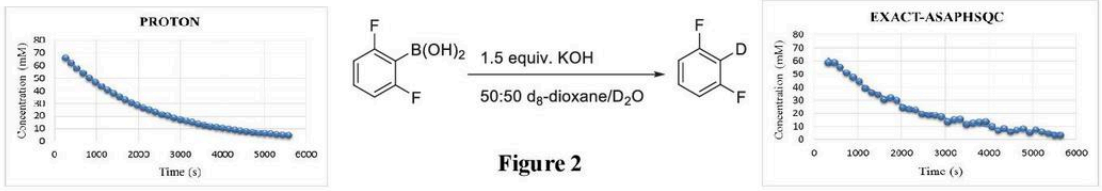

Figure 2

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Lithiation-Trapping of *N*-Boc Heterocycles: How Fast is Each Step?

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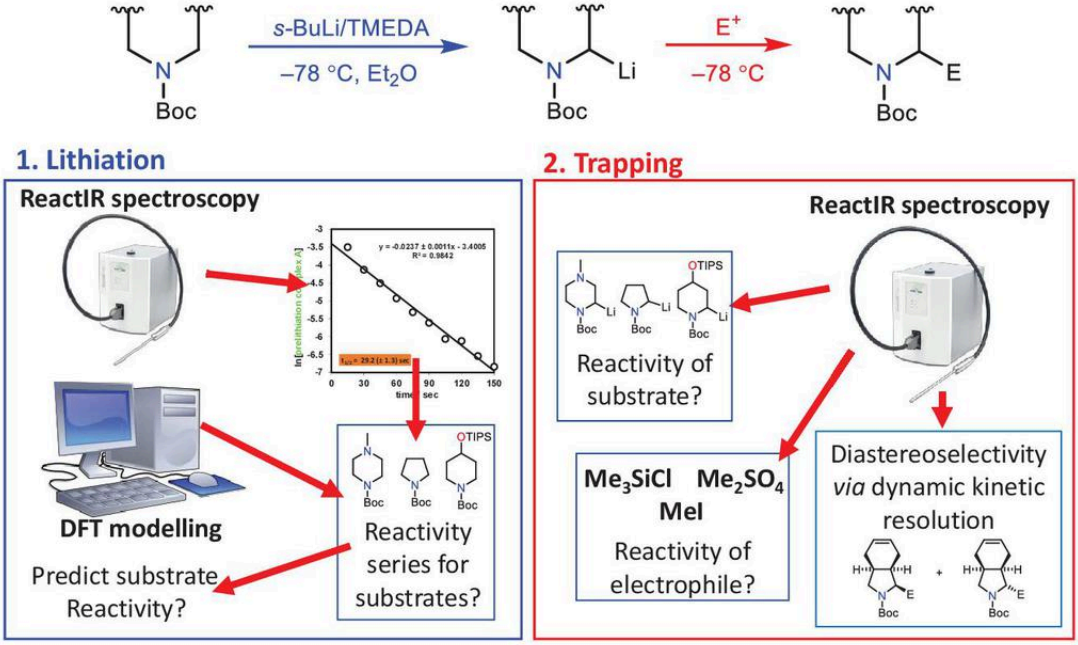
Introduction: Nitrogen heterocycles are important compounds, with 59% of US FDA approved small molecule drugs containing a *N*-heterocycle.[1] Beak's *N*-Boc α-lithiation protocol[2,3] has been widely used to synthesise 2-substituted *N*-Boc heterocycles, including the synthesis of Telaprevir (Hepatitis C drug) on a multi-kilogram scale.[4]

Project Outline: Our research combines organic synthesis, *in situ* IR (ReactIR) spectroscopy and computational DFT modelling to probe and obtain mechanistic information about both the α-lithiation and trapping steps. This will enable more efficient optimization of reactions conditions for the lithiation-trapping of novel substrates. This talk will present reactivity series obtained for both the lithiation and trapping reactions, constructed using ReactIR kinetic data. These reactivity series provide interesting trends of reactivity for electrophiles and substrates, which can be used to find optimal conditions and rationalize the products formed in the reaction.



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Submitted Presentation 24

Catalytic Reaction of Organometallic Ruthenium Complexes

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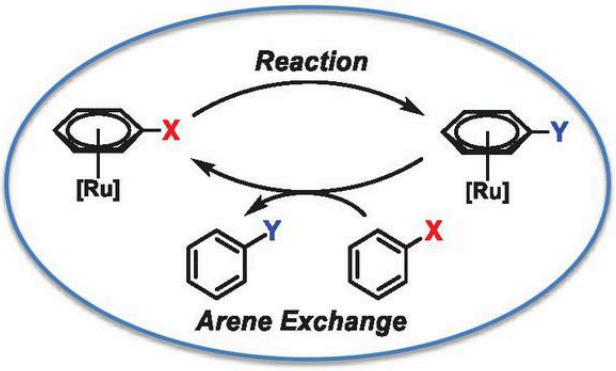
η^6-Coordination of aromatic molecules to transition metals alters the reactivity of the bound arene. Typically this η^6-coordination will increase the electrophilicity of the arene and stabilise negatively charged reaction intermediates. Since beginning our independent research group in 2014, we have been studying reactions of $[(\eta^6\text{-arene})RuCp]^+$ complexes. We will present successful S_NAr,[1] C–H activation[2] and trifluoromethylation[3] reactions based on the mechanism shown below.



Reaction

- ✓ C–H Activation
- ✓ Trifluoromethylation
- ✓ S_NAr

While η^6-coordination gives access to exciting new reaction of arenes, the requirement for stoichiometric metal is a drawback. To address this issue, our research also focusses on reactions that are catalytic in the activating metal fragment. Following reaction of η^6-bound arenes, exchange between the bound product and starting material will lead to catalytic systems (Figure). To achieve this, we need an understanding of the mechanism of arene exchange. We have recently reported a catalytic S_NAr process[1] and have shown that C–H activation[2] and trifluoromethylation[3] can proceed with recovery of the activating Ru fragment. This research has great potential to allow late-stage modification of arenes for application in drug discovery, as well as developing fundamental understanding of organometallic Ru complexes.

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Using ionic liquids as solvents for organic processes: Which one do you choose?

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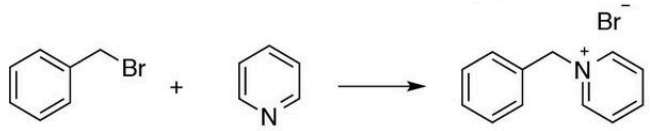
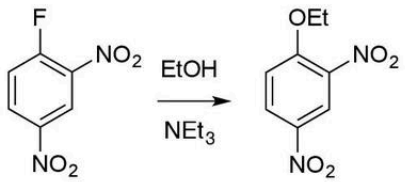
Ionic liquids (salts with melting points below 100 °C) can be considered as 'designer solvents',[1] as through changing either the cation and/or the anion, both the physical properties of the solvent[2] and the reaction outcome can be altered.[2] Because of this, there is the potential for components of an ionic liquid solvent to be rationally designed, leading to solvent controlled reactivity. To be effective, such rational design requires an understanding of the microscopic interactions responsible for the ionic liquid effects; the components of the ionic liquid can be varied to maximise these interactions. This concept has been investigated with two well-described organic reactions; a bimolecular nucleophilic substitution (S_N2, Scheme 1) process[3,4,5,6] and a nucleophilic aromatic substitution (S_NAr, Scheme 2) process.[7,8]



Scheme 1. The Menschutkin reaction between benzyl bromide and pyridine.



Scheme 2. The ethanolysis reaction of fluorodinitrobenzene.

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Submitted Presentation 26

Selective Fluorination Strategies

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The use of fluorinated systems in drug discovery programmes continues to grow and, at present, *ca.* 20-30% of new pharmaceutical and agrochemical systems that enter the market bear fluorine atoms. A number of fluorinating reagents have been developed recently for discovery scale reactions including DAST, Selectfluor, Phenofluor and NFSI, but for large scale synthesis of fluorinated APIs, in general, hydrogen fluoride, potassium fluoride or fluorine gas are the only fluorinating agents that are sufficiently inexpensive for process scale.

The use of fluorine gas for manufacturing APIs has not been developed to any extent despite the low cost, similar infrastructure to handling HF required and ready availability (fluorine gas is less toxic than chlorine gas and used widely on multi-tonne scale in the car, nuclear and semi-conductor industries). The Durham Fluorine group has developed extensive methodology for the use of fluorine gas as a reagent for the selective fluorination of 1,3-diketones, 1,3-ketoesters and 1,3-diesters using either batch or continuous flow fluorination techniques

Recently, as part of the European Union Innovative Medicine Initiative Network (115360, Chemical manufacturing methods for the 21st century pharmaceutical industries, CHEM21), along with industrial partners (Sanofi-Aventis, MEPI, GSK), we have developed effective process chemistry for two APIs using either flow fluorination (Flucytosine[1]) or a combined fluorination-biocatalytic approach (Fluoro-lactams[2]) and these projects will be described.

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Counter-Intuitive Nucleophilicities of Peroxide Anions

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Organic peroxide anions are powerful nucleophiles that have applications in industrial bleaching processes as well as in various lab-scale reactions.[1]

We have quantified the nucleophilic reactivities of various organic peroxide anions by analyzing the kinetics of their reactions with a series of benzhydrylium ions (Ar_2CH^+) (Fig. 1). We found peroxycarboxylates (RCO_3^-) to be stronger nucleophiles than anions AlkylOO$^-$ generated from alkyl hydroperoxides, which contrasts expectations based on the order of acidities, which is pK_a(AlkylOOH) > pK_a(RCO_3H).

The linear correlations of the second-order rate constants (log k_2) for the reactions of Ar_2CH^+ with peroxide anions with the electrophilicities E of Ar_2CH^+ provided the nucleophilicity parameters (N, s_N) of peroxide anions according to equation (1).[2,3] It was then tested whether the thus calibrated nucleophilicities of peroxide anions also hold for predicting their reactivities in Weitz-Scheffer epoxidations.

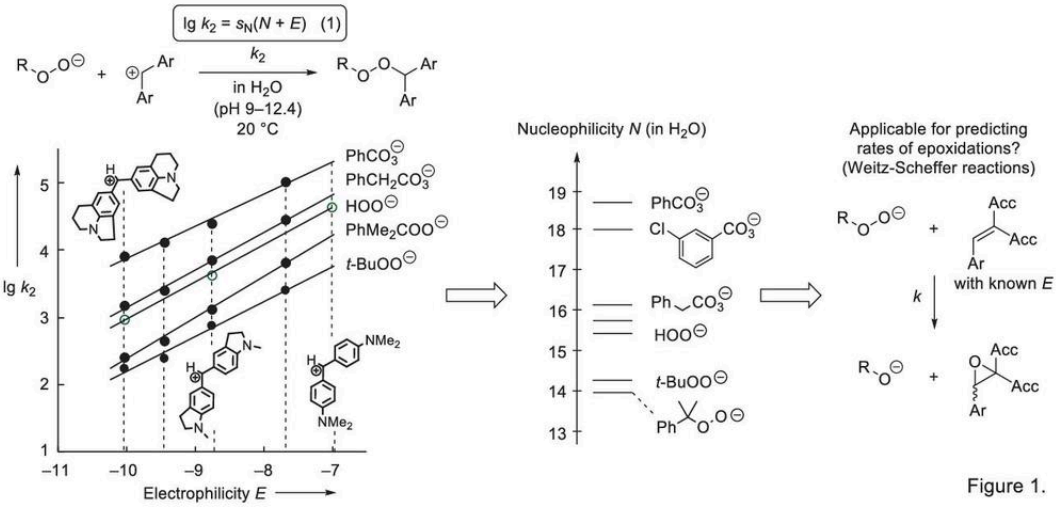

Figure 1.

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Submitted Presentation 28

Computational Study of Substituent Effects on Gas-Phase Stabilities of Phenylaminomethyl Cations

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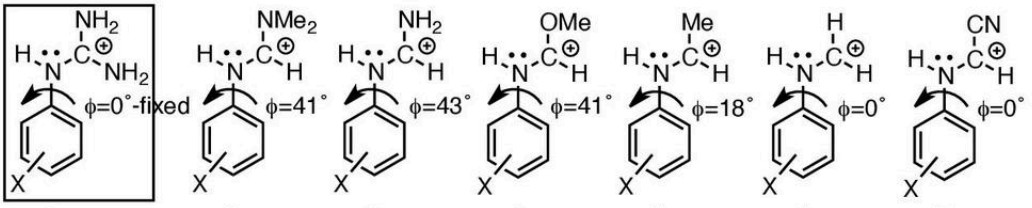
Substituent effects on the stabilities of cations of aromatic compounds are well described by the Yukawa-Tsuno equation (1): $-\Delta E_X = \rho(\sigma^0 + r^+\Delta\bar{\sigma}_R^+)$. The normal substituent constant (σ^0) measures the fundamental electron-donating or electron-withdrawing capability of all ring substituents. The resonance substituent constant ($\Delta\bar{\sigma}_R^+ \equiv \sigma^+ - \sigma^0$) measures the capability of through-resonance for *para* -R groups. The resultant r^+ value reveals the degree of through-resonance effect in a given system. The set of σ^0 has been determined by gas-phase stabilities of α,α-dimethylbenzyl cations in which the cationic p-orbital is orthogonally fixed to the benzene π-electron system. However, we recently found that the substituent effects on the stabilities of planarized N-phenylguanidinium ions (**1**) gave a negative r^+ value (-0.14), although the correlation is inferior due to a steric factor.[1] This shows that the present σ^0 reference system includes some through-resonance effect.

In the course of exploration of the optimum σ^0 reference system, we examined here the substituent effects on gas-phase stabilities of phenylaminomethyl cations (**2**-**7**). These cations were given by the replacement of the bulky NH_2 group in **1** to H and the replacement of another NH_2 group to various groups keeping the phenylaminomethyl skeleton. Relative gas-phase stabilities of the ring-substituted cations were determined computationally using isodesmic reactions at the B3LYP/6-311+G(2d,p) level of theory. Obtained substituent effects were analyzed by eq. 1.

Unexpectedly substantial through-resonance effects (r^+ values) were observed in **5**-**7**, although the corresponding canonical form cannot be drawn. The detailed mechanism of the through-resonance effects in these cations were investigated using NBO analysis.



1 r^+=-0.14 **2** r^+=-0.10 **3** r^+=-0.05 **4** r^+=0.02 **5** r^+=0.22 **6** r^+=0.36 **7** r^+=0.58

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Aromatic C-Nitroso Compounds and their Dimers: A Model for Physical Organic Chemistry of Reactions in Crystalline Molecular Solids

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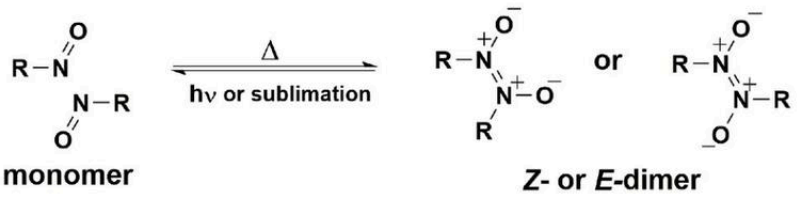
Dimerization of aromatic C-nitroso compounds and dissociation of the corresponding azodioxy dimers are represented as a model for studying the thermal organic solid-state reaction mechanisms. Reactivity of the model molecules in solid state is examined under the different topotactic conditions, especially as a function of disordering, surface defects, and phase transformations. The dependence of the reaction rate on the distance between reacting molecules (topochemical effect) is discussed in more detail. The investigation is also extended to the reactions in the condensed one- and two-dimensional molecular arrangements.



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Submitted Presentation 30

Catalyst choice aided by mechanistic understanding on AZD9496 Heck stage

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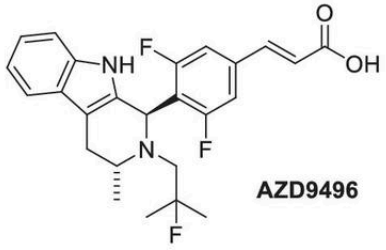
AZD9496 is an orally available SERD currently in development at AstraZeneca. The multi-kilo route to AZD9496 utilises a palladium-catalyzed Heck reaction to form the olefin in the functionalized *trans*-cinnamic acid side chain of the active pharmaceutical ingredient (API). A combination of $Pd_2(dba)_3$ and $P^tBu_3.HBF_4$ in iPrOAc provided this fragment in good yield and purity, however ahead of future scale up and further route development the opportunity to reduce the high catalyst loading and further improve process efficiency led to an exploration of alternative catalysts.



AZD9496

A combination of high throughput screening, design of experiments (DoE) and kinetics was used to optimise and assess the suitability of a number of potential new catalyst systems. An amalgamation of reaction progress kinetic analysis (RPKA)[1] with parallel experimentation helped to aid selection of a new catalyst and solvent combination quickly and efficiently by using same excess experiments to assess catalyst stability. The best set of conditions exhibited an interesting, linear reaction profile providing a trigger for further mechanistic understanding in order to ensure the new conditions would be scalable. Further study showed that the concentration of starting materials had no effect on the rate of reaction and that an inactive catalyst complex can be formed during the initial stages of the reaction.

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Towards the Design of New Anti-Parasitic Drug Candidates: Some Studies of the Reaction of Aromatic Nitro-Compounds with Anionic and Amino Nucleophiles.

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Several promising drug targets and lead molecules are being studied with the goal of developing new antiparasitic agents. Among the compounds currently been developed are the dinitroanilines which are widely used in herbicide formulations [1-3]. Dinitroanilines, trifluralin **1** and oryzalin **2** are known to bind with high affinity to plant tubulin, inhibit tubulin assembly, and disrupt the microtubules (MTs) of plants [4,5]. There is current interest in the mode of interaction of dinitroaniline-based antiparasitic drug candidates with cellular thiols. This interaction is believed to be important to the inhibitory activity of these drugs against protozoa parasites.

In the present investigation, we have synthesised a series of 2- and 4-substituted dinitrodiphenylamines **3,** diphenylethers **4,** diphenylthioethers **5** (with 4-substituents such as H, CH_3, SO_2R, COR, CO_2R, CN, NO_2, CF_3) and X-phenyl-4-nitrobenzofurazan ether **6**. The products from the reactions of **4-6** with amines were independently prepared and characterised. It is well established [6] that nitroactivated benzenes bearing suitable leaving group react with nucleophiles via a two step S_NAr mechanism which involves the formation of σ-adduct or the displacement of the leaving group via a zwitterionic intermediate.

A detailed kinetic, spectroscopic and quantitative structure reactivity investigation of the nucleophilic reactions of the **4-6** with amine and bioactive nucleophiles has been carried out. The knowledge of the intrinsic reactivities of these electrophilic antiparasitic drug candidates towards amine and bioavailable thiols is related to the inhibitory activities of the potential drugs against protozoa parasites. Thus, the S_NAr reactions of these electropliles **4**-**6** with amines or thiols serves as model reactions to identify the structural requirements in the design new anti-parasitic nitro-arene drug candidates.

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Submitted Presentation 32

The Effects of Electronics and Strain on the Acidity and Reactivity of a Range of Systems

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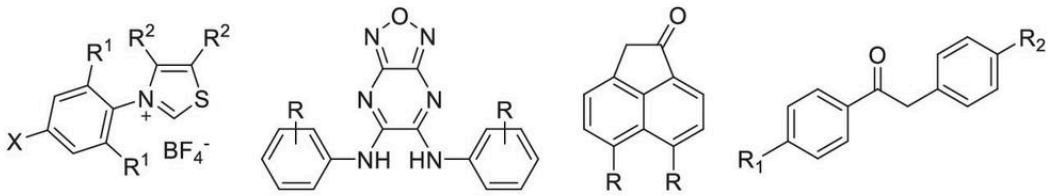
The reactivity of molecules can be significantly affected by electronic effects of substituents[1] and strained geometries.[2] This work examines, and quantifies where possible, how such effects alter the reactivity of a range of systems including thiazolium salts **1**, furazano[3,4-b]pyrazines **2,** acenaphthenones **3** and 1,2-diphenylethanones **4**.



1 **2** **3** **4**

In order to examine the properties of the series of compounds examined in this study, the pK_a values of the series **1**, **2**, **3** and **4** (along with the pK_a value of the second deprotonation of series **2**) in DMSO have been determined using the bracketing indicator method in which the equilibrium position of a series of acid-base titrations were followed using UV-Visible spectroscopy.[3] Correlations have then been made with the structures of the compounds, indicating the influence of structure and substituents on acidity.

The reactivity of each series of compounds is being investigated and compared with the corresponding pK_a values in DMSO in order to draw information regarding the electronic and steric properties of each series. The pK_a values of series **1** has been correlated with the electronic properties of substituents and the ability of the corresponding carbene to catalyse a Stetter reaction, the pK_a values of series **2** has been correlated with its biological activity and the pK_a values of series **3** and **4** have been correlated with the rates of deuteration, electronic and steric factors for each compound. These correlations have been examined in order to produce a series of rationales which provide insight towards the effects of electronics and strain on the reactivity of the representative systems **1**, **2**, **3** and **4**.

List of Poster Presentations

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University of Sheffield, UK

PO2 ***"The Interaction of Enzymes with Laundry Additives in HDL"***
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Durham University, UK

PO3 ***"Reactivity of Catalytic Zn Complexes at Bilayer Interfaces"***
Layla Alajmee
University of Sheffield, UK

PO4 ***"Influence of substituents on the inversion of nitrogen atom in the o-(N-dialkyl)aminomethylphenols."***
Oleg Allaberdiev
Ukraine State Scientific Research Institute for Plastics, Ukraine

PO5 ***"Catalysis by Cages"***
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University of Sheffield, UK

PO6 ***"Out of the blue: finding an old pigment in a 'new' book"***
Andrew Beeby
Durham University, UK

PO7 ***"The Dynamic Covalent Rearrangements of the Barbaralyl Cation"***
Aisha Bismillah
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PO8 ***"Deciphering the Mechanistic Complexity of Pd–Catalyzed Aryl Cyanation: 'Excess Water' is the Trigger for Heterogeneous Catalysis"***
Joshua Bray
University of York, UK

PO9 ***"Intelligent Chemical Synthesis – an Informed Approach using Robotics and Mechanistic Investigations"***
Geroge Clarke
University of York, UK

PO10 ***"The Impact of the Intrinsic Barrier on Relative Reactivities of Leaving Groups"***
Bernard Denegri
University of Zagreb, Croatia

PO11 ***"Approaching DFT accuracy for 3JCH calculation using empirical equations"***
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PO12 ***"Using a Dearomatising Intramolecular Acylation Strategy to Develop a 'Reverse-Biomimetic' Synthesis of Arogenate and its Analogues"***
Louise Eagling
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PO13 ***"Ionic Liquids like extractant of RS-propranolol in liquid-liquid extractions"***
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Universidad del Desarrollo, Chile

PO14 ***"Benzoylguanidinium Cations as the Anion Sensing Groups. UV/Vis and Theoretical Study"***
Zoran Glasovac
Ruđer Bošković Institute, Croatia

PO15 ***"Stereocontrolled Synthesis of Resveratrol Dimers and Tetramers via Persistent Radicals"***
Markus Griesser
University of Ottawa, Canada

PO16 ***"The effect of an ionic liquid solvent on two SNAr reactions"***
Rebecca Hawker
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PO17 ***"Synthesis of fluorinated pyrroles using electrophilic N-F reagents"***
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PO18 ***"Lithiation-Trapping of Oxygen-Containing Heterocylces"***
Kevin Kasten
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PO19 ***"The solvolysis mechanism of simple tertiary substrates in 50% TFE"***
Dian Li
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PO20 ***"Development of a Technology for the Discovery of Protein Carbamates"***
Victoria Linthwaite
Durham University, UK

PO21 ***"Fluorinated dicarbonyl systems: chemical Swiss Army knives"***
Etienne Lisse
Durham University, UK

PO22 ***"Revisiting the Mechanism(s) of GTP Hydrolysis in Small GTPases"***
Malin Lüking
Uppsala University, Sweden

PO23 ***"Solvolytic Reactivity of Organic Phosphates"***
Mirela Matic
University of Zagreb, Croatia

PO24 ***"Towards understanding microscopic interactions in ionic liquidsand their effects on SN2 processes"***
Karin McHale
University of New South Wales, Australia

PO25 ***"Computational Study of Substituent Effects on Gas-Phase Stabilities of 2-Phenylethyl Anions"***
Kazuhide Nakata
Hosei University, Japan

PO26 ***"Proton transfer reactions of triazolyl acyl anions: determination of Breslow intermediate pKa values"***
Peter Quinn
Durham University, UK

PO27 ***"Ortho-Substitued Arylsilanes in Oxidative Gold Catalysis"***
Matthew Robinson
University of Edinburgh, UK

PO28 ***"Amplification of Emission in Donor–Acceptor Aggregates"***
Ketaki Samanta
Durham University, UK

PO29 ***"Effects of Binary Solvent Mixtures on Rates of Reaction"***
James Scotson
University of Sheffield, UK

PO30 ***"Molecular modeling of radical SAM enzyme lysine 2,3-aminomutase"***
Damiano Spadoni
University of Nottingham, UK

PO31 ***"New Blatter-type Radicals from a Bench-stable Carbene"***
David Tucker
Durham University, UK

PO32 ***"Towards Redox Active Warped Nanographenes"***
Andrew Turley
Durham University, UK

PO33 ***"Site-selective C-C bond formation in unprotected monosaccharides using photoredox catalysis"***
Steven Wan
University of Groningen, The Netherlands

PO34 ***"A systematic structural series to elucidate the inner workings of thermally activated delayed fluorescence"***
Jonathan Ward
Durham University, UK

PO35 ***"Combining Supramolecular Solvation and 'No Barrier Theory' to Predict Reactivity"***
Matthew Watson
University of Sheffield, UK

PO36 ***"On the Mechanism of Electrophilic Fluorination of Enol Esters"***
Susanna Wood
University of Strathclyde, UK

PO37 ***"Towards an Organocatalytic Route for the d1-Deuteration of Aldehydes"***
Jiayun Zhu
Durham University, UK

The Effect of Multiple Hydrogen Bonding on Reactivity

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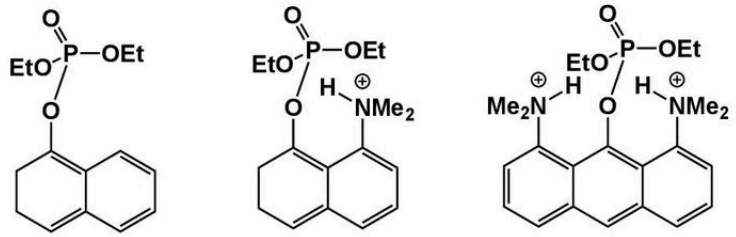
Enzymes catalyse reactions by stabilising the transition state relative to the uncatalyzed process. Hydrogen bonds have considerable potential to achieve this, and it is often proposed that multiple hydrogen bonds interactions are used by eznymes,[1] such as in the oxyanion hole.[2] However, achieving the same kinds of rate accelerations as enzymes in artificial systems is still a challenging issue. One of the most effective systems has been reported by Kirby and Asaad, who found that the hydrolysis of phosphate triester **2** is catalysed by a strong intramolecular hydrogen bond, and reacts 10^6 fold faster than triester **1**.[3]



1 **2** **3**

Our aim is to investigate the effect of multiple hydrogen bonds in this type of system. We have designed an initial model **3** with two hydrogen bond donors acting on the leaving group to provide insight into whether the hydrogen bonding is the key for catalysis or if general acid catalysis is essential. We will report our progress in this and related systems.

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Poster Presentation 2

The Interaction of Enzymes with Laundry Additives in HDL

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The study of enzyme inactivation in liquid laundry formulations (HDL) has long been hindered by the vast number of freely interacting components, high surfactant concentrations and highly viscous and coloured nature of solutions. It is believed that anionic surfactant, alongside chelant and proteases, is the greatest sources of strain on enzyme stability, but its mechanism of denaturation is poorly understood. The current industry standard for monitoring loss of enzyme activity over time involves lengthy storage experiments and activity assays. These offer little insight into the interactions and structural changes experienced by the enzymes, and the root causes of instability.

This work presents an evaluation of the capability of a range of analytical technologies in providing further insight into the processes which cause enzyme inactivation in HDL. This is with an aim to detect early indicators of instability and produce predictive models of enzyme inactivation. Techniques such as circular dichroism, differential scanning fluorimetery, differential scanning calorimetry, isothermal titration calorimetry, microscale thermophoresis and fast pulse proteolysis[2] were screened for their capabilities in accessing enzyme Tm values in HDL formulations. Sample complexity, alongside the highly viscous and UV-active nature of the anionic surfactant LAS, present at up to 20% w/v in HDL, posed the greatest challenge in analysing these samples.

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Reactivity of Catalytic Zn Complexes at Bilayer Interfaces

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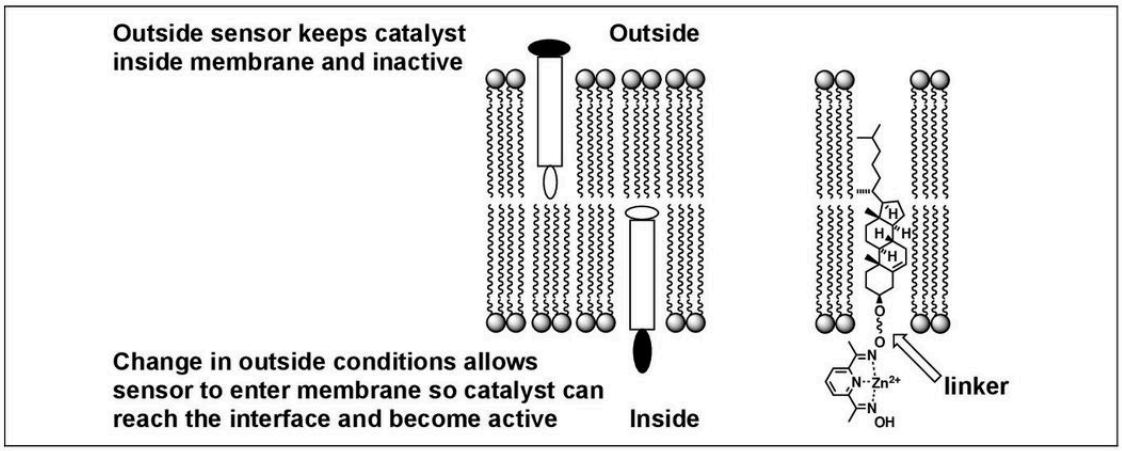
(ljalajmee1@sheffield.ac.uk)

Bilayer membranes allow the chemistry inside cells to be separated from the exterior environment. Changes in the exterior conditions are transmitted to the interior through a number of mechanisms, such as opening and closing pores or changing the conformation of membrane spanning proteins, so that the cell can respond.[1] We are interested in creating supramolecular systems where the presence of new molecules outside a cell is transmitted to the inside without transferring the material itself. Recently, we have reported how to achieve this using a carefully constructed transducer molecule can be used to control the activity of a catalytic Zn complex:[2]



To improve the system, we need to make the Zn complex more effective and to optimise the conditions under which it operates. Here we investigate how the catalytic efficiency depends on how the Zn complex is linked to a membrane anchor. We also compare how the activity at the interface affects the properties of the complex relative to solution.

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Poster Presentation 4

Influence of substituents on the inversion of nitrogen atom in the o-(N-dialkyl)aminomethylphenols.

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The internal dynamics of organic compounds(rotation,inversion) has a significant effect on the thermodynamic, electrical,optical,chemical properties of organic compounds, it is of particularly important for biochemical processes - understanding of their mechanisms of action, and the creation of new biologically active substances.

The equilibrium geometry of p-substituted o-(N-dialkyl)aminomethylphenols, $XC_6H_5CH_2Y$ (X=p-OCH_3, CH_3, H, F, Cl, Br, $COCH_3$,$COOCH_3$, CHO, CN and NO_2, Y=*o*-N $(C_2H_5)_2$, o-DEAMPH and $–N(CH_3)_2$ and changes in the energy and structural parameters due to the internal rotation and the inversion of the nitrogen atom in the amino fragment were calculated by the density functional theory (DFT). The frequencies of torsional and inversion transitions were determined by the B3LYP 6-311+ G (d,p) level of theory. Computational analysis showed the influence a steric and electrical effects on the nitrogen inversion in the aminomethylphenols. The decrease the volume of substituents on the nitrogen atom, i.e. in Y= -$N(CH3)_2$, the nitrogen inversion barrier decreases. The inversion barriers, E_{inv} of the *o*-DEAMPH are linearly correlated with substituent constants, σ_p^- (R^2=0.9902). Pyramidal the nitrogen inversion hindered by an intramolecular hydrogen bond formation in the *o*-DEAMPH. The effect strength of intramolecular H-bond on the nitrogen inversion also was established. The linear correlation was observed between the nitrogen inversion, E_{inv} values and the hydrogen bond enthalpy of formation (experimental NMR data), -ΔH: E_{inv} =-4.4027+1.1042 -ΔH (R^2 =0.9849). Inclusion of substituents containing the carbonyl moiety ($COCH_3$, $COOCH_3$ and OCH) in the correlation for the o-DEAMPH series results in large deviations of these substituents from the correlation lines and a considerable deterioration in goodness of fit. The nitrogen inversion barrier these molecules increases in the order: $COCH_3$<$COOCH_3$<COH. The influence of the carbonyl substituents on the E_{inv} of the *o*-DEAMPH is analyzed. The investigation of nitrogen inversion dynamics provides useful information about the configuration of nitrogen atom in *o*-DEAMPH. It is found that the linear relationship between the nitrogen inversion and the pyramidality of the nitrogen atom (R^2=0.9816). The interest has attached also to the correlation between the E_{inv} values and the total energy density at the bond critical point of the proton-acceptor (H-N) distance, ρ^{cp} evaluated within the quantum theory atoms in molecules: E_{inv} =2,2722+198.8390ρ^{cp} (R^2=0.9912). which can be used for estimation the nitrogen inversion in compounds containing intramolecular H-bond.

Catalysis by Cages

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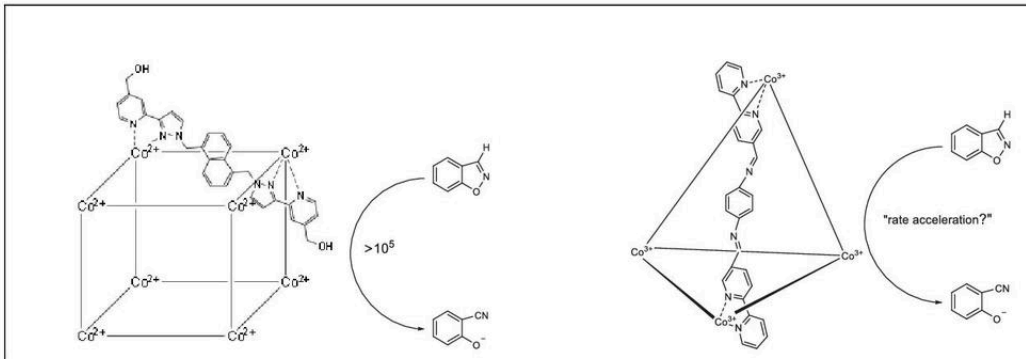
Cage complexes, formed by the self assembly of ligands around metal ions, can show substantial catalytic properties.[1] Typically, this involves binding substrates in a cavity where their conformation and chemical potential is modified. Recently, it was reported that a cubic cage showed substantial activity, but through a mode of action that is quite different. Here, solvation effects and proximity appear to be the major factors, offering the prospect of efficiently catalysing bimolecular reactions in a new way.[2] In this work, we explore whether these features are unique to this cubic cage, or whether the same activity can be designed into other cages.



Scheme1. The catalytic reaction in cubic cage(left) and tetrahedral cage(right).

We designed a self-assembled tetrahedral structure $[Co(III)_4L_6]^{12+}$ that incorporates twelve bipyridyl ligands with four metal ions via an assembly followed by oxidation protocol using cobalt(II). Cobalt is was chosen for this purpose because although Co(II) is labile, it can be readily oxidized to substitutionally inert Co(III) without alteration of the coordination geometry to make a more stable final complex. The cage structure shares key features with the cubic cage structure, and we will report whether it behaves similarly.

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Poster Presentation 6

Out of the blue: finding an old pigment in a 'new' book.

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Egyptian blue was probably the first man-made chemical, produced by the ancient Egyptians ca. 3000BC. This blue ceramic is made by heating lime, sand and copper in a very hot fire, and the technology to prepare this material was believed to be lost with the Egyptian civilization. There is limited evidence of some production of the pigment in southern Italy in ca. 75AD, and Davy reported its presence in some ancient Italian wall painings.[1] Whilst examining a series of medieval manuscripts produced in Canterbury between 950 and 1200 AD we discovered a small number of texts that contain a mixture of lapis lazuli mixed with a significant fraction of Egyptian blue, identified by its characteristic fluorescence at ca. 900 nm, and its extraordinarily long fluorescence lifetime, τ_f =100 μs. The discovery of this pigment in the manuscripts is exceptionally rare, prior to our investigation only three examples of this pigment had been noted, and there is no evidence that the pigment has been produced within Britain or Europe in the 10th century.

We suggest that at some point during the trade of the lapis lazuli form Afghanistan to Britain, via the Silk route and Europe there has been an adventitious dilution of the precious pigment with a recycled ancient Egyptian artifact.

1 Sir Humphry Davy "Some experiments and observations on the colours used in painting by the ancients," *Philosophical Transactions of the Royal Society of London*, (1815) **105** 97–124

The Dynamic Covalent Rearrangements of the Barbaralyl Cation

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Shapeshifting molecules[1], in which low-energy rearrangements bring about the rapid interconversion of distinct regioisomers, have the potential to address challenges in binding and detecting specific ions, complex small molecules and macromolecules. The shapeshifting 9-barbaralyl cation exists as mixture of 362,800 degenerate forms, interconverting rapidly through dynamic covalent rearrangements at temperatures as low as –135 °C. It has been reported[2] recently that gold-catalysed isomerisation of simple alkynyl cycloheptatrienes to indene products first passes through a fleeting barbaralyl cation intermediate that can be observed by NMR isotopic labelling experiments. Using gold catalysis, we have targeted stabilised, shapeshifting barbaralyl cations. Herein we report (**Figure 1**) synthetic and spectroscopic investigations of di-substituted barbaralols (e.g. **1**). Low temperature NMR spectroscopic investigations are performed after the addition of acid to form **2**. We will also present preliminary syntheses of highly substituted alkynyl cyclo-heptatrienes, which can give access to highly substituted barbaralols bearing several stabilising groups, which also have the potential to form stabilised barbaralyl cations.

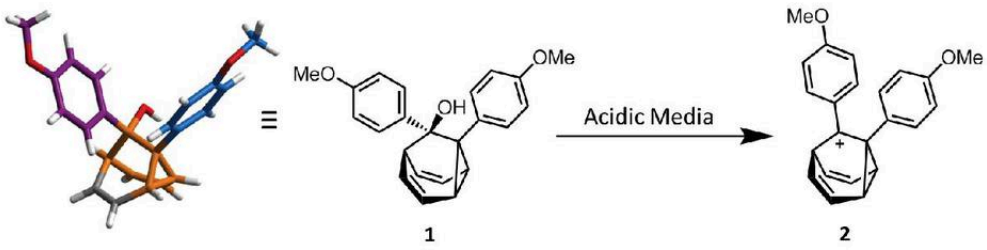

Figure 2. Dehydration of (±)1,9-bis(4-methoxyphenyl)tricyclo[3.3.1.$0^{2,8}$]nona-3,6-dien-9-ol (**1**) in acidic media produces a fluxional cation (**2**).

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Poster Presentation 8

Deciphering the Mechanistic Complexity of Pd–Catalyzed Aryl Cyanation: 'Excess Water' is the Trigger for Heterogeneous Catalysis

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Pd-catalyzed cyanation of aryl/heteroaryl halides is among the most commonly used synthetic methods for the preparation of aromatic nitriles.[1] Despite this, the precise reaction mechanisms under catalytic conditions remain poorly understood.

A kinetic study on the catalytic behavior of Pd species, deriving from exemplar Pd^{II} precatalysts, in aryl cyanation reactions is detailed in this poster. The use of *in situ* infra-red spectroscopy *in operando* mode facilitated quantitative analysis of the rates of appropriate reactions, and the unprecedented, qualitative study of intermediate, solubilized $K_4[Fe(CN)_6]$ concentrations throughout the course of aryl cyanation reactions at Pd. The study led to the surprising finding that the presence of water triggers the reaction from being homogeneous to heterogeneous in terms of catalyst behavior.[2]

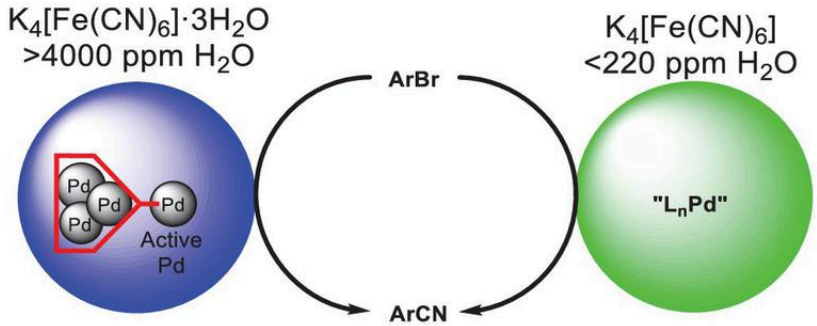

Figure 1: Pd-catalysed arylcyanation reactions operate in a heterogenous catalytic manifold in the presence of excess water (>4000 ppm H_2O) but under anhydrous conditions (<220 ppm H_2O) undergo homogeneous catalysis.

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Intelligent Chemical Synthesis – an Informed Approach using Robotics and Mechanistic Investigations

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Chemical synthesis is a very important area which underpins scientific research, allowing novel compounds to be designed and synthesised for agrochemical and pharmaceutical applications. The synthesis of a given target molecule is often a major bottleneck in the development work. High-throughput robotics offers a solution to these problems by speeding up the reaction discovery and optimisation of a given reaction.

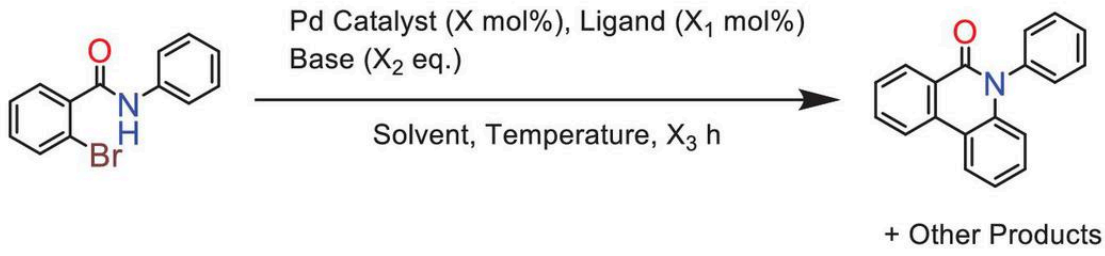

Figure 1. A complex palladium-catalysed reaction, where the distribution of products is dependent on reaction conditions.

An automated approach to optimising chemical reactions using a Chemspeed robotics platform has been developed, with a focus on understanding a complex palladium-catalysed C-H bond functionalisation reaction. The complex reaction (Figure 1) involves one substrate forming over 13 different products (some of which are novel) in one reaction system. The products synthesised are similar to molecules with already known pharmaceutical activities. Reaction screening of solvents and temperatures has been carried out and the LC-MS data obtained analysed by statistical pattern recognition methods such as principal component analysis.

Poster Presentation 10

The Impact of the Intrinsic Barrier on Relative Reactivities of Leaving Groups

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A comprehensive nucleofugality scale, based on both LFER equation (1) and the set of reference benzhydryl electrofuges, has been established.[1–3] The nucleofugality of a particular leaving group is determined with two parameters: N_f (the negative intercept on the abscissa of the log k vs. E_f correlation plot) and s_f (the slope of the correlation plot). Whereas N_f values represent the approximate solvolytic reactivity of dianisylmethyl derivatives in a given solvent (in the logarithmic scale), the reaction constant s_f indicates the variation in relative reactivities of leaving groups with electrofugality (E_f), i.e. the reactivity of an electrofuge in a substrate.

$$\log k\ (25\ ^\circ\mathrm{C}) = s_f\,(E_f + N_f) \qquad (1)$$

Comparison of s_f values of phenolate leaving groups with s_f of carboxylates and carbonates with similar reactivities reveals the noticeably higher values for the former which is manifested with intersecting the corresponding log k vs. E_f correlation lines and inversion of relative reactivities of leaving groups in the region of kinetic measurements.[4] The inversion of relative reactivities with a series of benzhydryl electrofuges clearly demonstrates that nucleofugalities of leaving groups are not determined only with stabilities of free anions but also with a differential impact of the intrinsic barrier, caused by different types of stabilizing effects that are operative in diverse leaving groups during heterolysis.

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Approaching DFT accuracy for $^3J_{CH}$ calculation using empirical equations

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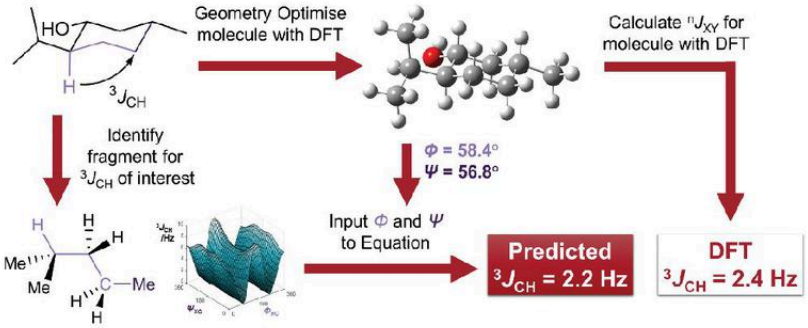
NMR spectroscopy has a wide application in the determination of three-dimensional molecular structure and the use of three-bond scalar couplings is common in solution-state NMR. Scalar coupling between nuclei separated by three bonds can be described empirically by homonuclear (^{1}H-^{1}H)[1] and heteronuclear (^{1}H-^{13}C)[2,3] equations relating the magnitude of the scalar coupling constant to the dihedral angle between the nuclei. Computational methods can also predict NMR properties such as chemical shift and scalar coupling constants for a given molecular structure[4].

Over 140,000 density functional theory (DFT) calculations were used to examine the relationship between $^3J_{CH}$ and dihedral angles (Φ and Ψ) for >75 different molecular fragments. The effects of bond angle, substituent pattern and coupling pathway were examined. These DFT-calculated $^3J_{CH}$ were then used to identify and parameterize suitable equations relating $^3J_{CH}$ to the dihedral angles Φ and Ψ for different fragments.

The performance of this library of equations was tested using computationally determined $^3J_{CH}$ as shown below. This fragment-based approach achieved an accuracy of ~0.5Hz compared to ~1.0 Hz for literature methods.



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Poster Presentation 12

Using a Dearomatising Intramolecular Acylation Strategy to Develop a 'Reverse-Biomimetic' Synthesis of Arogenate and its Analogues

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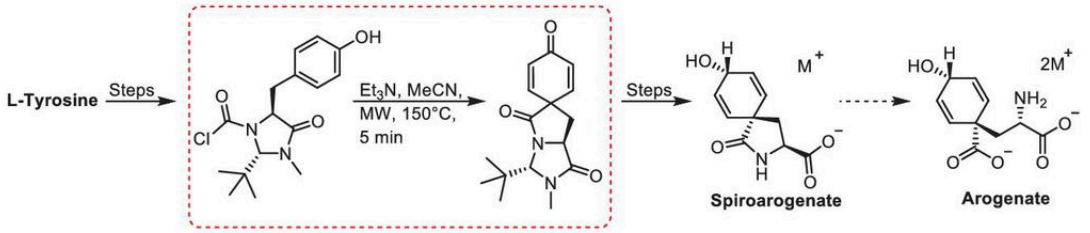
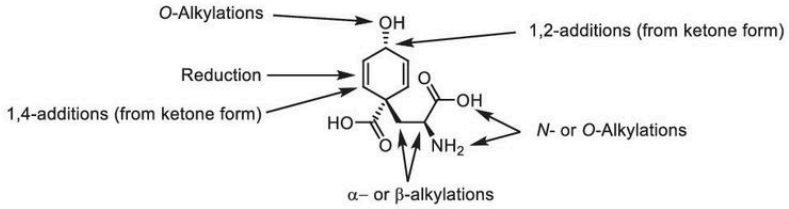
Arogenate is a key intermediate in the shikimate biosynthetic pathway to aromatic amino acids tyrosine and phenylalanine. Only two syntheses of arogenate have been reported, neither of which exploit the obvious starting material, L-tyrosine itself.[1,2] Uniquely, our work focuses on a 'reverse-biomimetic' synthesis of arogenate starting from this inexpensive, enantiopure amino acid. Interestingly, the synthetic route proceeds *via* a novel and mechanistically unusual dearomatising spirocyclisation reaction. This intramolecular acylation, which utilises a carbamoyl chloride tether to produce a spirocyclic lactam, can be performed using low-cost reagents and without the need for heavy metals or toxic species. Using this strategy, a quick and efficient route to spiroarogenate has been achieved, and current work seeks to optimise the hydrolysis of spiroarogenate to arogenate itself.



Scheme 1: Overview of the synthetic concept.

The biosynthetic pathways to aromatic amino acids are present in plants, bacteria and fungi but completely absent in animals.[3] Targeting the enzymes involved in this pathway with synthetic analogues of arogenate could enable the development of new, safe, and selective herbicides.



Scheme 2: Derivatisation of arogenate for agrochemical studies.

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Ionic Liquids like extractant of RS-propranolol in liquid-liquid extractions

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Liquid–liquid extraction is a separation processes that employs two immiscible phases, usually an organic solvent and an aqueous solution.[1] In this work we propose the use of ionic liquids as extractant to replace traditional solvents that are generally toxic, flammable, and volatile.[2]

We report the separation of RS-propranolol employing liquid-liquid technique, 5 organic solvents and 12 commercial ionic liquids to compare the efficiency of ionic liquids in comparison with organic solvents. The extraction efficiencies were determined through a chiral liquid chromatography method.

This work was supported by Fondecyt grant 11140172, Project ICM-MINECON, RC-130006-CILIS, granted by Fondo de Innovación para La Competitividad Del Ministerio de Economía, Fomento y Turismo and Instituto de Ciencias e Innovación en Medicina (ICIM-CAS UDD).

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Poster Presentation 14

Benzoylguanidinium Cations as the Anion Sensing Groups. UV/Vis and Theoretical Study

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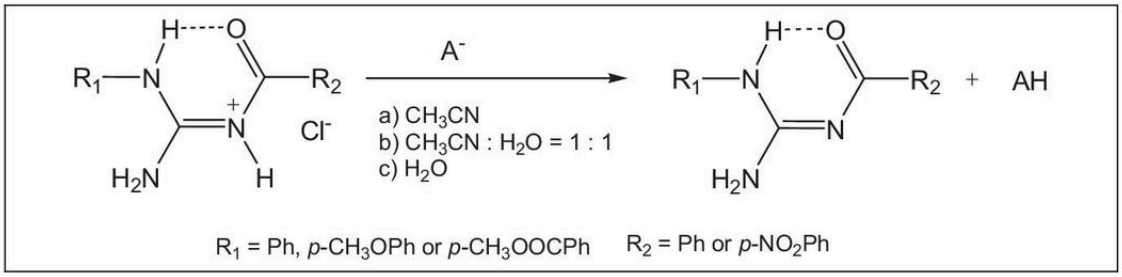
Guanidinium cation as a functional group has been recognized long time ago as the powerful anion binding moiety which interacts with anions through multiple hydrogen bonding and Coulombic interaction.[1,2] Therefore, it has been often used as a part of various anion sensors.[1,2] Sensor response could be triggered either by deprotonation or by the anion binding where the former process usually gives a larger effect, as shown for some thiourea derivatives.[3]

As a continuation of our interest in chromophore-guanidinium systems,[4] we prepared a series of benzoylguanidium hydrochloride salts (Scheme) and tested their interactions with different anions (AcO^-, F^-, $H_2PO_4^-$, NO_3^- and ClO_4^-). The role of water was also investigated. The measured UV/Vis spectra were compared with those calculated using TD-DFT methods. Obtained results indicate that the deprotonation is dominant process during the titration with moderate and strongly basic anions.



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Stereocontrolled Synthesis of Resveratrol Dimers and Tetramers via Persistent Radicals

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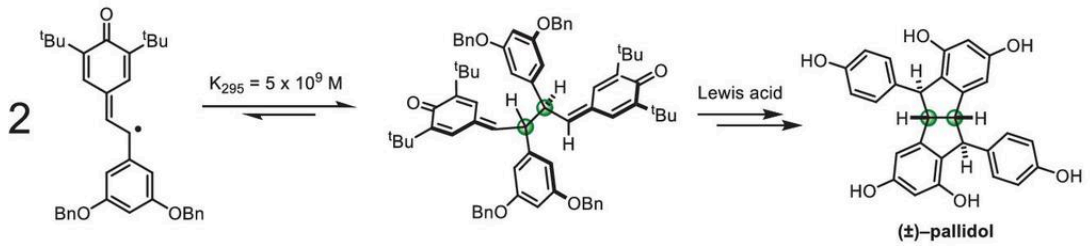
Resveratrol is a prominent example of the polyphenolic molecules ubiquitous in nature, to which a wide range of biological activities and health benefits have been ascribed. In addition, resveratrol is a building block for a myriad of oligomers that also exhibit promising biological properties. Here we present a biomimetic route to several resveratrol dimers and tetramers. During the course of this work, we identified a room temperature equilibrium between bisquinone methides and their monomeric radicals. We were able to characterize the properties of the radical species as well as the kinetics and thermodynamics of the equilibrium employing steady-state and transient absorption UV-Vis spectroscopy as well as EPR. This equilibrium plays a major role in dictating the stereochemistry of dimerization of different quinone methide building blocks. That is, although a mixture of products was expected from cyclizations of the different diastereomers of the quinone methides, the reactions yield a single diastereomer. This is caused via what we have termed as “dynamic homolytic stereocontrol”. Exploiting this mechanism we were able to synthesize several of the resveratrol oligomers, such as the dimers pallidol and quadragularin A and tetramers nepalensinol B and vateriaphenol C. We are now expanding on this technique with the help of computational modelling (DFT) to access a wider range of resveratrol oligomers.



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Poster Presentation 16

The effect of an ionic liquid solvent on two S_NAr reactions

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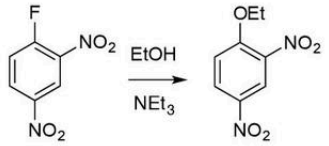
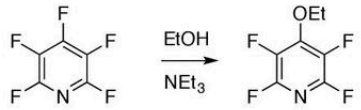
Ionic liquids can affect the reaction outcome of a range of organic processes.[1] In particular, the ethanolysis of 1-fluoro-2,4-dinitrobenzene **1** (Scheme 1), a nucleophilic aromatic substitution (S_NAr) process, occurs with an increase in the rate constant when an ionic liquid solvent is used.[2] It is of interest to extend this work to other reactions proceeding through an S_NAr mechanism.



1 **2**

Scheme 1. The S_NAr reaction between 1-fluoro-2,4-dinitrobenzene **1** and ethanol.[2]

2,3,4,5,6-Pentafluoropyridine **3** is a useful precursor for a range of molecules of interest to the life science and materials industries, due to the ease of nucleophilic substitution.[3] There is preference for reaction at the 4-position of pyridine **3**[3-4] and the electron poor nature of the heterocycle makes a good comparison to the previously mentioned reaction (Scheme 1).



3 **4**

Scheme 2. The S_NAr reaction between 2,3,4,5,6-pentafluoropyridine **3** and ethanol.

This project focuses on the influence of an ionic liquid solvent on the reaction described above (Scheme 2) and describes the kinetic analyses of the reaction with both a molecular solvent, ethanol and the ionic liquid 1-butyl-3-methylimidazolium *bis*(trifluoromethanesulfonyl)imide. This poster will cover how different proportions of ionic liquid affect the rate constant and investigate the temperature dependence of these data to determine the microscopic origins of any effects.

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Lithiation-Trapping of Oxygen-Containing Heterocylces

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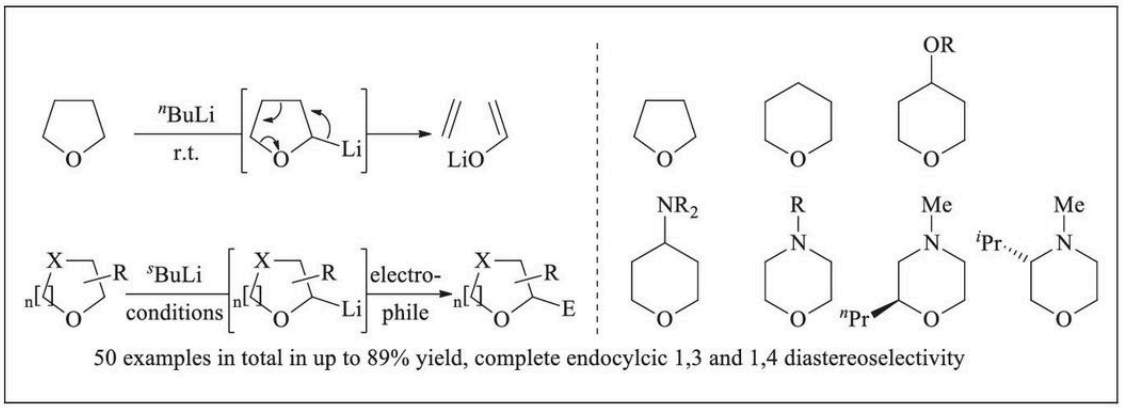
In the last 30 years, the α-lithiation and trapping of *N*-substituted-heterocycles has been extensively studied.[1] Pioneering studies by Bates on the lithiation of tetrahydrofuran employing ^{n}BuLi at room temperature revealed a fast retro [3+2] cycloaddition of the highly unstable lithiated species. This made trapping of the lithiated heterocycle by addition of an electrophile impossible.[2] As a result, lithiation-trapping of oxygen-containing heterocycles has been much less explored.

We discovered that careful selection of reaction conditions can lead to selective C-H activation and decomposition of THF can be minimised using ^{s}BuLi at low temperature. The so generated nucleophilic species can be trapped by a range of appropriate electrophiles. We present a novel, versatile route for the synthesis of α-substituted, five- and six-membered oxygen-containing heterocycles *via* a lithiation-trapping protocol. Employing optimised conditions for each system, products were obtained in high yields chemo- and regionselectively.



50 examples in total in up to 89% yield, complete endocylcic 1,3 and 1,4 diastereoselectivity

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Poster Presentation 18

The solvolysis mechanism of simple tertiary substrates in 50% TFE

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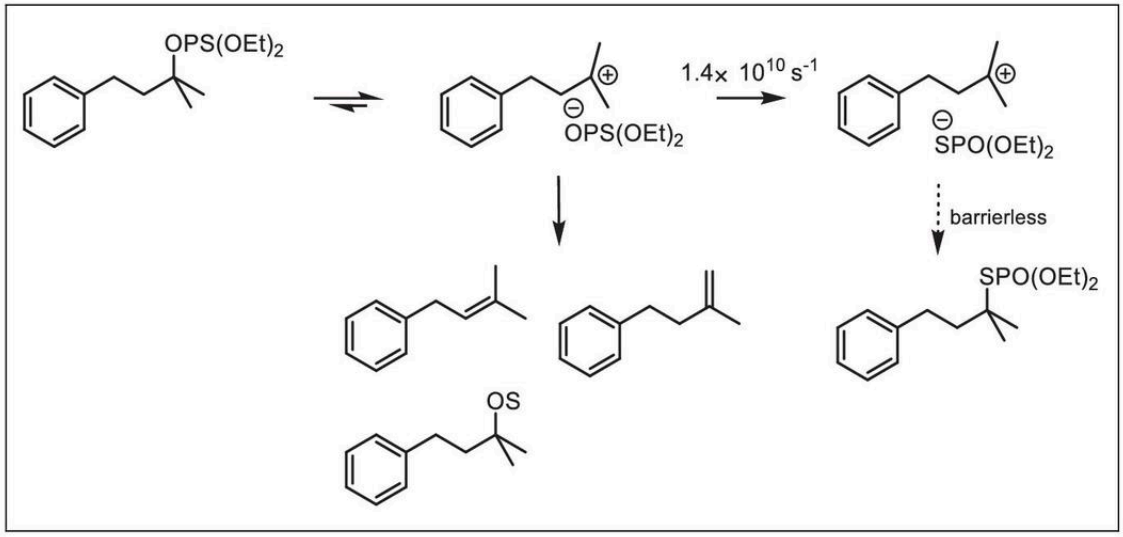
The solvolysis reaction of simple tertiary substrates is generally assumed to follow one of the most well-known substitution pathways: S_N1. However, the correlation between a cation's lifetime and its precursor's solvolysis rate, shows that the intrinsic lifetime of simple tertiary cation is only 1 ps in 50% TFE, indicating a solvent-reorganization dominated step-wise pathway.[1] On the other hand, this correlation-extrapolation method has been criticized[2] as it may *underestimate* the lifetime of unstable cations. Therefore, the real lifetime of simple tertiary cations in 50% TFE and the corresponding solvolysis mechanism are still ambiguous.

In this work, we choose a thiono-thiolo exchange probe[3] to determine the lifetime of simple tertiary cations. The reaction mechanisms with strong nucleophiles and bases are also discussed.



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Revisiting the Mechanism(s) of GTP Hydrolysis in Small GTPases

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GTPases are a broad super class of hydrolytic enzymes that play important roles in almost every cellular process from protein synthesis to regulated cell death [1]. They accelerate the hydrolytic cleavage of guanosine triphosphate and are activated by interaction partners, like the GTPase activating proteins (GAPs) [2]. Although broadly studied from a biological perspective, their precise chemical mechanisms remain controversial. For example, in the case of the small GTPase Ras, the absence of an obvious general base in the active site has led to a range of mechanistic proposals, from a substrate-assisted mechanism [3] to mechanisms with no general base at all [4]. We revisit here the mechanism(s) of GTP hydrolysis by Ras and related small GTPases using free energy perturbation molecular dynamic simulations and the empirical valence bond approach [5] to obtain free energy profiles.

In light of our recent, detailed, computational studies of uncatalyzed phosphate hydrolysis [6], we present an alternate model for GTP hydrolysis by these enzymes that removes the need for a general base in the active site.

1. Pylayeva-Gupta, Y., E. Grabocka, and D. Bar-Sagi, *RAS oncogenes: weaving a tumorigenic web.* Nature reviews. Cancer, 2011. **11**(11): p. 761-74.
2. Scheffzek, K., M.R. Ahmadian, and A. Wittinghofer, *GTPase-activating proteins: Helping hands to complement an active site.* Trends in Biochemical Sciences, 1998. **23**(7): p. 257-262.
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5. Shurki, A., et al., *How valence bond theory can help you understand your (bio)chemical reaction.* Chemical Society Reviews, 2015. **44**(5): p. 1037-1052.
6. Barrozo, A., et al., *The effect of magnesium ions on triphosphate hydrolysis.* **89**(6): p. 715-727.

Poster Presentation 20

Development of a Technology for the Discovery of Protein Carbamates

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Carbon dioxide (CO_2) is fundamental to life with critical roles in respiration, photosynthesis and acid-base homeostasis[1]. Despite this there is very little known about its molecular interactions with cellular components. CO_2 combines rapidly but reversibly with amines, by the nucleophilic attack of an uncharged amine on CO_2, at physiological temperatures and pressures to form carbamates[2]. The presence of this post-translational modification has been demonstrated in a small number of key proteins, such as RuBisCO and haemoglobin, but remains unexplored in other systems.

Carbamates are labile and previous work on the post-translational modification involved their study under non-physiological conditions. We have developed a technology to identify new sites of CO_2 interactions within proteomes, using a chemical trapping technique to remove their labile nature[3] combined with tryptic digest-MS analyses. The methodology functions under aqueous conditions representative of a physiological environment.

Initial validation experiments demonstrated effective carbamate trapping at NH_2 sites within model substrates acetyl-lysine, Phe-Gly and Phe-Lys, a tetra-peptide and haemoglobin. These results were confirmed using ESI-MS combined with ^{12}C and ^{13}C isotope incorporation. Screening of *Arabidopsis thaliana* whole proteome homogenates identified several novel carbamylated proteins previously unknown to directly interact with CO_2.

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Fluorinated dicarbonyl systems: chemical Swiss Army knives

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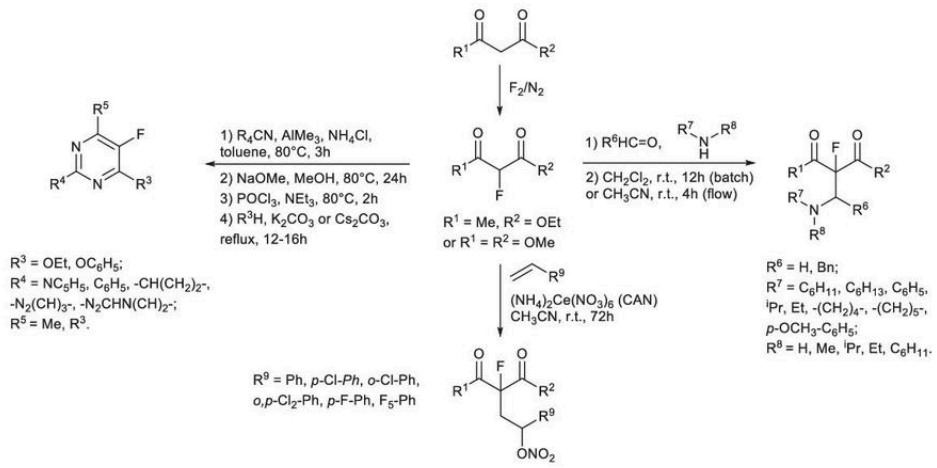
The incorporation of fluorine atoms into pharmaceutical candidate is a well established approach to, for example, affect lipophilicity, pKa and metabolic stability of new chemical entities as part of drug discovery programs. Consequently, effective and inexpensive methodologies for the synthesis of selectively fluorinated multifunctional building blocks for incorporation into drug synthesis campaigns are very desirable. Recently, the synthesis of 2-fluoromalonate esters has been optimized (>90% yield) by a one-step direct fluorination strategy which is very efficient, inexpensive, does not generate much waste and is readily scalable.[1,2]



As part of a general strategy aimed at assessing the effect of the carbon-fluorine bond attached to the reactive enolic site of the 2-fluoro-1,3-dicarbonyl system, we were using this reactivity profile for the synthesis of pharmaceutically relevant fluorinated intermediates from 2-fluoro-1,3-dicarbonyl substrates, such as functionalized fluorinated pyrimidinones and various nitro-oxy fluorinated products using a CAN-induced catalytic oxidative addition. Finally, we also developed a synthetic strategy using β-fluoroketoesters and β-fluoromalonate substrates as MCR components in Mannich reactions involving various aldehydes and amines, using both batch and flow processes.

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Poster Presentation 22

Revisiting the Mechanism(s) of GTP Hydrolysis in Small GTPases

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GTPases are a broad super class of hydrolytic enzymes that play important roles in almost every cellular process from protein synthesis to regulated cell death [1]. They accelerate the hydrolytic cleavage of guanosine triphosphate and are activated by interaction partners, like the GTPase activating proteins (GAPs) [2]. Although broadly studied from a biological perspective, their precise chemical mechanisms remain controversial. For example, in the case of the small GTPase Ras, the absence of an obvious general base in the active site has led to a range of mechanistic proposals, from a substrate-assisted mechanism [3] to mechanisms with no general base at all [4]. We revisit here the mechanism(s) of GTP hydrolysis by Ras and related small GTPases using free energy perturbation molecular dynamic simulations and the empirical valence bond approach [5] to obtain free energy profiles.
In light of our recent, detailed, computational studies of uncatalyzed phosphate hydrolysis [6], we present an alternate model for GTP hydrolysis by these enzymes that removes the need for a general base in the active site.

1. Pylayeva-Gupta, Y., E. Grabocka, and D. Bar-Sagi, *RAS oncogenes: weaving a tumorigenic web.* Nature reviews. Cancer, 2011. **11**(11): p. 761-74.
2. Scheffzek, K., M.R. Ahmadian, and A. Wittinghofer, *GTPase-activating proteins: Helping hands to complement an active site.* Trends in Biochemical Sciences, 1998. **23**(7): p. 257-262.
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4. Maegley, K.A., S.J. Admiraal, and D. Herschlag, *Ras-catalyzed hydrolysis of GTP: a new perspective from model studies.* Proceedings of the National Academy of Sciences of the United States of America, 1996. **93**(16): p. 8160-8166.
5. Shurki, A., et al., *How valence bond theory can help you understand your (bio)chemical reaction.* Chemical Society Reviews, 2015. **44**(5): p. 1037-1052.
6. Barrozo, A., et al., *The effect of magnesium ions on triphosphate hydrolysis.* **89**(6): p. 715-727.

Solvolytic Reactivity of Organic Phosphates

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Heterolytic reactivities (nucleofugalities) of some organic phosphate leaving groups have been determined in terms of N_f parameters from solvolysis rate constants of corresponding benzhydryl derivatives according to equation (1).[1] In this fashion, the nucleofugality of organic phosphates can be compared with nucleofugalities of numerous leaving groups in a wide range of reactivity in the existing nucleofugality scale.[1,2] N_f values can further be used for estimating the heterolytic reactivity of various substrates according to equation (1).[1]

$$\log k\ (25\ ^\circ\mathrm{C}) = s_f\,(E_f + N_f) \qquad (1)$$

It was previously established that the negative hyperconjugation is operative in heterolytic transition states of carbonate diesters as well as in free aryl/alkyl carbonate anions, transferring electron density out of the carboxylate moiety.[3] The difference in heterolytic reactivity between diphenyl phosphate and dimethyl phosphate leaving groups of even two orders of magnitude indicates that additional orbital effects exist in both heterolytic transition states and corresponding free phosphate anions since a direct transfer of the anionic charge to the aromatic rings of diphenyl phosphate is not possible. In order to investigate stabilizing effects that occur in leaving groups along the heterolytic reaction coordinate of phosphates, quantum chemical calculations have been employed.

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Poster Presentation 24

Towards understanding microscopic interactions in ionic liquids and their effects on S_N2 processes

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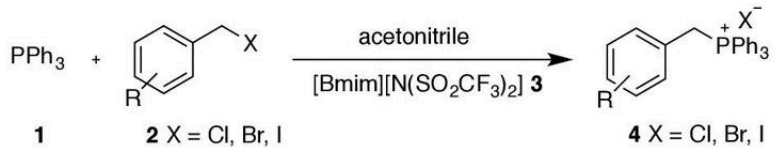
Ionic liquids, salts with normal melting points below 100 ºC,[1] have the potential to alter reaction outcomes relative to molecular solvents.[1-2] Previously it has been demonstrated that where pyridine undergoes an S_N2 reaction with benzyl halides **2** there is an entropically driven rate enhancement when the ionic liquids are used due to favourable cation-nucleophile interactions.[3-5] The effect of varying the constituent ions of ionic liquids on this interaction has been previously investigated, allowing a degree of predictability and therefore progress towards rational selection of an ionic liquid solvent for accelerating S_N2 processes.[6] However there is a comparatively limited understanding as to how variation of the chemical nature of reactive species affects S_N2 processes in ionic liquids.

Therefore this work has focused on variation of the electronics of the electrophile to probe the importance of interactions between the transition state and the components of ionic liquid **3** (Scheme 1). The effects of varying the nucleophilic heteroatom down group 15 have also been investigated to determine if there is a trend in the observed ionic liquid effect as you go down a group. The solvent effects have been investigated through studying the dependence of the rate constant on the amount of ionic liquid **3** in the reaction mixture, as well as temperature dependent kinetic studies to gain insight into the interactions between species along the reaction coordinate and the salt **3**.



1 **2** X = Cl, Br, I **4** X = Cl, Br, I

Scheme 1: Representative S_N2 reactions between a group 15-based nucleophile (triphenylphosphine **4**) and benzyl halides **2**.

R = 3,5-Me-4-MeO, 4-MeO, 4-Me, H, 4-CF_3, 4-Br, 4-NO_2

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Computational Study of Substituent Effects on Gas-Phase Stabilities of 2-Phenylethyl Anions

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For over a half century, it is well-known that the substituent effects on the stabilities of cations of benzene derivatives are well described by the Yukawa-Tsuno equation. On the other hand, the establishment of LFER for anions has been slow due to experimental difficulties. Recently, we computationally determined the substituent effects on gas-phase stabilities of various benzylic anions. Comparison of the substituent effects revealed that the stabilities of the anions are governed by three kinds of electronic effects, and an extended Yukawa-Tsuno equation (1) was proposed.[1]

$$-\Delta E_X = \rho(\sigma^0 + r^-\Delta\bar{\sigma}_R^- + s\Delta\bar{\sigma}_S) \quad (1)$$

To establish generality of eq. 1, we extended the research to 2-phenylethyl anions.

The relative stabilities of ring-substituted 2-phenylethyl anions were determined using an isodesmic reaction. Energies of respective species involved in the reaction were calculated at the B3LYP/6-311+G(2d,p) level of theory. Obtained substituent effects were analyzed by eq. 1.

The angle $\angle C^8\text{-}C^7\text{-}C^1$ (θ) of ring-unsubstituted 2-phenylethyl anion was optimized as 112.8°. The substituent effect analysis with eq. 1 gave a fine linear correlation with the ρ = 16.2, r^- = 1.74, and s = 0.47, as shown in Fig.1. The r^- value (through-resonance effect) in 2-phenylethyl anion is 1.7 times larger than that of phenoxide anion, which implies a participation of the benzene ring. The r^- value increased monotonically with the decrease of the angle θ. For spiro[2,5]octadienyl anion (θ = 60.0°), the ρ = 26.0, r^- = 2.40, and s = 0.71 were observed. The r^- and s values changed consistently reflecting the degree of participation, which confirms the validity of eq. 1.

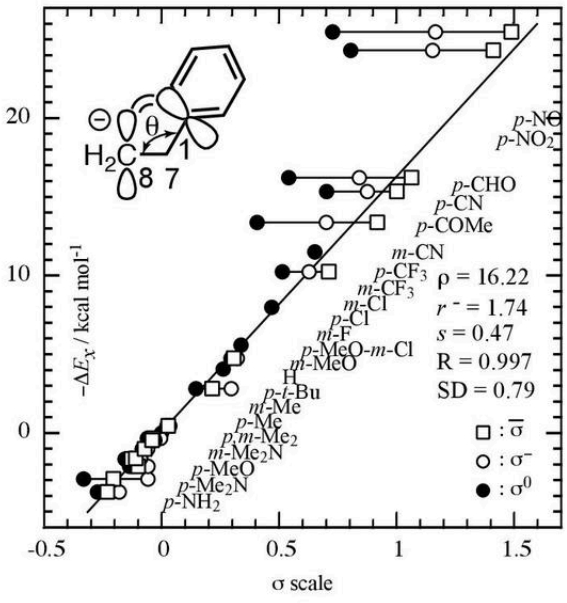

Fig. 1. Extended Y-T plots of 2-phenylethyl anion.

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Poster Presentation 26

Proton transfer reactions of triazolyl acyl anions: determination of Breslow intermediate pK_a values

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N-Heterocyclic carbenes (NHCs) are extensively used in contemporary organocatalysis in diverse C-C bond forming reactions. Acyl anion (Breslow[1]) intermediates feature in the majority of NHC-mediated transformations *e.g.* the benzoin condensation. Given the centrality of the Breslow Intermediate (BI) in NHC organocatalysis, understanding the structural effects on its formation and reaction is essential, in particular using synthetically-relevant triazolyl NHC catalysts.

The first unambiguous isolation and structural characterization of this intermediate was only recently achieved in 2012 for diamino enols from the less reactive, saturated imidazolinylidene NHC scaffold.[2] Relative nucleophilicities of a range of NHC-derived O-methylated BIs towards reaction with benzhydrylium carbocation acceptors have also been determined at low temperatures.[3] Herein, we report our kinetic studies towards the determination of a pK_a value for the conjugate acid of a triazolium-derived BI in aqueous solution. We have previously shown that the hydroxyaryl-NHC conjugate acids form reversibly in solution from NHC and aldehyde precursors thus a range of O-methylated adducts were prepared to prevent the reverse reaction.[4] Bulky *ortho*-substituents on both NHC and aryl aldehyde were also employed to suppress parallel hydrolytic decomposition reactions. Rate constants for BI formation from hydroxyaryl-NHC conjugate acid could be determined *via* kinetic analysis of deuterium exchange. Reverse rate constants for protonation of BI were accessed using stopped flow spectrophotometry.

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Ortho-Substitued Arylsilanes in Oxidative Gold Catalysis

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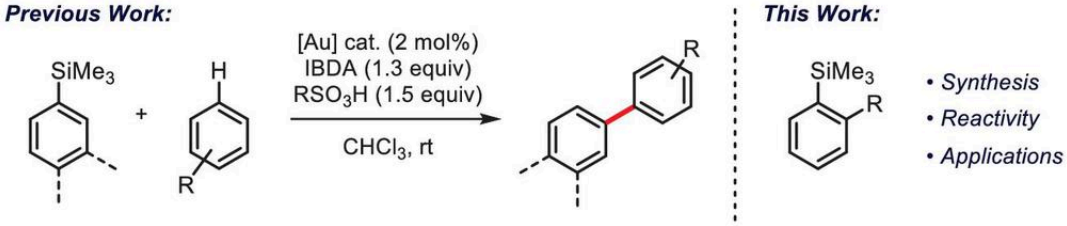
Oxidative gold catalysis is emerging as a powerful synthetic tool due to the unique reactivity of gold in comparison to the other late transition metals.[1] Our group recently reported the first gold-catalysed oxidative coupling of arylsilanes and arenes to form functionalised biaryls.[2] Reactions proceed under impressively mild conditions, and a diverse range of aryltrimethylsilanes and π-rich (hetero)arenes can be used. Notably, aryl halides and boronic esters are well tolerated, demonstrating orthogonality to other metal-catalysed cross-coupling reactions.



One limitation of the chemistry, however, is the profound unreactivity of arylsilanes bearing *ortho*-substitution. In fact, the only substituent tolerated under the originally reported conditions was a methyl group, requiring elevated temperature and a prolonged reaction time to reach high conversion.

Seeking to address this gap in reactivity, we have investigated the transmetalation of these reagents under catalytically relevant conditions, using a combination of *in situ* reaction monitoring and kinetic modelling. We have subsequently been able to design a class of *ortho*-substituted arylsilanes that are able to undergo coupling to form previously inaccessible products, significantly expanding the scope of the arylation reaction.

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[2] Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A. *Science* **2012**, 337, 1644.

Poster Presentation 28

Amplification of Emission in Donor–Acceptor Aggregates

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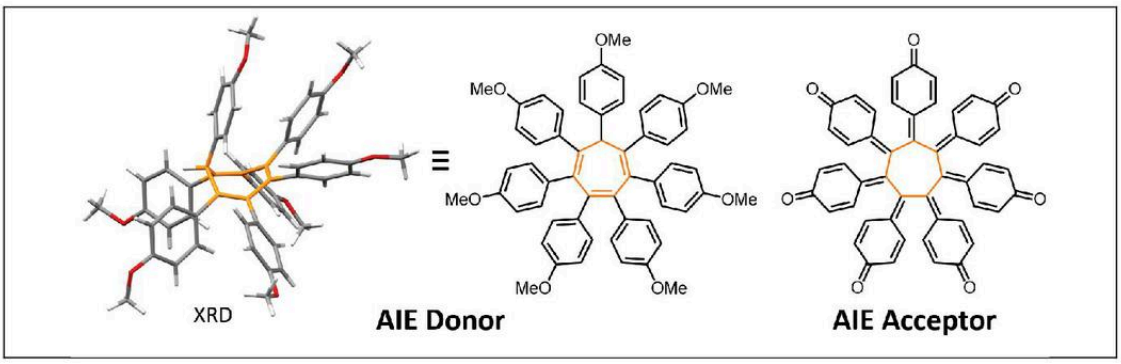
In recent times, organic donor–acceptor (D–A) architectures have been investigated for optoelectronic applications on account of their unique charge transfer properties.[1] Energy transfer between donors and acceptors also plays an important role in natural phenomena, e.g., photosynthesis. Emissive conjugates have a wide variety of applications in long wavelength emitters, biophotonics, organic lasers and so forth. A current frontier in this research area is the synthesis of D–A structured emitters that exhibit aggregation-induced emission (AIE) behaviour—that is, they fluoresce only weakly in solution, but become highly luminescent in the solid state.[2]

Our approach is to synthesise donor molecules which have AIE characteristics and then, using noncovalent interactions, to tune their luminescence by co-crystalizing with readily available electron deficient arenes, as well as with some AIE acceptors. This poster presentation will discuss the synthesis, reactivities and luminescence properties of the AIE donors and acceptors.



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Effects of Binary Solvent Mixtures on Rates of Reaction

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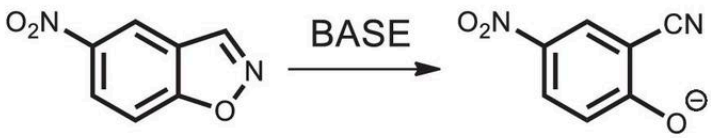
The solvent in which a chemical reaction is carried out can significantly affect the rate, pathway, or indeed, the outcome of the reaction. Hence, there have been many attempts to characterise solvent effects using a wide range of parameters, so that these effects can be understood and predicted.[1] One particularly attractive approach focuses on donor (α) or acceptor (β) hydrogen bond sites in the solvent to create a supramolecular model of the solvent.[2] This model has been very effective in predicting equilibria,[3] and now we want to explore whether it is equally effective in predicting reactivity. We are using the Kemp elimination as a test reaction because it is known to be highly sensitive to the solvent:



In this work, the second order rate constants of the Kemp elimination in various binary solvents containing alcohols and halogenated organic solvent have been measured. The rate of reaction is very sensitive to increasing alcohol concentration and the α value of the strongest hydrogen bond donor site. We will present our progress in quantitatively fitting these data to a model based on the molecular properties of these mixed solvents.

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Poster Presentation 30

Molecular modeling of radical SAM enzyme lysine 2,3-aminomutase

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The radical S-adenosyl methionine (SAM) enzyme superfamily represents an ensemble of proteins that are able to catalyse biochemical reactions involving organic radical intermediates.[1] These intermediate radicals then undergo a wide range of reactions, many of them difficult to accomplish in the laboratory. Virtually every enzyme belonging to this family is known to be unstable in air due to the requirement for a catalytic, oxygen-sensitive [4Fe-4S] cluster, resulting in loss of catalytic activity and making the study of these enzymes technically challenging.

Lysine 2,3-aminomutase (LAM),[2] a widely studied radical SAM enzyme, has an established natural oxygen-tolerant variant[3] whose structure has been predicted here through homology modeling with LAM's oxygen sensitive crystal structure as a template. The homology structure of the oxygen-tolerant LAM variant is evaluated and its dynamic behaviour studied and compared to its native form using molecular dynamics simulations. The goal is to explore the dynamics of oxygen diffusion inside the proteins and to understand the source of oxygen tolerance, which should allow us to transfer and exploit this feature to other members of the SAM family, enabling easier access to radical SAM enzymes in the laboratory and larger-scale applications.

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New Blatter-type Radicals from a Bench-stable Carbene

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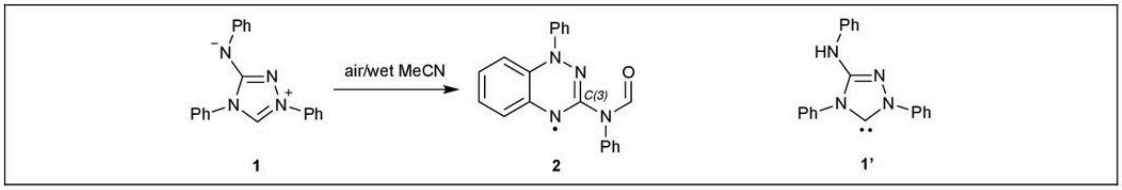
There has been increased recent interest in stable benzotriazinyl (Blatters') radicals owing to their potential applications as building blocks for functional materials. Existing synthetic routes to Blatters' radicals are problematic, however, and derivitisation is challenging. We have recently reported that an inexpensive, commercially available, analytical reagent Nitron **1** undergoes a previously unrecognized transformation in wet acetonitrile in the presence of air to yield a new Blatter-type radical **2** with an amide group replacing a phenyl at the C(3)-position.[1]

Our original interest in the chemistry of **1** was sparked by a recent report of the significance of the N-heterocyclic carbene (NHC) tautomer **1'** of this bench-stable analytical reagent.[2] To further probe the tautomeric distribution, we analysed the proton transfer properties in comparison with other NHCs, which revealed the unexpected transformation of **1** to **2**.

This one-pot reaction of **1** provides access to a range of previously inaccessible benzotriazinyl radicals with excellent stabilities. The scope of the new reaction was confirmed by the successful synthesis of several substituted derivatives. Our mechanistic studies demonstrate that the reaction starts with a hydrolytic cleavage of the triazole ring of **1** followed by oxidative cyclization. Our results provide access to novel C(3)-amido and amino functional handles, thus significantly expanding the scope of benzotriazinyls as radical building blocks.



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Poster Presentation 32

Towards Redox Active Warped Nanographenes

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Although normally associated with only neutral carbon frameworks, aromaticity can also be found in charged systems. Some unsaturated odd-numbered rings are known to exhibit the same type of stabilising electron delocalisation as traditional aromatics when they hold a positive or negative charge. High impact neutral carbon materials such as graphene can be redeveloped to possess the unique properties of charged aromatic systems through implementing unsaturated odd numbered rings (aromatic ions).[1]

Odd numbered carbon frameworks have previously been observed as typical defects of traditional graphene through the Stone–Wales rearrangement, causing disruption in the planarity of the graphene sheet. Nanographenes are used to model perfect hexagonal graphenes by representing a small section of the extended material.[2] The problem is that few models are defect free and there are few accurate models of defects graphene available for comparison.

Our approach to devising aromatic-ion nanomaterials focuses on synthesising a tropylium-centred nanographene, surrounded by fused benzene rings to produce a warped redox active nanographene that includes a counter ion to allow for solution processing. The resulting structure will possess the unique and versatile characteristics of a charged aromatic system as well as a non-planar structural effect dictated by the odd-numbered central ring.[3]

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Site-selective C-C bond formation in unprotected monosaccharides using photoredox catalysis

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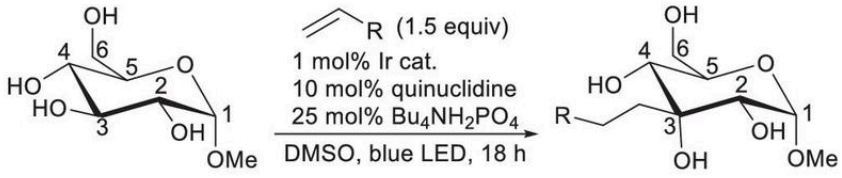
Site-selective photoredox reactions with somophiles readily enable branching of the carbon skeleton of unprotected glucosides, allosides and xylosides regioselectively at C3. These reactions open the possibility of selective C-C bond formation in monosaccharides without multi-step protection-deprotection strategies.

A photoredox reaction developed by MacMillan and coworkers allows the activation of alcohol C-H bonds.[1] With this information in hand, in addition to the previous efforts of regioselective oxidation of carbohydrates in our group, we recognized the intrinsic reactivity of carbohydrates and the possibility of regioselective C-H activation.[2] The activated C-H bond turned out to be C3. The regioselectivity is currently under investigation.



Literature:

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Poster Presentation 34

A systematic structural series to elucidate the inner workings of thermally activated delayed fluorescence

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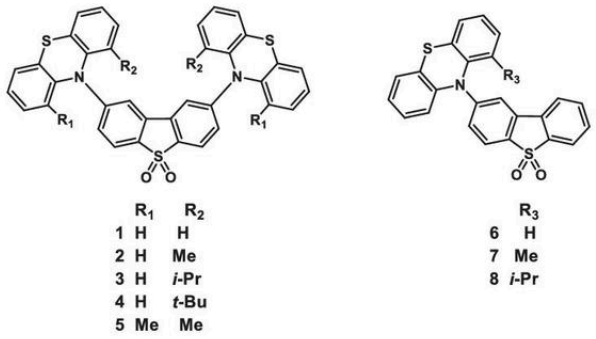
Thermally activated delayed fluorescence (TADF) is an important emission pathway for OLED device photophysics. Conversion of triplet excited states to singlets, allows for high efficiency OLED devices. A series of molecules with variations on the donor were synthesised to assess how rigidifying the molecule would affect the emission properties. (Figure 1).[2]



	R_1	R_2
1	H	H
2	H	Me
3	H	*i*-Pr
4	H	*t*-Bu
5	Me	Me

	R_3
6	H
7	Me
8	*i*-Pr

Figure 1. Structure of synthesised series of molecules

Introduction of bulkier groups gave unexpected strong room temperature phosphorescence (RTP) in the solid state, which could have interesting further applications.

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Combining Supramolecular Solvation and "No Barrier Theory" to Predict Reactivity

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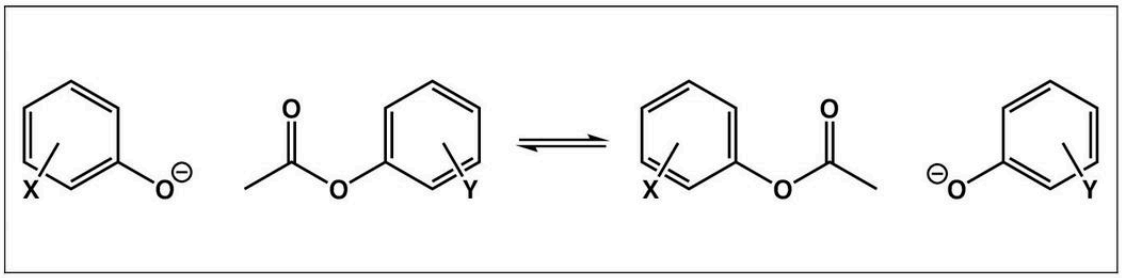
A supramolecular model based primarily on hydrogen bond donor (α) and acceptor (β) parameters have been used to predict binding equilibria very successfully.[1] The model characterizes the solvent as a collection of molecular sites with relatively easily obtained parameters, rather than using bulk solvent properties or computationally expensive quantum mechanical modeling, and allows mixtures of solvents to be treated simply and intuitively. Despite its success with binding events, its utility for predicting the rates of chemical reactions is unclear. In this work, we describe our progress in using phenolate exchange as a probe to see how the β parameter of anionic nucleophiles and leaving groups affect the rate of reaction:



The β values for series of phenolates were obtained through titration experiments with a common hydrogen bond donor and the rates of the reactions are correlated with this parameter. We consider whether the charge and structural changes involved in this simple acyl transfer reaction can be combined into a simple predictive model, extending Guthrie's "no barrier" description of reactions pathways.[2]

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Poster Presentation 36

On the Mechanism of Electrophilic Fluorination of Enol Esters

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The introduction of fluorine into molecules can have a marked effect on solubility, pK_a, lipophilicity, geometry, permeability in biological systems and binding affinity at biological targets. Fluorinated molecules have therefore found widespread use in pharmaceutical applications.[1] Widely applicable synthetic strategies are required for the introduction of fluorine into these molecules. With the advent of safe, bench stable electrophilic fluorinating reagents such as SelectFluor[2] the reaction of carbon nucleophiles with "F^+" sources has become a convenient means of introducing fluorine atoms into organic molecules. Enol esters are often used as nucleophiles in this manner, and there are several examples of their use to fluorinate steroid scaffolds.[3,4] However, whilst the fluorination of alkenes has been studied in some depth[5,6] the mechanism of enol ester fluorination with common electrophilic fluorinating reagents is not well understood. This work illustrates initial investigations into the mechanism of the electrophilic fluorination of enol esters with common fluorinating reagents.

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Towards an Organocatalytic Route for the d^1-Deuteration of Aldehydes

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Triazolium and bis(amino)cyclopropenium salts, precursors to N-heterocyclic carbenes (NHCs) and bis(amino)cyclopropenylidenes (BACs), have been recognised as versatile organocatalysts for a range of synthetic transformations.[1-3] Recently, a kinetic evaluation of the benzoin condensation in the presence of NHCs[4] and BACs[5] suggested potential pathways towards d^1-deuterated aldehydes.

Overall, sixteen N-aryl triazolium salts and two bis(amino)cyclopropenium salts have been prepared. During synthetic preparations, novel NHC-dialkoxy adducts were isolated and X-ray crystallography provided structural confirmation. Kinetic evaluation of the NHC/BAC-catalysed self-condensation of aryl-aldehydes was subsequently performed. Equilibrium and rate constants were determined for the reactions of triazolium catalysts with aldehyde, clearly highlighting differential effects of the fused-ring size of catalysts. Moreover, the extent of H/D-exchange of aldehyde at the d^1 position was evaluated, with up to 70% of d^1-deuterium incorporation obtained.

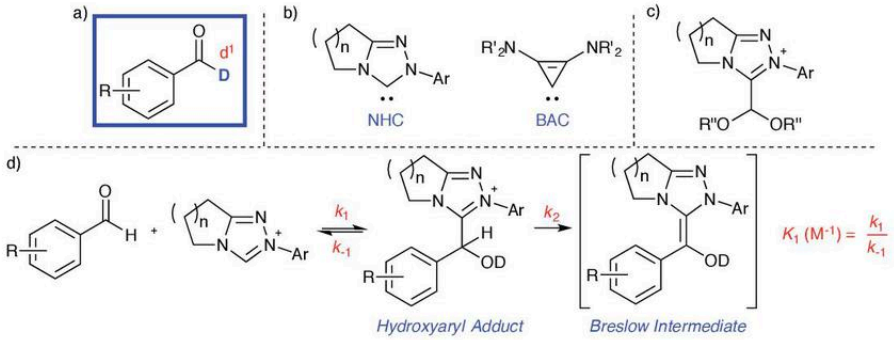

Fig. 1 a) d^1-Deuterated aldehyde, b) N-heterocyclic carbene (NHC) and bis(amino)cyclopropenylidene (BAC), c) novel NHC adducts, d) kinetic evaluation of the benzoin condensation.

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b) D. E. Tucker and A. C. O'Donoghue, unpublished results.

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ESOR 2017 3 - 8 September 2017, Durham UK

Schedule

Time	Sunday 3 September	Monday 4 September	Tuesday 5 September	Wednesday 6 September	Thursday 7 September	Friday 8 September
09:00		Plenary Sijbren Otto 09:00 - 09:40	Plenary Franziska Schoenebeck 09:00 - 09:40	Plenary John Richard 09:00 - 09:40	Plenary Albrecht Berkessel 09:00 - 09:40	Plenary Guy Lloyd-Jones 09:00 - 09:40
09:10						
09:20						
09:30						
09:40		Invited Rainer Herges 09:40 - 10:10	Invited Peter Schreiner 09:40 - 10:10	Invited Nick Williams 09:40 - 10:10	Invited John Murphy 09:40 - 10:10	Invited Michael Page 09:40 - 10:10
09:50						
10:00		Dave Carbery 10:10 -10:30	Markus Griesser 10:10 -10:30	Heidi Korhonen 10:10 -10:30	Craig Butts 10:10 -10:30	Robert Cox 10:10 -10:30
10:10						
10:20						
10:30		coffee break 10:30-11:00	coffee break 10:30-11:00	coffee break 10:30-11:00	coffee break 10:30-11:00	coffee break 10:30-11:00
10:40						
10:50						
11:00		Invited Anke Kruger 11:00 - 11:30	Invited Manube Abe 11:00 - 11:30	Invited Lynn Kamerlin 11:00 - 11:30	Invited María Paz Muñoz 11:00 - 11:30	Invited Maria Cristiano 11:00 - 11:30
11:10						
11:20						
11:30		Leo Frkanec 11:30 - 11:50	Victor Chechik 11:30 - 11:50	Ian Fairlamb 11:30 - 11:50	Adam Islip 11:30 - 11:50	Chuks Isanbor 11:30 - 11:50
11:40						
11:50		Kirill Nikitin 11:50 - 12:10	Götz Bucher 11:50 - 12:10	Moisés Canle 11:50 - 12:10	James Walton 11:50 - 12:10	N. Konstandaras 11:50 - 12:10
12:00						
12:10		Ian Ashworth 12:10 - 12:30	Christof Jäger 12:10 - 12:30	Jiří Váňa 12:10 - 12:30	Rebecca Hawker 12:10 - 12:30	Closing Remarks 12:10 - 12:30
12:20						
12:30		lunch break 12:30 - 14:00 Grey College	lunch break 12:30 - 14:00 Grey College	packed lunch served from Chemistry Café	lunch break 12:30 - 14:00 Grey College	packed lunch served from Chemistry Café
12:40						
12:50						
13:00				Excursions (optional)		
13:10						
13:20						
13:30						
13:40						
13:50						
14:00	registration and University accommodation check-in at Grey College 14:00 - 20:30	Plenary Michael Ward RSC Award for Supramolecular Chemistry 14:00 - 15:00	Plenary Ivan Huc 14:00 - 14:40		Olah Symposium Introduction & Surya Prakash 14:00 - 15:00	
14:10						
14:20						
14:30						
14:40			Invited Ian Williams 14:40 - 15:10			
14:50						
15:00		Invited Jason Harper 15:00 - 15:30	Simon Webb 15:10 - 15:30		Invited H.-U. Siehl 15:00 - 15:30	
15:10						
15:20						
15:30		coffee break 15:30-16:00	Paul McGonigal 15:30 - 15:50		Graham Sandford 15:30 - 15:50	
15:40						
15:50			coffee break 15:50-16:20		coffee break 15:50-16:20	
16:00		Siying Zhong 16:00 - 16:20				
16:10						
16:20		Ivana Biljan 16:20 - 16:40	Fernanda Duarte 16:20 - 16:40		Armin Ofial 16:20 - 16:40	
16:30						
16:40		Fujio Yagihashi 16:40 - 17:00	Anna Vetter 16:40 - 17:00		Kazuhide Nakata 16:40 - 17:00	
16:50						
17:00	Introduction & Opening Lecture: Chris Hunter 17:00 - 18:00		Ivan Kodrin 17:00 - 17:20		Hrvoj Vancik 17:00 - 17:20	
17:10						
17:20			Peter Byrne 17:20 - 17:40			
17:30		Poster presenters to hang posters 17:30 - 18:00				
17:40						
17:50						
18:00	Welcome Party 18:00 - 20:30	Posters: Durham Cathedral Cloister 18:00 - 20:00				
18:10						
18:20						
18:30						
18:40						
18:50						
19:00					Conference Dinner (optional) 19:00 onwards	
19:10						
19:20						
19:30						