

1 > 6 July 2018

UNIVERSITY OF ALGARVE

FARO

PORTUGAL



24th IUPAC

INTERNATIONAL CONFERENCE
ON PHYSICAL ORGANIC CHEMISTRY



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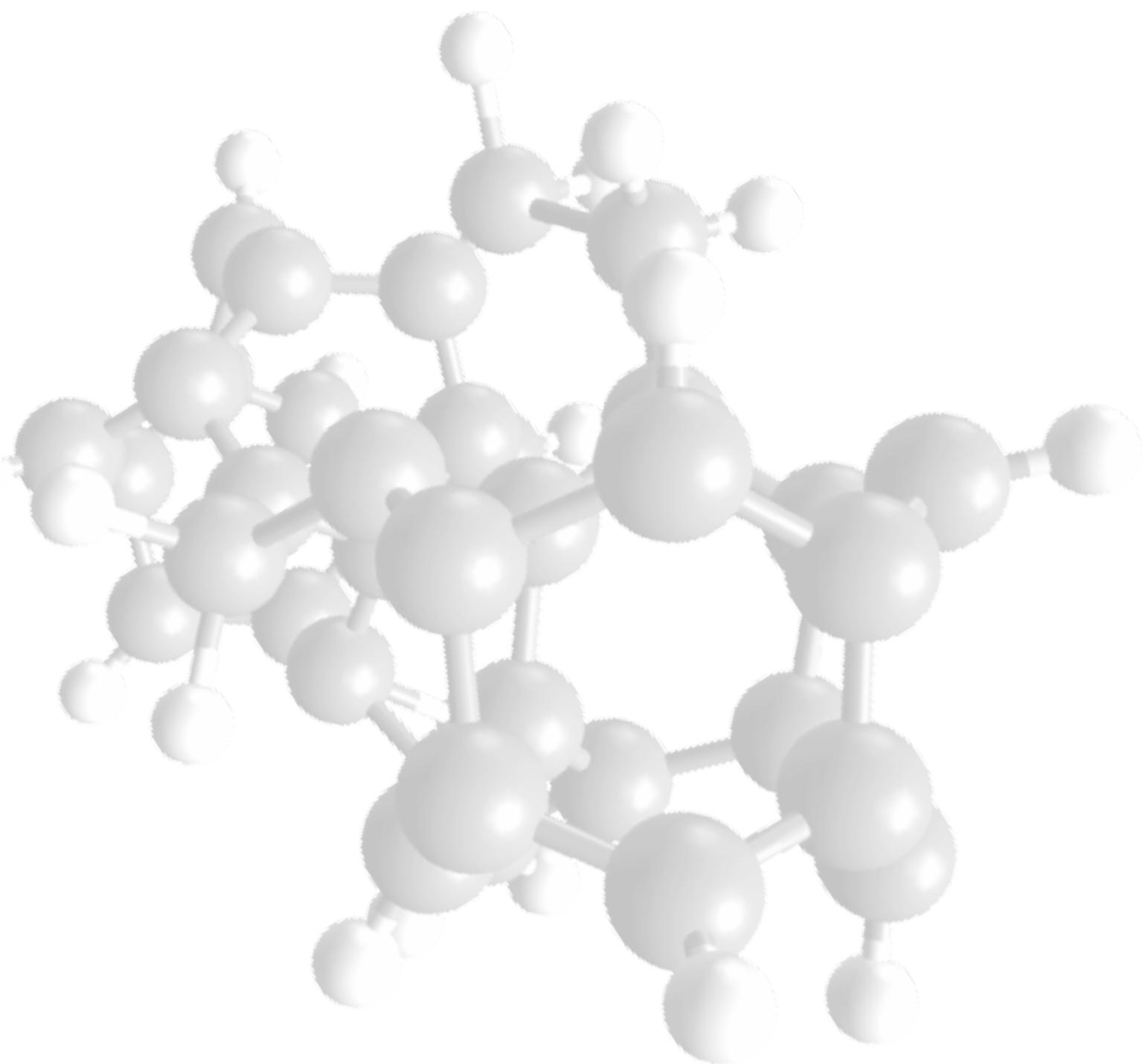
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24th IUPAC International Conference on Physical Organic Chemistry

**University of Algarve
Faro, Portugal**

1-6 July 2018

ICPOC 24



Welcome Address

Dear Colleagues,
Dear Friends,

I am happy and honoured to welcome you to the University of Algarve. I wish you an active, stimulating and rewarding participation in the 24th IUPAC International Conference on Physical Organic Chemistry (ICPOC 24).

Since their start, in 1972, ICPOC conferences have been the leading international gatherings on Physical Organic Chemistry.

Today, Physical Organic Chemistry encompasses a broad range of context, including the study of structure, reactivity, mechanism and equilibrium in organic systems, aiming at the quantitative, molecular level understanding of their properties, and further expanding into materials science, biology and systems chemistry.

As organisers of ICPOC 24, our main goal has been to offer a scientific program that reflects this comprehensive and multidisciplinary approach and pinpoints current developments in the area.

The scientific program of ICPOC 24 comprises 12 plenary lectures, 11 keynote lectures, 11 invited lectures, 58 oral communications and 113 poster presentations, associated to the three streams of the conference: Physical Foundations of Organic Reactivity, Mechanism and Catalysis, Supramolecular and Systems Chemistry.

We are confident that it will provide ample opportunity for vibrant and enlightening scientific discussions, paving ways toward further developments in Chemical Sciences.

The venue of the conference is Faro, is the main city of Algarve. Not far from Faro, near the southwestern most point of continental Europe, lies Sagres, a sacred promontory to the Romans. It was in Sagres that, legendarily, prince Henry the Navigator dreamed and planned the Portuguese discoveries in the 15th century, searching for the unknown while expanding frontiers, in the quest to discovering a sea route to India.

All participants of ICPOC 24 are invited to visit Sagres and the nearby city of Lagos during our conference excursion and, in addition to the history and traditions, will be exposed to the colours, flavours and tastes of Portugal.

We thank you wholeheartedly for participating in ICPOC 24 and wish you a pleasant and fruitful stay in Portugal.



Maria de Lurdes Cristiano

Chair, IUPAC – ICPOC 24 Organising Committee



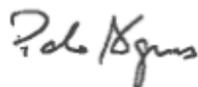
Message from the Rector of the University of Algarve

Dear participants,

It gives me great pleasure to extend to you all a very warm welcome and to express how grateful we are to host the 24th IUPAC International Conference on Physical Organic Chemistry in the University of Algarve, Faro, Portugal, 1- 6 July 2018.

The University of the Algarve is a young state comprehensive university founded in 1979. In this academic year we have 7,500 enrolled students, of those 1,200 are foreigners, from 70 different nationalities. Research and Innovation is a top priority for the University of Algarve.

I sincerely hope you will enjoy a full week of debate and networking. Thank you for your participation.



Paulo Águas

Rector of the University of Algarve



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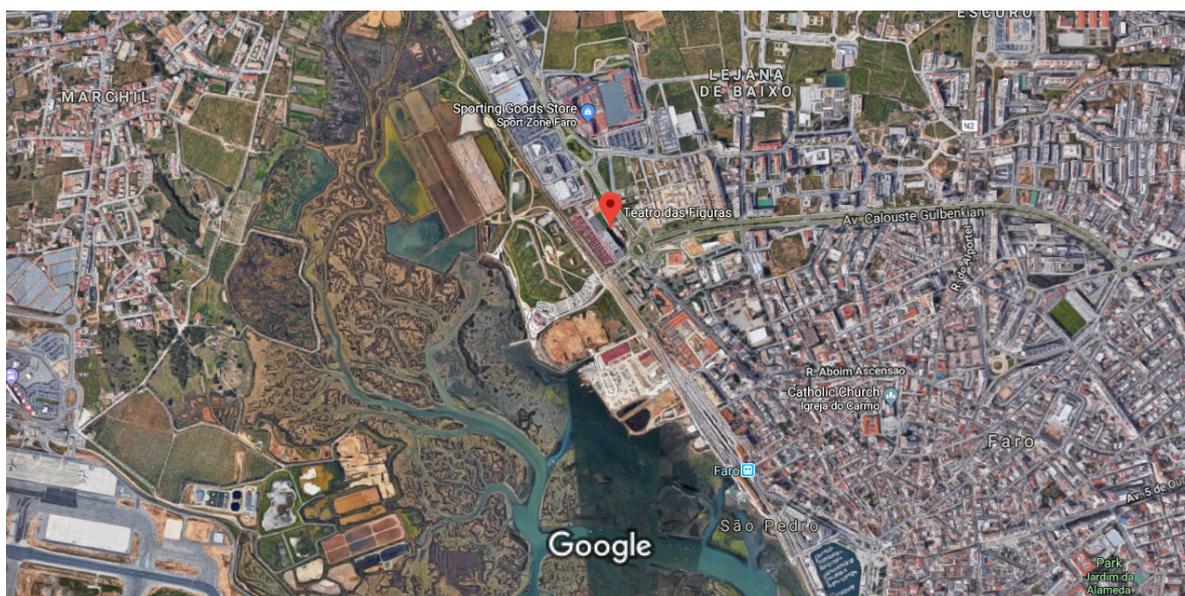
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General information

Conference Location

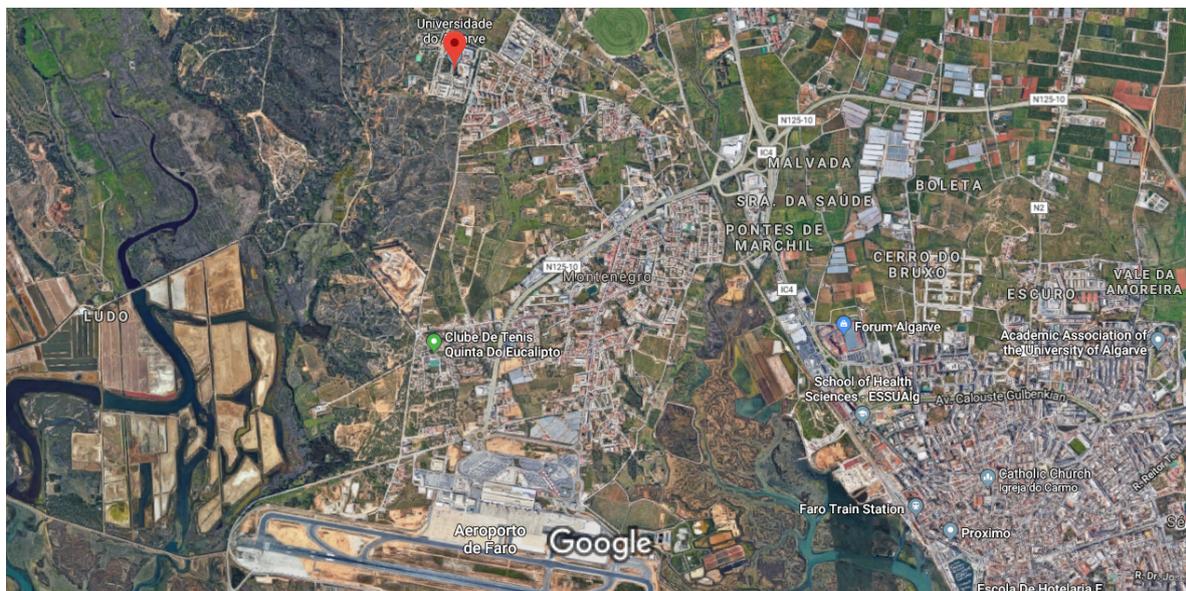
The Conference opening will be on Sunday (July 1) at the “Teatro das Figuras” in Faro. The Conference, from Monday to Friday (July 2-6), will be held at *Campus de Gambelas* of the University of Algarve, about 5-6 Km away from Faro.

Google Maps Teatro das Figuras



Imagery ©2018 Google, Map data ©2018 Google 200 m

Google Maps University of the Algarve



Imagery ©2018 Google, Map data ©2018 Google 500 m

Lecture Halls

On Sunday (July 1) the Plenary will be at the Auditorium of “Teatro das Figuras” in Faro. From July 2 to 6, the conference presentations will be held at University of Algarve - *Campus* de Gambelas. The Plenary and Keynotes lectures will take place at the University Auditorium and the invited lectures and oral presentations in parallel session will be at CP building auditoriums (see figure below).

The Conference poster session will be in the arcades of the building CP (see figure below).



Legend:

1. University Auditorium
2. Parallel sections rooms
3. Poster session place
4. Lunch restaurant (ground floor)
5. Gambelas *Campus* main entrance

Rooms are equipped with desktop computer. Speakers are recommended to bring their presentations in ppt, pptx or PDF format on a USB pen drive. [Speakers should upload their presentations in advance.](#) Speakers who want to use their Mackintosh should bring DVI-VGA or DisplayPort-VGA adapter.

WiFi - A temporary login for the wireless has been created, the credentials will be given at conference office.

Conference Office

The Conference desk will be located on Sunday (July 1) at the atrium of the Teatro das Figuras, and from Monday to Friday (July 2-6) will be at the hall near the University Auditorium.

Conference Office timetable

Sunday, July 1	14:00-19:00	Teatro das Figuras atrium
Monday, July 2	08:00-19:00	UAlg - Auditorium hall
Tuesday, July 3	08:30-19:00	UAlg - Auditorium hall
Wednesday, July 4	08:30-13:00	UAlg - Auditorium hall
Thursday, July 5	08:30-17:00	UAlg - Auditorium hall
Friday, July 6	08:30-13:00	UAlg - Auditorium hall

Meals

Lunch is free for active participants and will be served every day at the university restaurant, building near de conference rooms (indicated with the number 4 in the *Campus* map).

Badges

Upon registering, participants will receive a badge showing their identification. It is mandatory to use the badge during all Conference activities.

Local Transportation

Several bus routes, provided by the Proximo company (urban bus), are available everyday from and to Faro (terminal station, near center city). For Gambelas you can take bus 18 from Faro, but if you are coming from Montenegro or Faro Island you will need to take bus 16.

Banking

There is no bank dependence near *Campus* de Gambelas, however at the main entrance of the *Campus* there is an ATM service.

Social Program

Conference excursion

A conference excursion to Lagos and Sagres will be offered to all participants. Some historical and touristic information on Lagos and Sagres is available through the links indicated below.

Lagos

<https://lagos.algarvetouristguide.com/>

https://portugalvirtual.pt/_tourism/algarve/lagos/index.html

Sagres

<http://www.sagres.net/>

Conference dinner

The conference dinner will take place at the Pousada Palace of Estoi, a recovered eighteenth century palace featuring a combination of classical, baroque and contemporary architectural and artistic elements. The palace is surrounded by gardens with a French and Italian inspiration and offers a splendid view over a marvellous landscape encompassing the Algarve countryside, where the Palace is situated, and, further away, the Atlantic coast.

Some information about Pousada Palace of Estoi is available through the following link:

<https://www.pousadas.pt/en/hotel/pousada-estoi>

Scientific Program

Conference Timetable

Sunday - 1 July

14:00-16:00	Registration
16:00-17:00	Opening Ceremony Introductory Remarks Plenary Session 1a - Chair: Artur Silva
17:00-18:00	PL1 - <i>Dynamic Molecular Systems</i> , Bernard Feringa Plenary Session 1b - Chair: Ian Williams
18:00-19:00	PL2 - <i>Innovation by Evolution: Bringing New Chemistry to Life</i> , Frances Arnold
19:00	Welcome Reception

Monday - 2 July

	Plenary/ Keynote Session 2 - Chair: Manabu Abe		
09:00-09:50	PL3 - <i>Bond Strengths in the Gas Phase, in Solution, and in Silico: Dispersion Effects and Big Molecules</i> , Peter Chen		
09:50-10:20	KN1 - <i>Carbohydrate Formation in the Absence of Biosynthesis</i> , Peter R. Schreiner		
10:20-11:00	Coffee Break		
	Plenary/ Keynote Session 3 - Chair: Jason Harper		
11:00-11:50	PL4 - <i>Revitalize Bond Energetics for Understanding Ionic Liquid Chemistry</i> , Jinpei Cheng		
11:50-12:20	KN2 - <i>Competitive and Cooperative Counterion Effects on Supramolecular Recognition</i> , Luís Garcia-Río		
12:20-14:00	Lunch		
	Parallel sessions		
	Session 1a Chair: S. Fornarini	Session 2a Chair: P. Schreiner	Session 3a Chair: U. Pischel
14:00-14:30	IL1 - <i>Ottosson</i>	IL2 - <i>Mayr</i>	IL3 - <i>Hiraoka</i>
14:30-14:50	OP1 - Itoh	OP10 - Page	OP19 - Sato
14:50-15:10	OP2 - Bucher	OP11 - Alabugin	OP20 - Brotin
15:10-15:30	OP3 - Jones	OP12	OP21 - Vančik
15:30-15:50	OP4 - G.-Poranne	OP13 - Humeres	OP22 - Nekipelova
15:50-16:20	Coffee Break		
	Session 1b Chair: U. Wille	Session 2b Chair: A. O'Donoghue	Session 3b Chair: L. Garcia-Río
16:20-16:40	OP5 - Milo	OP14 - Uggerud	OP23 - Lainé
16:40-17:00	OP6 - Perrin	OP15 - Kaneno	OP24 - Basílio
17:00-17:20	OP7 - Cruzeiro	OP16 - Faria	OP25 - Salonen
17:20-17:40	OP8 - Mardyukov	OP17 - Ignatchenko	OP26 - Guieu
17:40-18:00	OP9 - Nakata	OP18 - Buurma	OP27 - Reany

Tuesday - 3 JulyPlenary/ Keynote Session 4 - Chair: **Rui Fausto**

09:00-09:50	PL5 - <i>Development and Application of Low-Cost Quantum Chemistry Methods</i> , Stefan Grimme
09:50-10:20	KN3 - <i>Chiral Induction in Asymmetric Dual Catalysis</i> , Raghavan Sunoj
10:20-10:50	Coffee Break

Plenary/ Keynote Session 5 - Chair: **Carlos Afonso**

10:50-11:40	PL6 - <i>Chemistry and Physics: Synthesis and Vectorization of Drugs Towards the Tumors</i> , Janine Cossy
11:40-12:10	KN4 - <i>Solvent Control of Reaction Outcome Using Ionic Liquids</i> , Jason B. Harper
12:10-12:40	KN5 - <i>Use of Modelling in Pharmaceutical Process Development</i> , Rui Loureiro
12:40-14:30	Lunch

Parallel sessions

	Session 1c Chair: S. Kozuch	Session 2c Chair: M. P. Muñoz	Session 3c Chair: R. Herges
14:30-15:00	IL4 - <i>R. Fausto</i>	IL5 - <i>H. Szatyłowicz</i>	IL6 - <i>S. Luo</i>
15:00-15:20	OP28 - Williams	OP33 - Zipse	OP38 - Sekiya
15:20-15:40	OP29 - Wallis	OP34 - Chechik	OP39 - Auras
15:40-16:00	OP30 - Váňa	OP35 - Thamattoor	OP40 - Kurth
16:00-16:20	OP31 - Duarte	OP36 - Canle	OP41 - McConnell
16:20-16:40	OP32 - Reva	OP37 - Viegas	OP42 - Medronho
16:40	Poster Session and Refreshments		

Wednesday - 4 JulyPlenary/ Keynote Session 6 - Chair: **Hugh Burrows**

09:00-09:50	PL7 - <i>Organic Photocatalysis with Metal-Decorated Titanium Dioxide</i> , Tito Scaiano
09:50-10:20	KN6 - <i>Molecular Assemblers, Molecular Machines Performing Synthesis</i> , Rainer Herges
10:20-10:50	Coffee Break

Plenary/ Keynote Session 7 - Chair: **Igor Alabugin**

10:50-11:40	PL8 - <i>Structure-Reactivity-Selectivity Relationships in Alkali Metal Chemistry</i> , David Collum
11:40-12:10	KN7 - <i>Understanding How Enzymes Work</i> , Maria João Ramos
12:10-12:40	IL7 - <i>Toward Computational Molecular Technology of complex Chemical Reaction Systems: Applications of Red Moon Methodology</i> , Masataka Nagaoka
12:40-13:50	Lunch
14:00	Excursion

Thursday - 5 July**Plenary/ Keynote Session 8 - Chair: Einar Uggerud**

09:00-09:50	PL9 - <i>Exploring Catalytic Landscapes: Don't be Inhibited</i> , Guy Lloyd-Jones
09:50-10:20	KN8 - <i>Understanding Chemoselectivity in Umpolung Acyl Anion NHC Catalysis</i> , AnnMarie O'Donoghue
10:20-10:50	Coffee Break

Plenary/ Keynote Session 9 - Chair: Henrik Ottosson

10:50-11:40	PL10 - <i>Diverse Reactivity of Furan Based Biorenewable Resources</i> , Carlos Afonso
11:40-12:10	KN9 - <i>Quantum tunneling: Computational predictions in exothermic and isothermic reactions</i> , Sebastian Kozuch
12:10-12:40	KN10 - <i>Binding Motifs of Cisplatin with Amino Acid Targets Probed by IR Spectroscopy of Isolated Species</i> , Simonetta Fornarini
12:40-14:30	Lunch

Parallel sessions

	Session 1d Chair: E. Humeres	Session 2d Chair: M. Ludwig	Session 3d Chair: H. Vančik	Session 3e Chair: M. Canle
14:30-15:00	IL8 - U. Wille	IL9 - M. Muñoz	IL10 - A. Gerola	IL11 - S. Hoz
15:00-15:20	OP43 - Shainyan	OP47 - Usui	OP51 - Setaka	OP55 - Lima
15:20-15:40	OP44 - Siehl	OP48 - Frija	OP52 - Pischel	OP56 - Simões
15:40-16:00	OP45 - Maguire	OP49 - Branco	OP53 - Ryan	OP57 - Aureliano
16:00-16:20	OP46 - Khmelinskii	OP50 - Souza	OP54 - Baleizão	OP58 - Ostos
	Conference Dinner			

Friday - 6 July**Plenary/ Keynote Session 10 - Chair: José Gaspar Martinho**

09:20-10:10	PL11 - <i>Organic and Organic-Inorganic Hybrid Materials for Light Emission and Sensing</i> , João Rocha
10:10-10:40	KN11 - <i>Defective Graphenes from Biomass Wastes as Photocatalysts for Solar Fuels Production</i> , Hermenigildo Garcia
10:40-11:10	Coffee Break

Plenary/ Keynote Session 11 - Chair: Hans-Ullrich Siehl

11:10-12:00	PL12 - <i>Is π Single-Bonding (C-π-C) Possible? A Challenge in Organic Chemistry</i> , Manabu Abe
12:00-12:30	Concluding Remarks-
12:30	Lunch

Plenary Lectures

PL1	Bernard Feringa	Dynamic molecular systems
PL2	Frances Arnold	Innovation by evolution: Bringing new chemistry to life
PL3	Peter Chen	Bond strengths in the gas phase, in solution, and in silico: Dispersion effects and big molecules
PL4	Jinpei Cheng	Revitalize bond energetics for understanding ionic liquid chemistry
PL5	Stefan Grimme	Development and application of low-cost quantum chemistry methods
PL6	Janine Cossy	Chemistry and physico-chemistry: synthesis of bioactive molecules and vectorization of antitumor agents towards the tumors
PL7	Tito Scaiano	Organic photocatalysis with metal-decorated titanium dioxide
PL8	David Collum	Structure-reactivity-selectivity relationships in alkali metal chemistry
PL9	Guy Lloyd-Jones	Exploring catalytic landscapes: don't be inhibited
PL10	Carlos Afonso	Diverse reactivity of furan based biorenewable resources
PL11	João Rocha	Organic and organic-inorganic hybrid materials for light emission and sensing
PL12	Manabu Abe	Is π single-bonding (c- π -c) possible? A challenge in organic chemistry

Keynote Lectures

KN1	Peter R. Schreiner	Carbohydrate formation in the absence of biosynthesis
KN2	Luis Garcia-Rio	Competitive and cooperative counterion effects on supramolecular recognition
KN3	Raghavan Sunoj	Chiral induction in asymmetric dual catalysis
KN4	Jason B. Harper	Solvent control of reaction outcome using ionic liquids
KN5	Rui Loureiro	Use of modelling in pharmaceutical process development
KN6	Rainer Herges	Molecular assemblers, molecular machines performing synthesis
KN7	Maria João Ramos	Understanding how enzymes work
KN8	AnnMarie O'Donoghue	Understanding chemoselectivity in umpolung acyl anion NHC catalysis
KN9	Sebastian Kozuch	Quantum tunneling: Computational predictions in exothermic and isothermic reactions
KN10	Simonetta Fornarini	Binding motifs of cisplatin with amino acid targets probed by IR spectroscopy of isolated species
KN11	Hermenegildo García	Defective graphenes from biomass wastes as photocatalysts for solar fuels production

Invited Lectures

IL1	Henrik Ottosson	Relating the triplet state Baird-aromaticity of the macrocycle to that of the monocycle
IL2	Herbert Mayr	Nucleophilicity and electrophilicity parameters for the analysis of cycloaddition reactions
IL3	Shuichi Hiraoka	Nanocube: hyperthermostable discrete self-assemblies in water
IL4	Rui Fausto	A magic wand to control molecular structure
IL5	Halina Szatyłowicz	Physical interpretation of the substituent effect – the quantum chemistry approach
IL6	Sanzhong Luo	Stereo-ionic interaction of protonated amines in asymmetric catalysis
IL7	Masataka Nagaoka	Toward computational molecular technology of complex chemical reaction systems: applications of red moon methodology
IL8	Uta Wille	Position matters: Amide neighbouring group participation facilitates the rate of phenylalanine oxidation in peptides
IL9	María Paz Muñoz	Precious metal catalysis in allene chemistry: from divergent systems to heterobimetallic catalysis
IL10	Adriana Gerola	Reactive and selective supramolecular artificial enzymes for phosphate transfer reactions
IL11	Shmaryahu Hoz	Reaction mechanism diagnostic tool for the reaction of Sml_2

Oral presentations

OP1	Yoshimitsu Itoh	Ring inversion kinetics of photoexcited chiral $[4n]$ annulene derivatives: energetic impact of Baird aromaticity
OP2	Goetz Bucher	Quenching of triplet and singlet excited states by carbon dioxide
OP3	Gavin Jones	Theoretical studies on ring-opening polymerizations by alkoxides and (thio)ureas
OP4	Renana Gershoni-Poranne	Aromatic additivity in three dimensions
OP5	Anat Milo	Physical organic principles for controlling the secondary sphere in organocatalysis
OP6	Charles Perrin	Approach control. Stereoelectronic origin of geometric constraints on N-to-S and N-to-O acyl shifts in peptides
OP7	Leonor Cruzeiro	A kinetic pathway for protein folding <i>in vivo</i>
OP8	Artur Mardyukov	Unravelling Lawesson's reagent – the structure of monomeric (4-methoxyphenyl)phosphine disulfide
OP9	Kazuhide Nakata	Computational study of substituent effects on gas-phase stabilities of amino(phenylboranyl)methyl anions
OP10	Michael Page	The kinetics and mechanism of organo-iridium-catalysed reactions
OP11	Igor V. Alabugin	Coupling N-H deprotonation, C-H activation and oxidation: metal-free $\text{C}(\text{sp}^3)\text{-H}$ aminations with unprotected anilines

OP12

OP13	Eduardo Humeres	Desulfurization route of carbons modified with SO ₂ . Polymerization of the sulfur allotropes intermediates
OP14	Einar Uggerud	C–C bond formation of Mg and Zn activated carbon dioxide
OP15	Daisuke Kaneno	Regioselectivity and reaction mechanism on tricyanovinilation of pyrrole derivatives
OP16	Joaquim Faria	Chemical modification of g-C ₃ N ₄ by β-cyclodextrin for enhanced H ₂ photocatalytic generation
OP17	Alexey Ignatchenko	Beta keto acids: structure, reactivity, and formation as elusive intermediates in heterogeneous catalysis
OP18	Niklaas J. Buurma	Predicting racemisation risk to avoid pointless stereoselective syntheses
OP19	Sota Sato	Chiral intertwined spirals and chiroptical properties - dictated by cylinder helicity
OP20	Thierry Brotin	Molecular recognition of cations by enantiopure cryptophanes
OP21	Hrvoj Vančik	Reaction mechanisms in crystalline molecular solids and their general importance in physical organic chemistry: a case study
OP22	Tatiana Nekipelova	Aggregation-induced chemical reaction: annulation of acetylenes with mixed phosphonium-iodonium ylides
OP23	Philippe Lainé	From single-electron processes to multielectron handling and storage at the molecular level: designing super-electrophores for the next generation of prototypes of photochemical molecular devices for man-made photosynthesis?
OP24	Nuno Basílio	Stimuli-responsive supramolecular systems based on bio-inspired molecular switches
OP25	Laura Salonen	A supramolecular strategy to high-quality covalent organic frameworks
OP26	Samuel Guieu	Organic fluorophores in confined environment: properties and applications
OP27	Ofer Reany	Hetero-Bambusurils
OP28	Ian Williams	Influence of Dielectric Environment upon Isotope Effects on Glycoside heterolysis: computational evaluation and atomic hessian analysis
OP29	John Wallis	New studies of interactions and bond formation in peri-naphthalenes
OP30	Jiří Váňa	On the way from understanding of basic principles to rational design of reaction conditions for palladium catalysed C–H activation reactions
OP31	Luís Duarte	Interaction of formic acid with nitrous oxide and carbon monoxide
OP32	Igor Reva	Spontaneous and photochemically induced reactions of triplet 2-formyl-phenylnitrene in low-temperature matrix
OP33	Hendrik Zipse	Size-induced chemoselectivity in esterification reactions
OP34	Victor Chechik	A new approach to detect short-lived radicals: application to atmospherically-relevant radicals
OP35	Dasan M. Thamattoor	Generation and trapping of 3-thiacyclohexyne

OP36	Moisés Canle	In search for truly green photocatalysts
OP37	Luis Viegas	Reactivity of the atmospherically important hydrofluoropolyethers towards OH: a cost-effective implementation of multiconformer transition state theory
OP38	Ryo Sekiya	Chemical functionalization of nanographene
OP39	Florian Auras	Solvatochromic donor-acceptor covalent organic frameworks
OP40	Dirk Kurth	Metallo-supramolecular polyelectrolytes: From growth kinetics to electrochromic properties
OP41	Anna McConnell	Metal-organic cages: expanding the toolbox of stimuli-responsive behaviour
OP42	Bruno Medronho	Advances in cellulose dissolution and regeneration: From scattering and rheology to a new NMR approach (with some controversial thoughts in between)
OP43	Bagrat Shainyan	Structural, electronic and mechanistic features of unsaturated triflamides
OP44	Hans-Ullrich Siehl	The conundrum of the $C_4H_7^+$ cation Dedicated to George A. Olah
OP45	Oliver Maguire	How to cope with change? The effects of dynamic environments on out-of-equilibrium chemical reaction networks: behaviour diversification and early warning signals
OP46	Igor Khmelinskii	ADH1A - catalysed ATP hydrolysis is coupled to ethanol dehydrogenation by energy transfer
OP47	Satoshi Usui	In-cage reaction of intermediates generated in the photosolvolytic of 3-substituted 2-benzoyloxy-naphthalene
OP48	Luis Frija	Broad-spectrum azole-based molecules: from strong ligands in coordination chemistry to organocatalysts
OP49	Luis Branco	Task-specific ionic liquids for CO_2 capture and catalytic conversion in fuels
OP50	Bruno S. Souza	Aminolysis of 1,8-naphthalic anhydrides in aprotic solvents involves two reaction paths
OP51	Wataru Setaka	Thiophenediyl-bridged macrocages as crystalline molecular dipolar rotors
OP52	Uwe Pischel	Light-induced release of guests from host-guest complexes in water
OP53	Sean Ryan	Light-controlled molecular encapsulation
OP54	Carlos Baleizão	Tuning particle diameter and morphology of hybrid mesoporous silica nanoparticles and application to controlled drug release
OP55	Carlos Lima	Influence of molecular symmetry on the entropy of pure phases
OP56	Ricardo Simões	Development of novel autoreactive and ecological monocomponent adhesives
OP57	Manuel Aureliano	Recent insights into the biological activities of polyoxometalates
OP58	Francisco José Ostos	Influence of the surfactant degree of oligomerization on the formation of cyclodextrin:surfactant inclusion complexes

Poster presentations

Physical Foundations of Organic Reactivity

PP1	Antony J. Stasyuk	Reliable charge assessment on encapsulated fragment for endohedral systems
PP2	Aicha Hassani	Biological activities and phytochemical study of <i>Cistus Salviifolius</i>
PP3	André K. Eckhardt	Spectroscopic evidence for aminomethylene ($\text{H}-\ddot{\text{C}}-\text{NH}_2$) - The simplest amino carbene
PP4	Amin Ismael	Insights into the photochemistry of 5-aminotetrazole derivatives; effect of the saccharyl moiety on the photostability
PP5	Bernard Denegri	Different solvolytic behavior of aryl/alkyl carbonates, carboxylates and phenolates
PP6	Carolina Rio	The termolecular reaction $\text{H} + \text{O}_2 + \text{M} \rightarrow \text{HO}_2 + \text{M}$
PP7	Charles Perrin	Polynomial coefficients. Application to spin-spin splitting by N equivalent nuclei of spin $I > 1/2$
PP8	Cláudio Nunes	Cyclization of triplet 2-formyl-phenylnitrene to 2,1-benzisoxazole: A new heavy-atom tunneling event?
PP9	Davide Corinti	Structural insights into non-covalent halide adducts with tyrosine and 3-nitrotyrosine using ion-spectroscopy
PP10	Elisa M. Brás	The structure and properties of a novel sulphanyl-bridged thiadiazolyl-saccharinate ligand
PP11	Ephrath Solel	Fulvalene: computationally tuning aromaticity and tunneling
PP12	Fynn Röhricht	Anisotropy of the current induced density (ACID) - a new method for prediction and explanation of Diels-Alder reactions
PP13	James Scotson	Effects of binary solvent mixtures on reactivity
PP14	Jan M. Schümann	A synthetical approach to 1,4-di-substituted-cyclooctatetraene based dispersion balances
PP15	Jesús Sanjosé-Orduna	Road to a full understanding of the C-H Activation using $\text{Cp}^*\text{Co(III)}$ metal complexes
PP16	Jin-Dong Yang	iBonD: a databank of measured pKa and BDE values
PP17	Kazuhide Nakata	Computational study of the through-resonance effect operating on (phenylamino)methyl cations
PP18	Lijuan Song	Understanding and utilizing the role of London dispersion interactions in catalysis
PP19	Luuk Kortekaas	Protonation of spiropyrans: revising acidochromism and electrochromism
PP20	Mika Maehara	Interaction of 3,6-dimethylfluorenylidene with ammonia and water at cryogenic temperatures
PP21	Mirela Matic	Solvolytic Reactivity Of Organophosphates And Organophosphinates
PP22	Moisés Canle	Photochemistry of thiazolidines in solution
PP23	Morten Peters	Development of a contrast agent based on Fe^{III} -recordplayer

PP24	Nadezhda Danilenko	Quantum chemical calculation of SuFEx reaction thermodynamics
PP25	Neshat Rozatian	Kinetics of fluorination of 1,3-dicarbonyls
PP26		
PP27	Pengju Ji	Homolytic bond dissociation enthalpies in room temperature ionic liquids
PP28		
PP29	Rikuo Akisaka	Kinetic stabilization of singlet-2,2-dialkoxy-1,3-diradical by introducing bulky substituents
PP30	Rui M. Borges dos Santos	Thermochemistry of peroxy radicals: a combined photoacoustic calorimetry, quantum chemistry, and molecular dynamics study
PP31	Jorn D. Steen	Proton dependent redox chemistry of spiropyrans
PP32	Sayaka Hatano	Development of a photo-induced fast spin-state switching molecule
PP33	Gulce Ogruç-Ildiz	Structural Aspects and Reactivity of 5-Methylhydantoin
PP34	Zoe Dominguez	Chiroptical properties of azabora[5]helicene architectures
PP35	Yusuke Inagaki	Rotation of the π -system rotor in crystalline molecular gyrotops
PP36	Zoran Glasovac	The role of intramolecular hydrogen bonds in construction of model donor-acceptor salt bridged crystals

Reaction mechanisms and Catalysis

PP37	Uta Wille	Decoding the mechanism of environmental radical polyester degradation
PP38	Xiuling Cui	Alkynone-based synthesis of heterocycles
PP39	Alba Pereira Vilar	Formation of pillar[5]arene based stable rotaxane with azobenzene
PP40	Alyssa Gilbert	Investigation of the effects of ionic liquids as solvents on a unimolecular substitution process
PP41	Anastasiia Kovrizhina	Methods for the preparation of new 11 <i>H</i> -indeno[1,2- <i>b</i>]quinoxalin-11-one oxime analogs as promising JNK inhibitors
PP42	André D. Lopes	Catalytic performance of pyridyl-benzimidazole oxidomolybdenum(vi) complex in olefin epoxidation
PP43	Anna Rovaletti	Theoretical investigation on the effect of ligand bulkiness on the reactivity of organometallic complexes
PP44	Thomas Dent	Investigation of the caesium effect in palladium catalysed coupling reactions
PP45	Barbara Ticconi	Oxidation of aliphatic and aromatic amino acids with H ₂ O ₂ catalyzed by a nonheme imine based iron complex
PP46	Christina McCulley	A mechanistic examination of the influence of alkene substitution on rates of biomimetic platinum-promoted polyene polycyclization

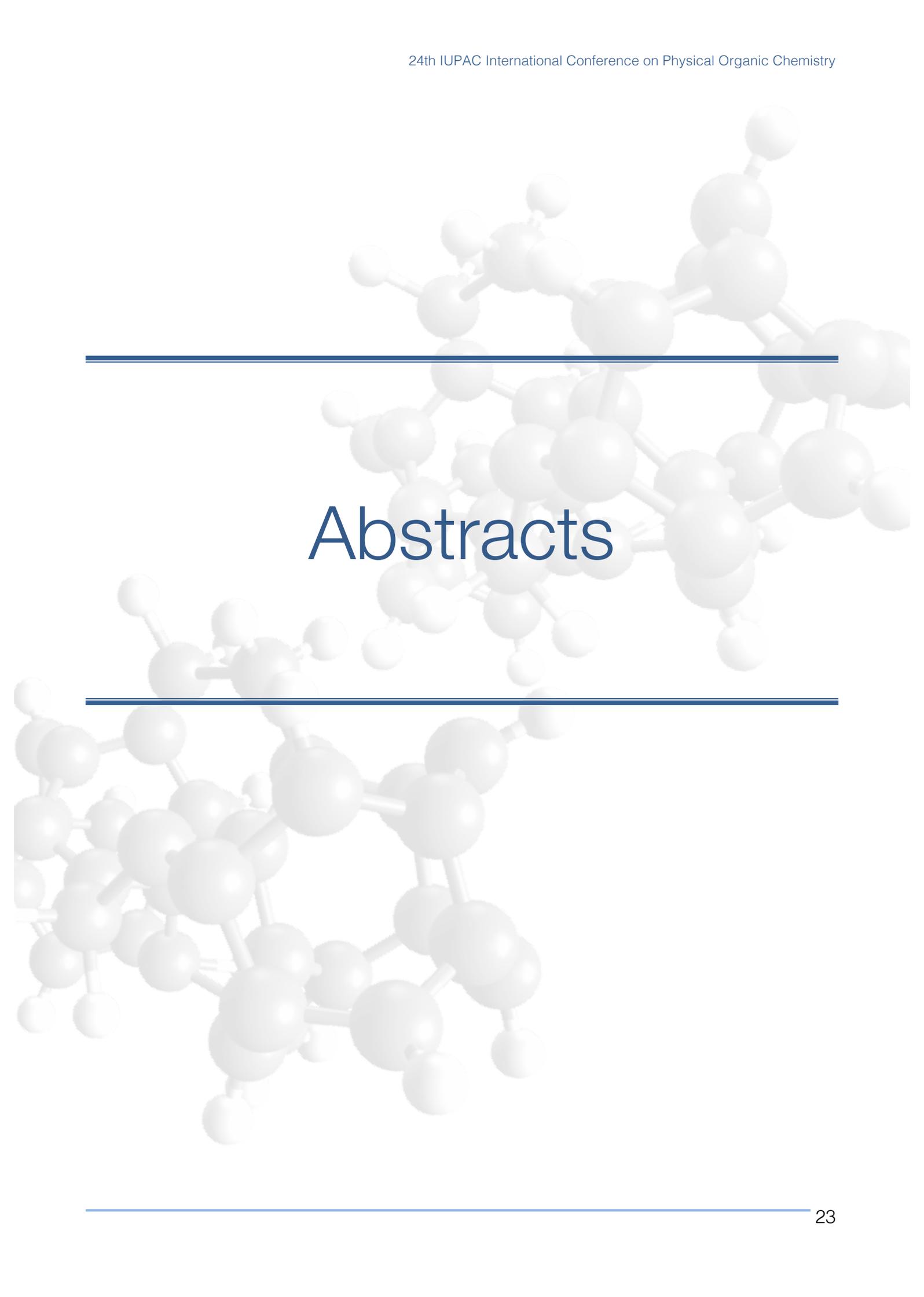
PP47	Christof Jaeger	Thermodynamic reaction control in radical enzymes and the role of orientated electric fields
PP48	Elisa M. Brás	UV-induced photolysis of a dispiro-1,2,4-trioxolane with antiparasitic activity
PP49	Gabriel J. Reyes-Rodríguez	Evans enolates: lithium hexamethyldisilazide-mediated enolization of acylated oxazolidinones
PP50	Hidetoshi Noda	On the mechanism of direct amidation catalyzed by the B ₃ NO ₂ heterocycle
PP51	Inmaculada Moreno	Oxidation of Desmetryn by Peroxynitrous Acid
PP52	Ivana Biljan	Self-assembly and dimerization of aromatic dinitroso derivatives on gold surface
PP53		
PP54	Jiayun Zhu	Towards an organocatalytic route for the d ¹ -deuterated of aldehydes
PP55	Ana R. Garcia	Chemistry of model catalytic systems at very low pressure: studies by RAIRS
PP56	Jiri Hanusek	Kinetics and mechanism of Cu(I)-catalyzed [3+2]cycloaddition between phenyl sydnone and phenylacetylenes
PP57	João Lourenço	Catalytic conversion of glycerol to value-added products
PP58	Joel Le Bars	Kinetic investigation of methyl bromide reaction with ethanolamine
PP59	Julian Helberg	The phosphane-catalyzed oligomerization of isocyanates – mechanistic study and identification of a transient intermediate
PP60	Karin Schaffarczyk McHale	Interactions of the components of ionic liquids with species along the reaction coordinate of substitution processes
PP61	Kevin O. Maduka	Synthetic and kinetic evaluation of triazolyl mimics of thiamine pyrophosphate (TPP) for biocatalysis
PP62	Lídia Cavaca	Oleuropein: a valuable chiral building block
PP63	Long Zhang	The enantiocontrol in primary amine catalysis
PP64	Patrick Jüstel	Concurrent S _N 1 and S _N 2 mechanisms in solvolysis reactions
PP65	Paulina Pavez	Dual function of amino acids ionic liquids (AAILs) on the degradation of organophosphate pesticide, Paraoxón®
PP66	Pedro Horta	Synthesis and Structure of a novel O-linked diazine-quinolone conjugate
PP67	Markus Schaueremann	NMR evidence for the aromatic, thiamine-like Breslow-Intermediate
PP68	Miroslav Ludwig	Push-Pull dicyanoimidazoles in photoredox catalysis
PP69	Nelaine Mora-Diez	Modelling the Repair of Damaged Proteins by Antioxidants
PP70	Rafael Gomes	Mechanistic studies on the formation of novel cyclopentenones from activated furans
PP71	Raquel Fernandes	Photocatalytic synthesis of benzaldehyde derivatives

PP72	Rebecca Hawker	Rational selection of the components of an ionic liquid solvent to control the reaction outcome of some organic processes
PP73	Roberto Colunga	A Radical twist in the mechanism of lithium-halogen exchange
PP74	Roberto Figueroa	Synthesis of amino acid ionic liquids (AAILs) and their effect in the reactivity of thiol-Michael addition reaction
PP75	Rodrigo Montecinos	Synthesis and characterization of pillar[5]arene functionalized with hydroxy-L-proline. Searching an asymmetric organocatalyst
PP76	Ricardo Ferreira Affeldt	Experimental and theoretical evidence of intramolecular bifunctional catalysis in amide cleavage
PP77	Roland Löw	Relaxation time measurements of azo functionalized TATA platforms
PP78	Romain Lepage	Computational study of the mechanism of glycosylation of L-idose derivatives
PP79	Tainah Dorina Marforio	A mechanistic insight into CNT-catalyzed oxidative dehydrogenation of ethylbenzene to styrene. A DFT computational study
PP80	Tatiana Nekipelova	Mechanism of the annulation of 4-ethynylanisole with mixed phosphonium-iodonium ylide

Supramolecular and Systems Chemistry

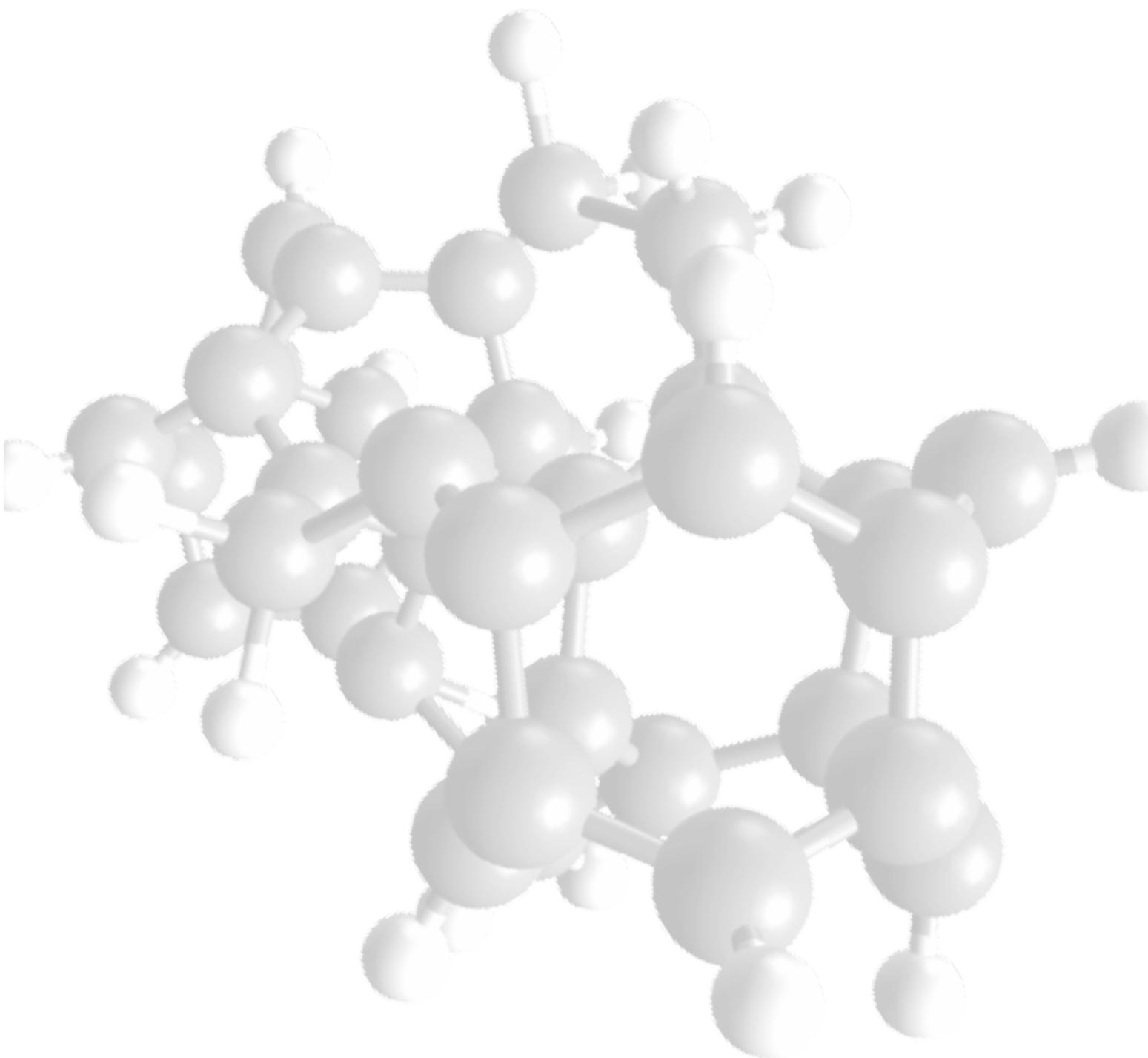
PP81	Sebastian Hamer	Dipolar molecular rotors in surface-anchored metal organic frameworks
PP82	Rui Fausto	The role of perchlorate anion on dimerization of a macrocyclic binuclear Cu(II) complex: comparison with a mononuclear Ni(II) macrocyclic complex
PP83	Silvia Hristova	Theoretical design and spectral investigations of tautomeric rotary switches
PP84	Agustin Morales	Use of photolabile Ru(II) complexes for supramolecular release
PP85	Alexandra Filipe	A brief survey on diffusion wave spectroscopy in soft matter systems
PP86	Alexandre Miranda	Synthesis and anion recognition by dinitrophenylurea-dihomooxalix[4]arene receptor
PP87	Alvaro Cañete	Synthesis and spectroscopic characterization of 4-(diethylamino)salicylaldehyde bearing at coumarin derivative. Effect of Cucurbit[7]uril encapsulation on its spectral properties
PP88	Andreas H. Heindl	Tuning the switching properties of macrocyclic azobenzenes by ring strain
PP89	Angel Acuña Barros	Nitric Oxide release from a cucurbituril encapsulated NO-donor
PP90	Baya Berka-Zougali	Comparison of the chemical composition and biological activities of essential oils obtained by classical steam distillation (SD), Instant Controlled Pressure Drop (DIC) and Ultrasound Assisted Extraction (UAE) from Myrtle Leaves Growing Spontaneously In Algeria
PP91	Davor Margetic	Self-Assembly of aromatic donor-acceptor systems by guanidine-carboxylate binding
PP92	Rubén Martín	Encryption of chemical information in a supramolecular assembly

PP93	Guntram Schwarz	Electrochromic properties of metallo-supramolecular polyelectrolytes (Mepes)
PP94	Joana Cristo	How does cholesterol affect the fluidity of model lipid bilayers at the molecular level?
PP95	João Ravasco	New double functionalizable trans-cyclooctenes for enhanced spatial and temporal resolution study of biological systems
PP96	Jackson Alcazar	Reactivity of carbonates and thiocarbonates derivatives toward hydrolysis reaction in the presence of calixarene
PP97	J.C. Mejuto	Stability of iprodione in AOT-based reverse micelles under alkaline conditions
PP98	Jorge Martins	Measuring dielectric constants of lipid bilayers: excluding experimental artifacts from pyrene fluorescence in liposomes
PP99	José G. Santos	Hydrolysis reactions of carbonates and thiocarbonates derivatives. Supramolecular catalysis by cucurbit[7]uril
PP100	Kajetan Dąbrowa	Dynamic control of ion-pair binding by photo-tunable azobenzene-derived hosts
PP101	Koki Ikemoto	Synthesis and structures of nanometer-sized geodesic phenylene bowl
PP102	Leandro Scorsin	A kinetic study with neutral and cationic dioxolanes catalyzed by CB7
PP103	Marcella S. H. Queiroz	Study of phase solubility of bioactive naphthoquinones
PP104	Margarita E. Aliaga	Cucurbit[7]uril encapsulation effect on tautomerism equilibrium in aza-coumarin and quinoxalinone scaffolds. Experimental and molecular modeling studies
PP105	Matthew Watson	Predicting reactivity in binary solvent mixtures using a supramolecular solvation model
PP106	Miguel A. Romero	Binding of terpenes by cucurbituril macrocycles
PP107	Nelaine Mora-Diez	Macroscopic pKa prediction of polyprotic acids from DFT calculations: the case of acetohydroxamic acid
PP108	Niklaas Jan Buurma	I2CITC : modular deconvolution of ITC data for complex equilibrium systems
PP109	Olimpo García-Beltrán	Synthesis and characterization of a new coumarin-derivative chemosensor to detect mercuric ions
PP110	Orlando Oliveira	Towards catalytic metalated covalent organic frameworks through supramolecular strategies
PP111	Patricia Remón	Chemical communication in a supramolecular cascade
PP112	Pravat Mondal	<i>Thio</i> -Bambusurils
PP113		
PP114	R. J. Mayer	From peroxides to hypohalites: towards a general understanding of the reactivities of anionic oxygen nucleophiles



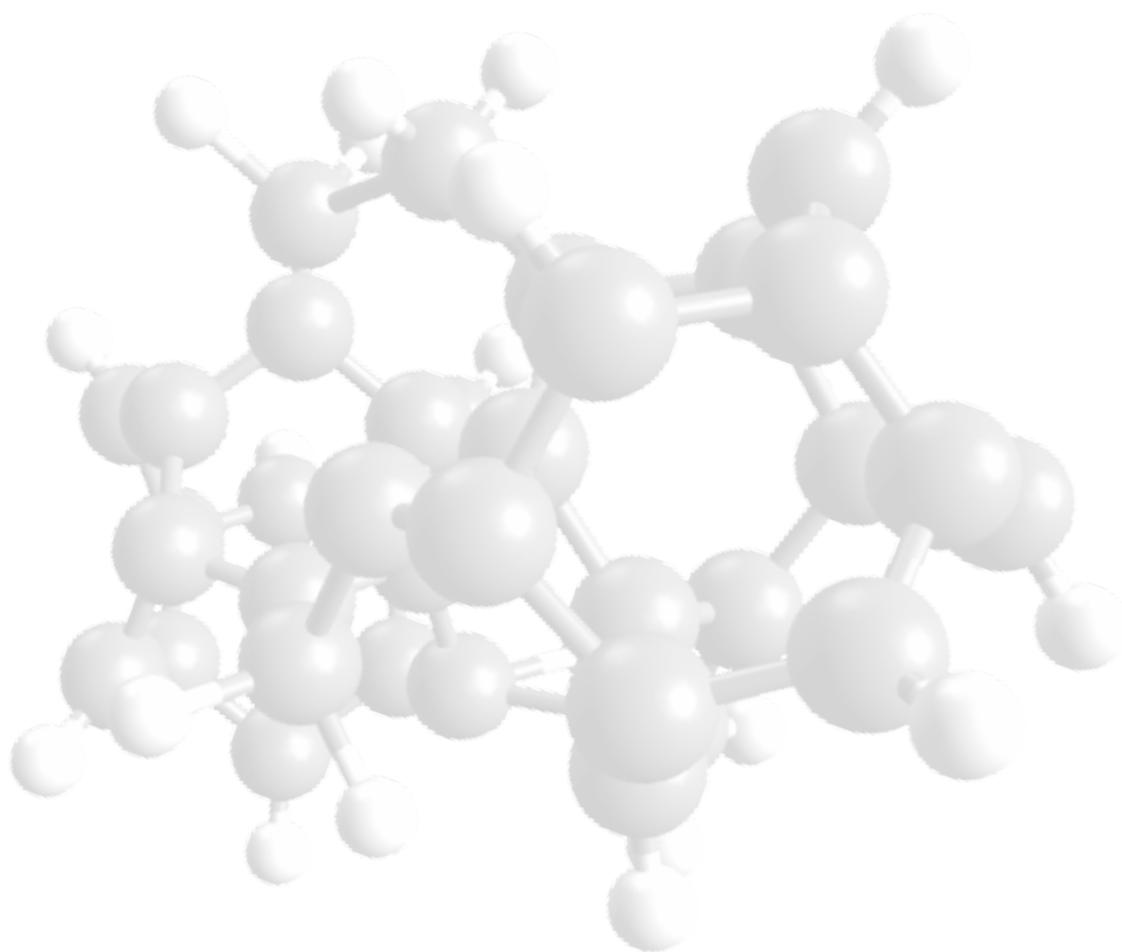
Abstracts

ICPOC 24



Plenary Lectures

ICPOC 24



Plenary 1



Professor Bernard L. Feringa obtained his PhD at the University of Groningen, where he was appointed full professor in 1988, after working as research scientist for Shell. Under his guidance the Feringa group has developed extensive expertise in the fields of organic chemistry, nanotechnology and asymmetric catalysis. Was awarded the 2016 Nobel Prize in Chemistry, together with Sir J. Fraser Stoddart and Jean-Pierre Sauvage, "for the design and synthesis of molecular machines.

Dynamic Molecular Systems

Ben L. Feringa

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The fascinating molecular motors and machines that sustain life offer a great source of inspiration to the molecular explorer at the nanoscale. Among the major challenges ahead in the design of complex artificial molecular systems is the control over dynamic functions and responsive far-from-equilibrium behaviour. Chemical systems ultimately require integration of structure, organization and function of multi-component dynamic molecular assemblies at different hierarchical levels. A major goal is to achieve and exploit translational and rotary motion.

In this presentation the focus is on the dynamics of functional molecular systems as well as triggering and assembly processes. We design switches and motors in which molecular motion is coupled to specific functions. Responsive behaviour will be illustrated in self-assembly, responsive materials and photopharmacology. The design, synthesis and functioning of rotary molecular motors will also be presented with a prospect toward future dynamic molecular systems.

Information on <http://www.benferinga.com>

- Molecular Machines: Nature, September 2015
- Molecular Switches: Chemistry World, June 2016

Plenary 2



Professor Frances Arnold is the Linus Pauling Professor of Chemical Engineering, Bioengineering and Biochemistry at the California Institute of Technology. Ph.D., Chemical Engineering, University of California, Berkeley, 1985; Postdoctoral, UC Berkeley, Chemistry, 1985; Postdoctoral, Caltech, Chemistry, 1986. Research focuses on protein engineering, directed evolution, creating new enzymes, biocatalysis.

Innovation by Evolution: Bringing New Chemistry to Life

Frances Arnold

California Institute of Technology, Pasadena, U.S.A.

Not satisfied with nature's vast catalyst repertoire, we want to create new protein catalysts and expand the space of genetically encoded enzyme functions. I will describe how we use the most powerful biological design process, evolution, to optimize existing enzymes and invent new ones, thereby circumventing our profound ignorance of how sequence encodes function. Using chemical intuition and mimicking nature's evolutionary processes, we can generate whole new enzyme families that catalyze synthetically important reactions not known in biology. Exploiting the vast world of non-natural carbene chemistry, we recently reported the first enzymes that forge C-Si and C-B bonds in living cells and other enzymes that catalyze alkyne cyclopropanation to make highly strained carbocycles. Uncovering the mechanisms of these new enzymes derived from natural iron-heme proteins provides a basis for discovering yet more new biocatalysts for increasingly challenging reactions. These new capabilities expand the scope of molecules and materials we can build using synthetic biology and move us closer to fully DNA-programmed chemical synthesis.

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Plenary 3



Professor Peter Chen has been Full Professor of Physical-Organic Chemistry since September 1994. From September 2007 to September 2009 he has been Vice President Research and Corporate Relations of ETH Zurich. His research combines detailed physical measurements with the planning and synthesis of molecules, making it possible to design and test intuitive models of the energetics and reactivity of reactive intermediates in organic and organometallic chemistry.

Bond Strengths in the Gas Phase, in Solution, and in Silico: Dispersion Effects and Big Molecules

Prof. Dr. Peter Chen*

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Van der Waals attractive forces have often been neglected because each individual interaction is small. Nevertheless, for organic and organometallic molecules of distinctly moderate size, e.g. 100-200 atoms, the large number of small, attractive interactions lost upon cleavage of a covalent bond can add up to a significant contribution to the bond dissociation energy, in the range of tens of kcal/mol. Whereas structural evidence for an “extra” stabilization has been reported, experimental measurement of bond dissociation energies for large molecules in the gas phase are surprisingly rare, given some not-so-obvious technical constraints. We report a comprehensive experimental and computational study of 36 proton-bound dimers for which a central $^+N-H\cdots N$ bond is constant, but the number and extent of non-bonding interactions can be varied systematically. We report experimental BDE measurements in the gas phase, and in solution, accompanied by computational studies using DFT and DLPNO-CCSD(T) methods taken to the CBS limit. Moreover, we include solvation with dispersion-corrected PCM models. Lastly, we take the experiments and computations on to more complicated systems with metal-metal bonds for which the same kind of constraints are even more serious.

Plenary 4



Professor Jin-Pei Cheng is since 1988 professor at Nankai University (as vice president in 1995-2000). He received his Ph.D. in 1987 from Northwestern University, Evanston, Ill., where he learned more details on chemical bonds. In 2012, he established the Centre of Basic Molecular Science (CBMS) at Tsinghua University where he serves as the director and a fulltime professor. The Cheng's groups at Tsinghua CBMS and at the State key Lab of Elemento-organic Chemistry at Nankai have primarily focused on bond energetics and its applications since late-80's.

Revitalize Bond Energetics for Understanding Ionic Liquid Chemistry -Taking absolute pK_a study as example

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Most chemical substances known today are organic compounds that are normally stable. The major work of organic chemists is hence to explore strategies to activate certain bonds and reorganize them into new molecules. In this regard, the basic concept "bond energy" should be most essential in study. Indeed, use of the bond parameters has played a primary role in advancing traditional chemistry into a more rational track, as evident from the landmarks of Hammett, Brønsted, and Marcus for a few examples. However, a hasty use of these simple guidelines to handle complicated situations like C-H activation, photocatalysis, etc., may often encounter problems. This should not be thought as a collapse of the central role of bond energy, but rather, it actually points out a definite need for many more relevant bond energetic data that are still unknown and a cogitative use of them in analysis.¹ In the past century, extensive bond energy parameters, such as BDE, pK_a, etc., have been accumulated.² However, those scales are derived almost entirely from gas phase or conventional molecular solvents, leaving the absolute bond energetic scales in ionic liquids (ILs) completely empty.

Ionic liquids, as an emerging primary category of media system, are comprised entirely of cations and anions that are highlighted as environmentally benign substitutes for volatile organic solvents. Over the past decades, enormous research efforts have been made on their applications in organic synthesis, catalysis, electrochemistry, and so on. By contrast, surprisingly little is known on many fundamental aspects such as the induced changes of bonding natures by this new medium system. Consequently, the significant differences between the chemistries in molecular solvents and in ILs are not yet well understood. Therefore, systematic and rigorous studies on the energies required for bond reorganizations in ILs are imperatively needed. In this respect, the most important and starting point of research should be equilibrium acidity (pK_a), due to its proven importance in chemistry.

In recent years, we have established a good number of absolute pK_a scales in several commonly used neat ILs by homogeneous approach (indicator method). These precisely measured bond energetic data provide us a good chance to disclose the insights behind the data for the mysterious "Ionic Liquid Effect" and for other interesting chemistries in this amazing new medium system.³

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Plenary 5



Professor Stefan Grimme, a theoretical chemist from the Mulliken Center for Theoretical Chemistry at University of Bonn, has been professor at the University of Bonn since 2011. The general Research Interests are the development of quantum chemical methods, DFT and density functionals, non-covalent interactions in large molecules and condensed matter systems, multi-level modelling, tight-binding QM methods, molecular crystals, excited state properties and electronic spectra, chiral molecules, reaction mechanisms.

Development and Application of Low-cost Quantum Chemistry Methods

Stefan Grimme

Mulliken Center for Theoretical Chemistry

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The computational treatment of large molecular systems in a multi-level scheme requires quantum chemistry methods which are able to provide good structures, vibrational frequencies as well as reasonable non-covalent interactions for more or less arbitrarily composed systems.

The talk presents our efforts in this context to develop physically sound and numerically well behaved mean-field quantum chemical approximations, namely composite schemes like HF-3c (minimal basis set), PBEh-3c (DZ hybrid level), or B97-3c (TZ GGA level).

Very detailed benchmarks for the huge GMTKN55 energy database, supramolecular non-covalent interactions, molecular crystals, as well as molecular structures are discussed. Furthermore, a recently developed a special purpose self-consistent density functional tight-binding scheme covering all spd-block elements up to $Z=86$ (GFN-xTB) is introduced. Key features of the Hamiltonian are the use of partially polarized Gaussian type orbitals, atomic-shell charges, diagonal third-order charge fluctuations, coordination number-dependent energy levels, and the well established D3 dispersion correction.

Application of this method and a very recent extension (GFN2-xTB) to various problems in chemistry will be shown like optimization of large supramolecular systems, computation of electron ionization mass spectra, automated search for protomers, or molecular conformation search for the automatic prediction of NMR spectra.

Plenary 6



Professor Janine Cossy graduated from the University of Reims. After a postdoctoral stay at the University of Wisconsin, she returned to Reims where she became CNRS Director of Research in 1990. The same year, she moved to Paris to become Professor of Organic Chemistry at the Ecole Supérieure de Physique et de Chimie Industrielles de la Ville de Paris (ESPCI). Her work focuses on radical, photochemical, organometallic reactions, on rearrangements, on the synthesis of bioactive products (antifungal, anti-inflammatory, antitumor agents), and on the vectorization of drugs toward tumors.

Chemistry and Physico-Chemistry **Synthesis of Bioactive Molecules and Vectorization of Antitumor Agents** **Towards the Tumors**

Janine Cossy

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The development of new synthetic tools is important to increase the chemical space and to have access to new bioactive compounds that can lead to new drugs.

For our part, we are particularly interested in the synthesis of anti-inflammatory and antitumor agents. We will show how we can synthesize these compounds by developing simple synthetic tools. In addition, in the case of antitumor agents, and in order to decrease their secondary effects, we will show how we can vectorize these molecules toward the tumor either by synthesizing immunoconjugates or by realizing the encapsulation of drugs into microdroplets and then how we can liberate the bioactive substance into the tumor.

Plenary 7



Professor J.C. (Tito) Scaiano currently holds the Canada Research Chair in Applied Photochemistry at the University of Ottawa. He has been recognized with many national and international awards for his work in photochemistry. His research interests include organic photochemistry, nanomaterials, catalysis, sunscreens, laser induced photochemistry, lithographic imaging, and single molecule spectroscopy. In June 2016, uOttawa appointed Scaiano as the founding Director of the newly created Centre for Advanced Materials Research (CAMaR), that promote the invention, characterization and use of a wide range of materials.

Organic Photocatalysis with Metal-Decorated Titanium Dioxide

Juan C. (Tito) Scaiano

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University of Ottawa, Ottawa, Ontario K1N 6N5, Canada*

Visible-light-mediated photo-redox catalysis has emerged as a valuable concept in organic synthesis to induce selective organic transformations avoiding the undesired photo degradation of organic molecules under UV light exposure. Titanium dioxide (TiO_2) is a well-known semiconductor and its use as a photocatalyst has been widely explored as an alternative heterogeneous photoredox catalyst. Heterogeneous photo-catalysis is a promising technology providing both facile catalyst separations, and potential reuse. The main disadvantage of the use of pure nanometric TiO_2 as a photocatalyst is the large band gap ($>3.1\text{eV}$) of this semiconductor that can only absorb UV light ($<400\text{ nm}$). Decorating TiO_2 with noble transition metals such as Pd, Au or Cu, among others, can overcome this problem as the resulting materials usually absorb light in the visible region and can be useful in isomerizations, hydrogenations,¹ C-C couplings² and click chemistry.³

We present here our efforts to develop hybrid catalysts based on TiO_2 decorated with noble metal or metal oxide nanoparticles, with emphasis on palladium, which can be suitable catalysts for different organic transformation under mild conditions. The first example involves Pd/PdO NPs-doped TiO_2 catalyst, known as an efficient photo-catalyst for olefin hydrogenation in the absence of H_2 gas upon UV irradiation. Its photocatalytic activity can be tuned in favour of hydrogenation or isomerization of benzyl-substituted alkenes simply by changing the irradiation wavelength. The isomerization can be thermally induced in air or driven by visible light irradiation at room temperature under Argon atmosphere, while switching to UV irradiation leads to efficient hydrogenation. The versatility of the catalyst is also tested for Sonogashira and Ullmann couplings upon visible light irradiation.

The use of heterogeneous catalysis has many advantages comparing to the homogeneous counterparts, such as easy catalyst separation and reusability. However, one of the main challenges yet to solve, is to ensure good performance after the first catalytic cycle. Active catalytic species being poisoned or inactivated during the catalytic process is usually the main reason behind the loss of catalytic efficiency. We propose a different approach in order to extend the catalyst lifetime based on the crop rotation system used in agriculture. Thus, the catalyst (Pd@TiO_2) is used alternating different catalytic reactions, which in turn reactivate the catalyst surface, extending the reusability of the material, preserving its selectivity and efficiency. As a proof of concept, different organic reactions (crops) were selected and catalyzed by the same catalyst during target-molecule rotation reactions.

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Plenary 8



Professor David B. Collum, professor of Chemistry and Chemical Biology at Cornell University, received his PhD in 1980 at Columbia University then returning to Cornell, as an assistant professor, where he had started his studies. He also runs the Collum group focuses on how aggregation and solvation dictate the reactivity and selectivity of organolithium compounds commonly used by synthetic chemists in both academia and the pharmaceutical industry. A combination of spectroscopic, kinetic, and computational methods bridge organic, organometallic, and analytical chemistry.

Structure-Reactivity-Selectivity Relationships in Alkali Metal Chemistry

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After decades of studying N-lithiated and C-lithiated species aided by detailed structural assignments based on X-Li scalar coupling, we have begun making progress in two new directions: the chemistry of lithium enolates and in organosodium chemistry. We will describe an overview of how solution structures influence reactivities and selectivities. In all studies the role of solvation is of paramount importance. Although we continue to emphasize structure and mechanism, connecting these with synthetic methodologies is of increasing focus.

Plenary 9



Professor Guy Lloyd-Jones, Fellow of the UK National Academy of Science and Fellow of the National Academy of Scotland, has been since 2013 the Forbes Chair of Organic Chemistry at University of Edinburgh. PhD in 1993 at University of Oxford. Research interest are related with the investigation of the mechanism of homogeneous chemical reactions, the design of new or improved chemical processes, and the development of new techniques and instrumentation to achieve this.

Exploring Catalytic Landscapes: Don't be Inhibited

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A selection of data from our recent mechanistic investigations into activation of catalysts (Au, Rh, Pd) and reagents (R_3RSiX and RBX_2) in coupling, addition, and substitution reactions will be presented, in addition to unpublished studies.¹⁻³

Gaining an understanding of the main mechanisms of action in these nominally simple processes - has required the acquisition of data under a broad range of conditions in order to fully elucidate some surprising inhibition effects. Indeed, such unusual kinetic behaviour can, when carefully interpreted, facilitate the design of new processes and applications in synthesis. These studies have involved collection of large sets of kinetic data, requiring redesign of analytical methods to allow this to be achieved in a time-efficient and material-efficient manner on standard instruments.⁴

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Plenary 10



Professor Carlos A. M. Afonso is currently Full Professor at Faculty of Pharmacy, University of Lisbon. Ph.D. in 1990 under the supervision of Professor Christopher Maycock, became Assistant Professor at New University of Lisbon and Associate Professor at the Instituto Superior Técnico in Lisbon (2004-2010). Research focuses on new catalyzed synthetic methodologies, green chemistry, synthetic valorisation of natural natural resources, biotransformations and synthesis of bioactive molecules.

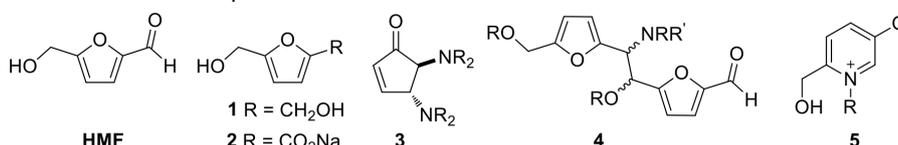
Diverse Reactivity of Furan Based Biorenewable Resources

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Due to the reduction of fossil resources for energy consumption and platform chemicals for different purposes, several building blocks derived from renewable resources such as ethanol, glycerol, lactic acid, furfural, succinic acid, levulinic acid, are already in use or considered with potential importance in the near future.¹ Among them, 5-hydroxymethyl-furfural (HMF) has been considered a very promising intermediate building block due to its potential rich chemistry that allows different transformations such as to biofuels, polymer monomers, levulinic acid, adipic acid, caprolactam and caprolactone and many other more specific molecules.² In line with our interest in the valorization of natural resources, will be described recent achievements from this laboratory on the transformation of HMF and furfural to several building blocks such as via Cannizzaro reaction 1,2, amine condensation-rearrangement-cyclization 3, homo Mannich reaction of trienamine/iminium-ion pair 4, N-alkyl-pyridinium salts 5, oxidation and Friedel-Crafts reaction by taking advantage of the reactivity of the furan core.³ In addition, will be presented some biological activity of the synthesized heterocycles and selection guidelines for human and environmental exposure of furfural-related compounds.⁴



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Plenary 11



Professor João Rocha got his Ph.D. in 1990 from the Department of Chemistry, University of Cambridge, UK, and in 1999 became Full Professor at Aveiro University, Portugal. He is member of the European Academy of Sciences and of the Lisbon Academy of Sciences, and Fellow of Royal Society of Chemistry. He has published ca. 500 papers with 15,000+ citations (h 58) and 4 patents. Research interests: nanoporous transition metal and Ln silicates, and other light emitting materials, and Metal Organic Frameworks for sensing; nanosystems for imaging and drug delivery; solid-state NMR and X-ray diffraction.

Organic and Organic-Inorganic Hybrid Materials for Light Emission and Sensing

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I shall review recent work carried out in Aveiro on the design, synthesis and characterisation of lanthanide (Ln)-bearing organic-inorganic hybrids, and organic solids, for light emission and temperature sensing.

Non-invasive, accurate, and self-referenced measurement of temperature at the submicrometer scale is of great interest in many fields. The thermal dependence of the phosphor's luminescence, provides high detection sensitivity and spatial resolution with short acquisition times in, e.g., biological fluids, strong electromagnetic fields, and fast-moving objects.¹

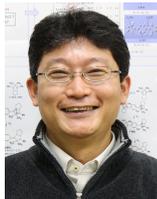
Ln-bearing materials are the most versatile probes used in luminescence nanothermometry. Metal organic framework thermometers ascertain the absolute temperature via the measurement of the intensity of two transitions of distinct emitting centres (so-called dual-centre thermometers):² a ligand (linker) and a Ln³⁺ ion (e.g., Eu³⁺ or Tb³⁺); two Ln³⁺ ions (so far, Eu³⁺ and Tb³⁺); or a dye hosted in the MOFs nanopores and a Ln³⁺ ion. The optical properties of such materials are amenable to tuning and so is their thermometry response.³⁻⁵ Another type of luminescent materials, oleic acid-capped core-shell NaYF₄:Yb/Er nanoparticles, dispersed into suitable solvents, perform as upconversion nanothermometers, allowing the investigation of the century-old problem of measuring the instantaneous Brownian velocity of 'ultramicroscopic' particles.⁶ Moreover, thermometers and heaters may be integrated offering potential applications in nanotechnology and biomedicine (e.g., hyperthermia).⁷ Such heater-thermometer nanoplatfoms are capable of measuring the plasmon-induced local temperature increase of (CTAB capped) Au nanorods via the ratiometric upconversion of (Gd,Yb,Er)₂O₃ nanothermometers, both linked together via a PSS polymer.

Finally, we have developed novel organic dyes exhibiting aggregation-induced emission enhancement (contrasting with most dyes that are non-emissive in concentrated solutions or in the solid state) and wish to report some intriguing findings.⁸

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Plenary 12



Professor Manabu Abe is doctor of Engineering from the Kyoto Institute of Technology, and became a Full Professor in Organic Chemistry at the Department of Chemistry, Graduate School of Science, Hiroshima University (HIRODAI) in 2007. His research focuses on reactive intermediates chemistry, especially on diradicals, organic photochemistry and unusual molecules.

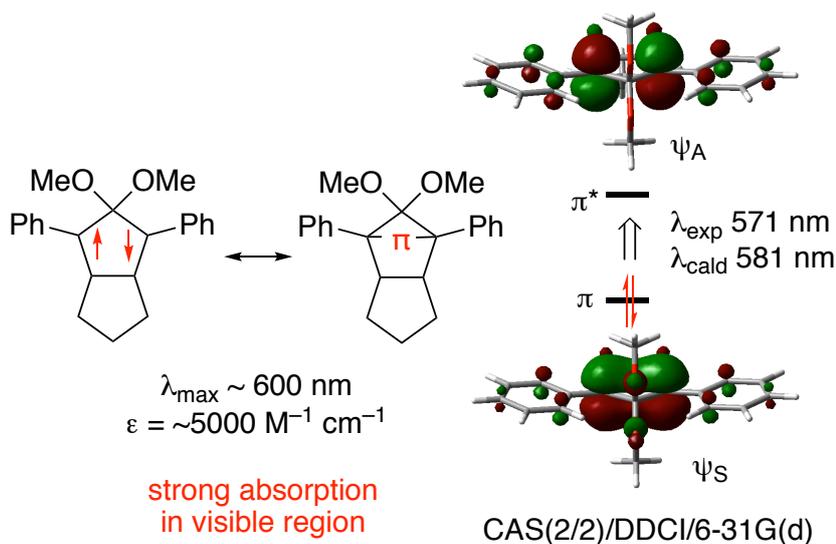
Is π -Single Bonding (C– π –C) Possible? A Challenge in Organic Chemistry

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Chemical bonding systems determine the nature of molecules. In organic chemistry, there are two bonding types for carbon–carbon connections: σ -bonding and π -bonding. In this lecture, several aspects of studies in the last two decades addressing a naive question “Is π -single bonding (C– π –C) possible?” will be presented: (1) features of π -single bonded species; (2) molecular design for π -single bonding; (3) generation and detection of singlet diradicaloids with a π -single bonding character; (4) future prospects of π -single bonded species.

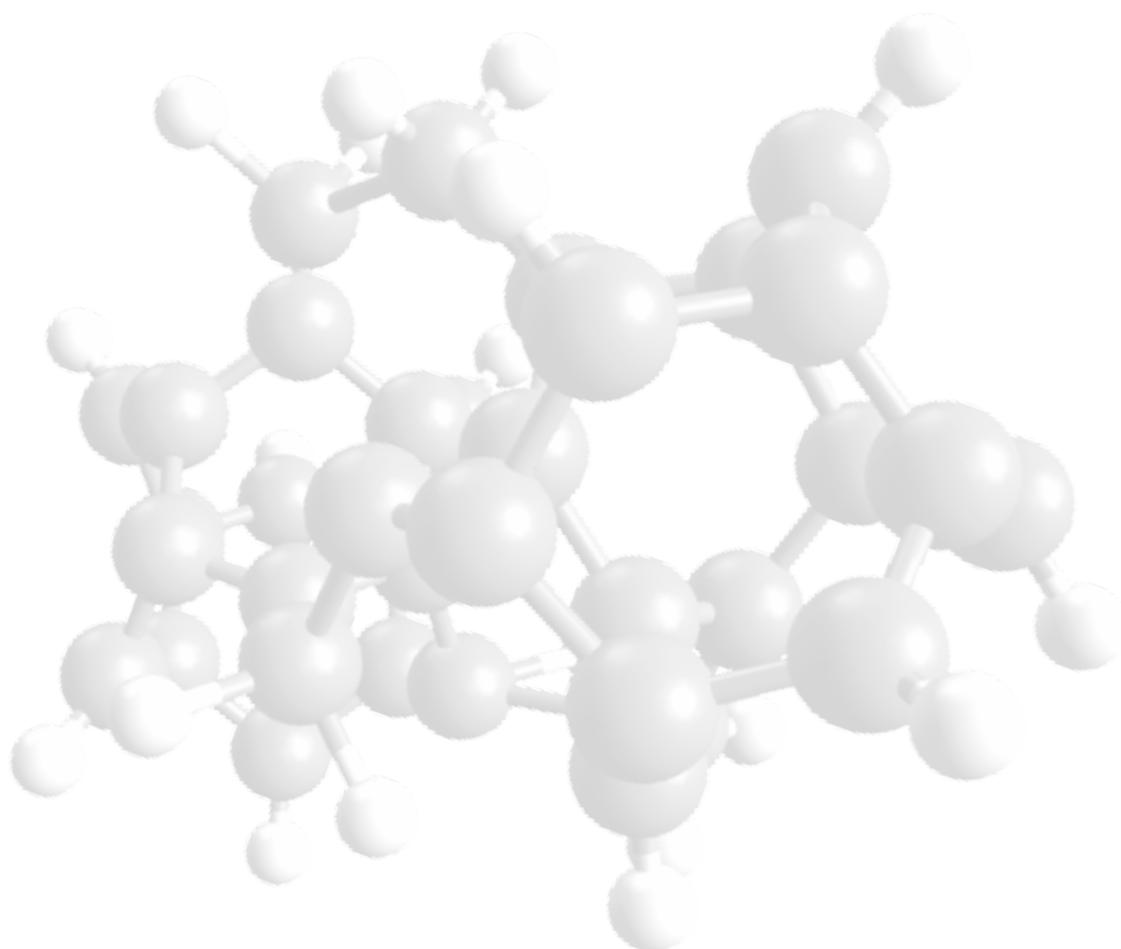


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Keynote Lectures

ICPOC 24



Keynote 1

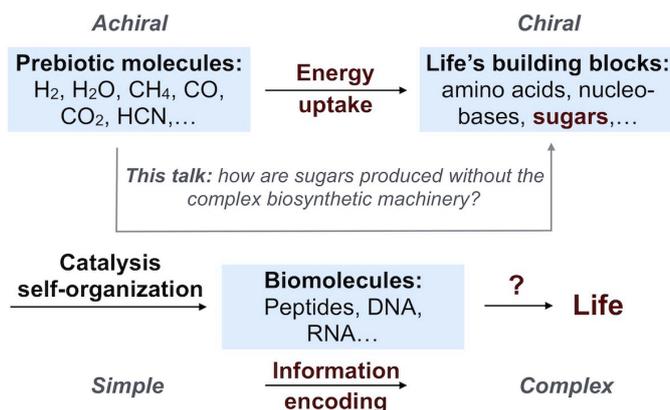


Carbohydrate Formation in the Absence of Biosynthesis

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What are the elementary reaction steps of the stereoselective synthesis of simple sugars as key molecules of life for energy and information storage? – Finding new strategies to answer this question is presented here. Although the simplest sugar, glycolaldehyde (HOCH_2CHO), has been generated in the laboratory from its constituents¹ and is suggested to be the first entry in the famous formose² (Butlerow³) reaction, the mechanism for the dimerization of two H_2CO molecules to glycolaldehyde and further to higher sugars (which are formaldehyde polymers) is a riddle to date; the finding of “glycolaldehyde autocatalysis” does not explain the fundamental chemistry, requires the presence of liquid water, a strong base, very high reactant concentrations, and ambient temperatures – all conditions unlikely to be present on early Earth or in extraterrestrial environments.⁴



In contrast to current hypotheses, we focus on non-aqueous reactions, ideally starting directly from the photoreaction of CO and H_2 to give hydroxymethylene (HCOH ⁵): Under appropriate conditions H_2CO and HCOH should react to glycolaldehyde and further to the chiral glyceraldehyde; an analogous sequence gives serine from glycine. One central question is whether HCOH is able to operate as an initiator and chain carrier for sugar formation and how this occurs mechanistically in the absence of liquid water and at the very low temperatures often encountered in space. We work employs organic synthesis, low temperature matrix isolation, flow pyrolysis, tunneling reactions,⁶ and high-level computations.

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Keynote 2



Competitive and Cooperative Counterion Effects on Supramolecular Recognition

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The vast majority of molecular components that are designed to assemble into supramolecular complex and mechanoestereochemical systems possess typically one or more formally charged atoms in either the host or the guest, or indeed in both. These charged species actively participate, with their associated counterions, in the assembly of higher ordered systems.

Competition between the host and counterion for binding sites on ionic guests can also contribute to the observed counterion effects. If the counterions, such as PF_6^- are weakly coordinating, then rigorous quantitative studies have revealed that host:guest complexation is relatively unaffected by the presence of the counterion, indicating that no competition exists between the host and counterion for the guest. Of course, these findings are specific to the host, guest, counterion, and the conditions of the investigation, and so each system needs to be studied individually to determine competitive effects, if any, of the counterion.

Water soluble calixarenes are obtained by introduction of polar substituents into their structure, being sulfonato[n]calixarenes (SCn) the most popular family. A large body of thermodynamic and structural studies have been carried out on binding of neutral and ionic guests by SCn showing their large ability hosting cationic species. A common feature of SCn family is that counterions are always present in their aqueous solutions. Despite SCn ability to host cationic guests the influence of counterions in their recognition process have been omitted. Counterion complexation by SCn was clearly established by studying the ^{23}Na self-diffusion coefficient. Both NMR and ITC experiments allow us to obtain the alkali cations binding constants implying that guest recognition processes should be considered as ion-exchange processes instead a single binding one.

Stoichiometry of host:guest complexes and host recognition ability are affected by counterion complexation. The reduction of the apparent host:guest binding constant results in a self-sorting process that is translated into the efficient translocation of the guest from the host cavity of the micellar pseudofease. In addition supramolecular catalysis is also affected by counterion recognition.

Keynote 3

**Chiral Induction in Asymmetric Dual Catalysis**

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Computational quantum chemistry has been increasingly employed toward rationalizing the stereochemical outcome in catalytic reactions.¹ The approach typically involves the identification of kinetically significant transition states and intermediates. In our laboratory, ab initio as well as DFT methods are employed to gain insights into carbon-carbon and carbon-heteroatom bond-forming reactions of immediate practical significance.² The key objective of our research is to gain molecular insights on the factors responsible for stereoselectivity and to exploit such insights toward in silico design of novel asymmetric catalysts.³

A number of examples wherein the conventional transition state models required systematic refinements toward accounting the observed product distribution and stereochemical outcome will be presented. Through this talk, we intend to propose the need for a timely rethink on a number of working hypotheses on asymmetric induction that places an over-emphasis on steric interaction. In general, the presentation would encompass a few contemporary themes in the domain of asymmetric multi-catalytic reactions.⁴ Interesting interpretations/rationalizations of experimental observations besides meaningful guidelines for rational improvements in the design of asymmetric catalysts would remain the key focus of the presentation. The contents are designed to cater to a broad and diverse group of audience; hence, the chemical insights would be emphasized, rather than a labyrinth of technical details.

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Keynote 4



Solvent Control of Reaction Outcome Using Ionic Liquids

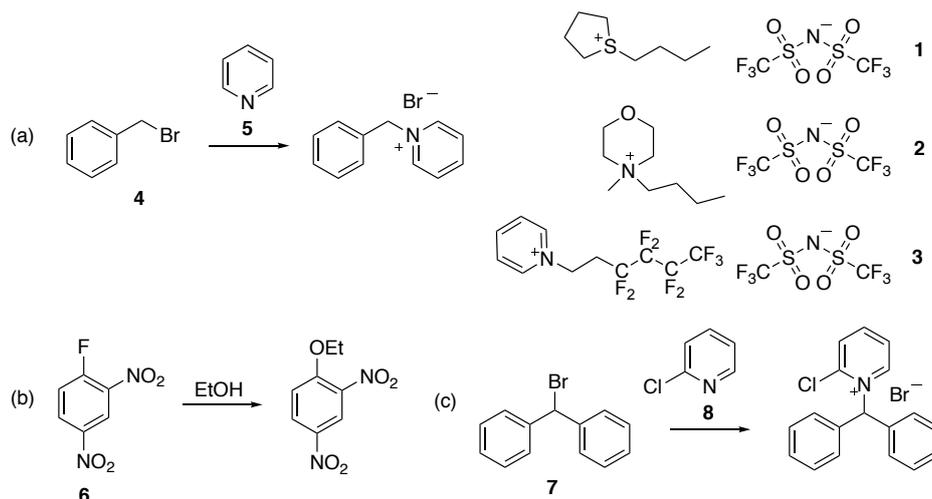
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A great deal of data has been accumulated on the origins of solvent effects in ionic liquids and, as a result, there are now a series of predictive principles for such solvent effects, particularly focussing on the key microscopic interactions responsible for the changes in reaction outcome.¹ Further development of this framework will allow the control of reaction outcome using ionic liquids.

The work described will discuss the challenges and opportunities associated with using the solvent effects of ionic liquids to achieve a desired outcome. This discussion will include demonstration of design of ionic liquids to control reaction outcome (such as using salts 1-3 to control the reaction of species 4 and 5, Scheme 1a,² and the effect of various salts on the ethanolysis of benzene 6, Scheme 1b³), use of these solvents to bias reaction outcomes (such as those between reagents 7 and 8, Scheme 1c⁴) along with methods for quantitatively assessing interactions in solution,⁵ in order to predict the effectiveness of an ionic liquid solvent.



Scheme 1. Examples that will be used to demonstrate the potential of ionic liquids to control reaction outcome. (a) Design of salts 1-3 to favour reaction of benzyl bromide 4 and pyridine 5.³ (b) Use of ionic liquids to favour ethanolysis of fluorodinitrobenzene 6. (c) Reaction of pyridine 6 with electrophile 7, which proceeds through two concurrent mechanisms.

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Keynote 5

**Use of Modelling in Pharmaceutical Process Development**

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The main goal of a process chemist is to scale-up a process in the shorter period of time possible doing this in a safe and robust manner while reducing the costs and improving efficiency. If these are not already sufficiently challenging requirements the chemist needs to reduce the risk of scaling-up a process from the lab to manufacturing scale. The process chemist needs to understand how the different components in the reaction mixture interact with each other and consider which side reactions take place due to unexpected reactivity of some of the reaction matrix.

The use of quality by design ensures that variability is better understood and that a prediction on product quality can be made throughout the process depending on the different occurrences. This approach is driven by the need to obtain process knowledge in a structured and systematic way. The use of modelling tools/calculations is a great enhancer of the fast and accurate development of knowledge with a minimal time

Keynote 6



Molecular Assemblers, Molecular Machines Performing Synthesis

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In chemical synthesis usually the reactants are dissolved in an organic solvent, the reactive molecules undergo stochastic collisions and form a bond if kinetic energy and relative orientation are favourable. However, the majority of biologically active molecules in nature are synthesized in ATP driven, molecular machine-type enzyme complexes such as non-ribosomal peptide synthetases (NRPS) or polyketide synthases (PKS). They operate like an assembly line by guiding reactions under positioning control driven by ATP. Notwithstanding the fact that there are a number of advantages to this assembler-like synthesis (less side reactions, easy stereo control, no protecting groups, preselection of reactants, driving unfavourable reactions...), there is (according to the best of our knowledge) no artificial system published so far. We are aiming at the design, synthesis and investigation of the first model system of a molecular assembler. In our preliminary work we designed and synthesized a light-switchable ditopic receptor which is able to drive the condensation of 4 molecules of vanadate to a cyclic tetravanadate. The reaction which is endergonic and therefore not spontaneous in the absence of the ligand is driven by the large and selective binding energy of the product tetravanadate inside the receptor. Photochemical isomerization (365 nm) of the ligand releases the product. Upon irradiation with 430 nm the original, "empty" state is restored and the cycle starts again.

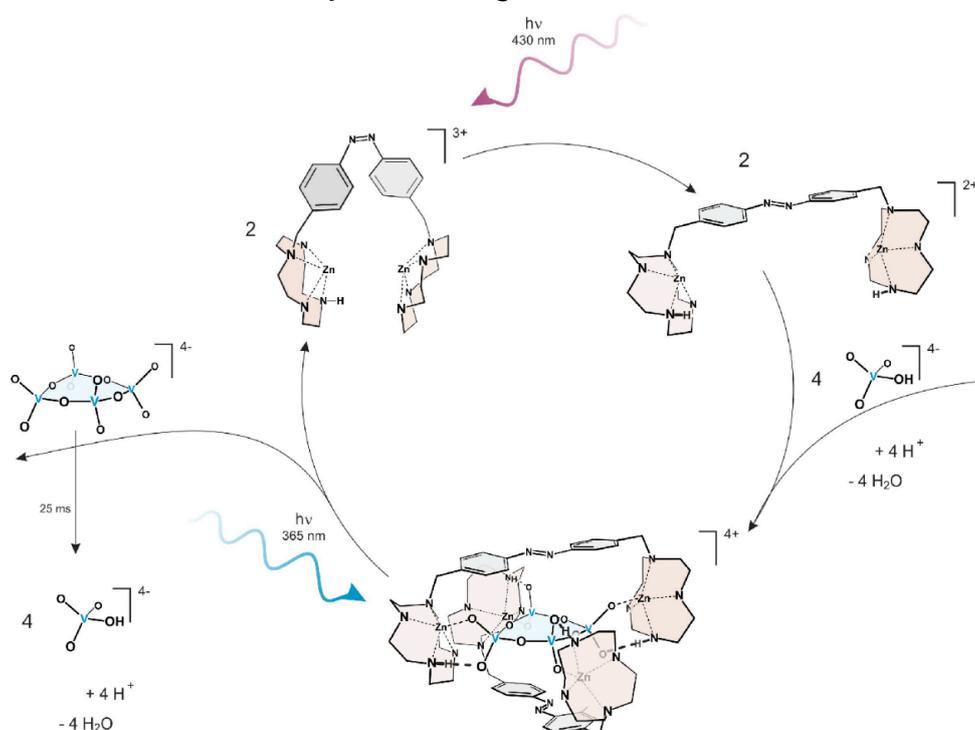


Figure 1. Thermodynamical cycle of a molecular assembler.

Keynote 7



Understanding How Enzymes Work

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We know that we can establish catalytic mechanisms of enzymatic reactions and, in doing so, explain the findings of experimentalists, but can we actually predict them? This talk is concerned with the computational needs that we come across to figure out results within computational enzymology. Calculations devised to study protein interactions and circumvent problems in some relevant systems will be reported as well as recent developments in the establishment of some catalytic mechanisms. We have resorted to QM/MM^{1,2} as well as other calculations^{3,4}, in order to analyse the energetics of processes related to the systems under study and evaluate their feasibility according to the available experimental data.

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Keynote 8



Understanding Chemoselectivity in Umpolung Acyl Anion NHC Catalysis

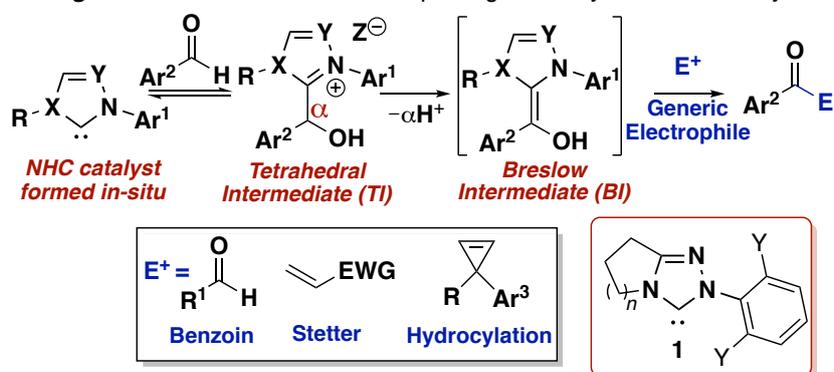
A. C. O'Donoghue,^{*a} J. Zhu^a and P. Quinn^a

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Despite many conceptual synthetic advances in organocatalysis by N-heterocyclic carbenes (NHCs), it is not understood why product distributions often differ dramatically with catalyst scaffold or with subtle substituent variation within a catalyst family.¹ In particular, a variety of chemo- and stereoselective reaction types are known for the archetypal acyl anion mode of NHC-reactivity, with a generally accepted mechanism shown in Fig. 1. Comparatively small changes in structure, e.g. variation of fused ring size (n=1-3) and inclusion of N-aryl ortho-substituents in triazolylidene **1**, can dramatically alter the product outcome.

Fig. 1: General mechanism underpinning NHC acyl anion chemistry.



Recent results have highlighted the diverse roles of 2-substituents in both N-aryl triazolium catalysts and benzaldehydes in controlling product outcomes in cross-benzoin reactions.^{2,3} The presence of 2-substituents, in either the aryl aldehyde or N-aryl group of triazolylidene catalyst, both kinetically favours addition of NHC to aldehyde and increases K values for formation of the tetrahedral intermediate, in contrast with the commonly assumed unfavourable steric effect of ortho-substituents. Proposed explanations include the formation of an adduct-stabilizing hydrogen bond between the developing OH and the 2-heteroatom, or a ground state effect due to increased aldehyde reactivity owing to removal of conjugation to the aryl substituent by steric twisting. Herein we report our further structural and kinetic analysis of the synthetically relevant ortho-substituent effect in NHC catalysis for a broader range of 2-substituents. We also report our new mechanistic studies of the impact of the fused ring size in **1**.

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Keynote 9

**Quantum Tunneling: Computational Predictions in Exothermic and Isothermic Reactions**

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Quantum mechanical tunneling of “heavy” atoms is extremely atypical, but also exceptionally rich chemistry, especially at cryogenic conditions. The only requirements are a rather low activation energy and, much more important, a narrow barrier. Through the theoretical analysis of the quantum tunneling driven reactions of carbenes and some degenerate rearrangements we will evaluate the novel concepts of isotopic controlled selectivity, tunneling stability and tunneling in antiaromatic systems.

Special emphasis will be put in the fulvalene system (an unsaturated, non-aromatic double-ring hydrocarbon), where by selectively introducing electron withdrawing and donating substituents we can design a molecule that exhibits a plethora of physical organic effects, including: Hückel and Baird (anti)aromaticity, Jahn-Teller distortion, NMR detection of tunneling, kinetic isotope effect, and, obviously, quantum tunnelling.

Keynote 10



Binding Motifs of Cisplatin with Amino Acid Targets Probed by IR Spectroscopy of Isolated Species

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Crucial issues coping with either challenging analytical problems or fundamental properties of ions find an increasing array of solutions based on novel mass spectrometric tools. Among the several MS-based approaches, we have largely exploited IR multiple photon dissociation (IRMPD) spectroscopy, an MS/MS method that allows to obtain vibrational spectra of bare isolated ions. In recent studies, IRMPD spectroscopy has allowed us to unveil the geometry and vibrational features of adducts of cisplatin, a widely used antineoplastic drug, with histidine (His) and methionine (Met). Electrospray ionization (ESI)-MS has permitted us to isolate the primary complex of cisplatin with these amino-acids, representing a key step in the interaction of the drug with proteins, on the way to platination at DNA. The IR spectrum of bare ions is directly compared with calculated spectra, thus allowing to relate the ion vibrational features with a particular conformer or a set of them. In the case of the cisplatin-histidine adduct, $\text{cis-}[\text{PtCl}(\text{NH}_3)_2(\text{His})]^+$, a complex mixture of isomers and conformers is verified.¹ Thus, IRMPD kinetics on conformer-specific vibrational modes were employed to evaluate the contribution of particular conformers within the gas-phase population. The so-obtained conformer ratio was used to produce an experimentally determined averaged theoretical spectrum finally obtaining good agreement with the IRMPD data. The same methodology was employed to evaluate the differences arising from the interaction of cisplatin and a structural isomer of the former, transplatin, with methionine, yielding cis/trans- $[\text{PtCl}(\text{NH}_3)_2(\text{Met})]^+$.² Comparing the IRMPD spectrum of the cis isomer with theoretical ones confirmed the preference for platination at the thioether group of methionine, in contrast with the more balanced binding motifs displayed by the trans isomer. Differences in the photofragmentation kinetics on a same, selected vibrational mode has revealed that the trans- $[\text{PtCl}(\text{NH}_3)_2(\text{Met})]^+$ population comprises a mixture of isomers presenting platinum coordination at either the amino or the thioether group, with a preference for the former. These results show how IRMPD-based techniques can be used as powerful tool to analyze complex mixtures of isomers and conformers as well as to obtain a fine characterization of structural features.

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Keynote 11

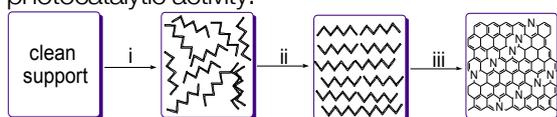


Defective Graphenes From Biomass Wastes as Photocatalysts for Solar Fuels Production

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Graphene as one carbon atom thick layer of sp^2 carbons in hexagonal arrangement is almost transparent in the spectral UV-visible range and is a zero-band gap semiconductor with high electron mobility.¹ However, in contrast to ideal, defectless, single layer graphene, the presence of defects in graphene as well as stacking as few or multilayer assemblies changes completely the properties of these materials, converting them into semiconductor exhibiting photocatalytic properties.² As an example, graphene oxide behaves as a semiconductor with UV response.³ The initial uses of graphenes in photocatalysis were as additives of semiconductors to enhance their photocatalytic activity.⁴



Scheme 1. Procedure for the preparation of N-doped graphenes by pyrolysis under inert atmosphere of natural chitosan

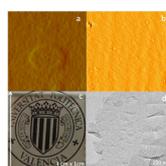


Figure 1. Optical profilometry (a) and AFM image (b) of films of natural biopolymer before pyrolysis and photograph (c) and transmission electron microscopy image of the resulting graphene films

In this presentation, a new procedure for defective graphene film preparation, containing or not dopant elements and metal nanoparticles, with semiconducting properties for overall water splitting in the absence of sacrificial electron donor or for photoassisted CO_2 reduction will be shown.⁵ The process is summarized in Scheme 1, while Figure 1 shows photographs and images by microscopy of the resulting films. Photocatalytic activity can be achieved by doping the graphene layer with heteroatoms and by deposition of metal nanoparticles. In this way, photocatalytic activity for hydrogen evolution was achieved by preparing a P-doped defective graphene.⁶ The hydrogen evolution activity increases upon incorporation of Pt nanoparticles by photodeposition. Figure 2 shows a transmission electron microscopy image of the P-doped defective graphene containing the Pt nanoparticles.

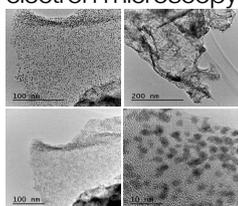


Figure 2. TEM images of P-doped defective graphene containing Pt nanoparticles formed by photodeposition

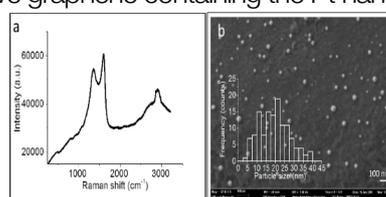


Figure 3. Raman spectrum (excitation at 514 nm) and SEM image of Au nanoparticles grafted on defective graphene. The inset shows the particle size distribution.

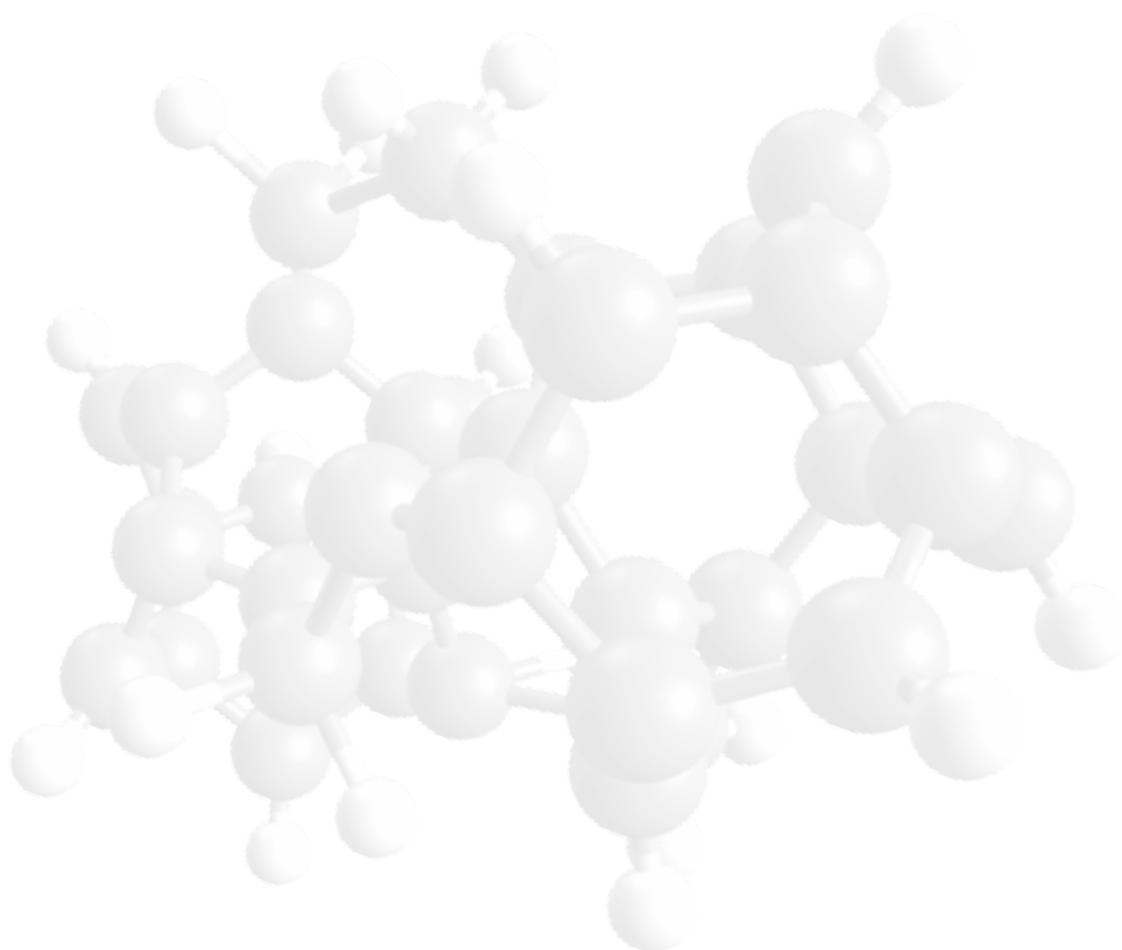
Among the most active photocatalyst for overall water splitting using pure water in the absence of sacrificial agents, the preparation of defective graphene containing facet oriented Au nanoplatelets will be presented (Figure 3).⁷ Characterization data show that due to the pyrolytic preparation procedure Au nanoplatelets are strongly grafted on the defective graphene as indicated by the shift in the Au 4d binding energy, the morphology of the Au particles wetting the graphene sheet and the relatively small particle size. Besides hydrogen generation, the presentation will show also the activity of the series of defective graphenes containing metal and metal oxide nanoparticles for the photoassisted CO_2 methanation.⁸ The reasons why the process requires temperatures above 175 °C, the role of H_2O as poison and the reaction mechanism will be commented based on available kinetic data. Overall, the presentation will show the potential of defective graphenes in the area of sustainable photocatalysts.

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Invited Lectures

ICPOC 24



Invited 1



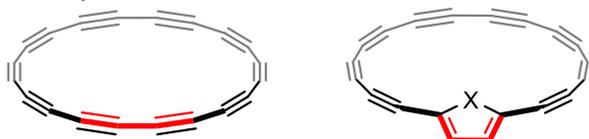
Relating the Triplet State Baird-Aromaticity of the Macrocycle to that of the Monocycle

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Aromaticity and antiaromaticity in the first pp^* excited states, as given by Baird's rule,^{1,2} have received gradually more attention in recent years.³⁻⁸ In short, Baird's rule tells that the p -electron counts for aromaticity and antiaromaticity are opposite in the first triplet and singlet excited states (T_1 and S_1 , respectively) as compared to the electronic ground state (S_0). Thus, cyclic fully p -conjugated compounds with $4n$ p -electrons are aromatic in their T_1 and S_1 states while those with $4n+2$ p -electrons are antiaromatic. In strict sense the rule applies only to monocyclic compounds, yet, it has also been used for both macrocyclic and polycyclic systems,^{4,6-8} although its potential limitations in macrocycles has not been fully examined. Using quantum chemical computations we now probed the connection of T_1 state Baird-aromaticity in a selection of compounds that allow us to gradually go from monocycles to macrocycles which have a multitude of circularly conjugated $4np$ -electron paths. We start at cyclic C_{4n} polyynes and successively replace 1,3-butadiyne segments with monocyclic units that each contribute four p -electrons to the conjugation of the full macrocycle. We explore various effects that lead to localization of the triplet diradical character to shorter segments versus full delocalization over the macrocycle leading to Baird-aromaticity. The selection of compounds also allows us to study to what extent the calculated degree of Baird-aromaticity in macrocyclic compounds vary with computational methods. Here we compare the results from DFT methods with results calculated with coupled cluster theory. Trends as well as recommendations for the study of potentially Baird-aromatic macrocycles using quantum chemical computations will be presented.



X = CHCH, CH₂CH₂, CH₂, NH, O or S

A 1,3-butadiyne segment in C_{20} and a monocyclic unit that participates with the same number of p -electrons in macrocyclic conjugation.

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Invited 2



Nucleophilicity and Electrophilicity Parameters for the Analysis of Cycloaddition Reactions

Herbert Mayr, Armin R. Ofial, Hendrik Zipse, Dominik Allgäuer, Harish Jangra, and Quan Chen

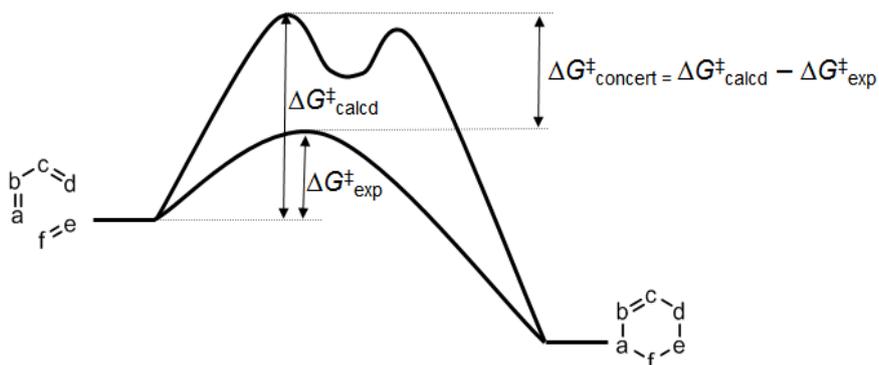
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Extensive kinetic investigations carried out during the last two decades have shown that the rates of reactions of electrophiles with nucleophiles follow equation (1)¹ when only one new bond is generated in the rate-determining step.

$$\lg k_{20^\circ\text{C}} = s_{\text{N}} (E + N) \quad (1)$$

This equation, where electrophiles are characterized by one parameter (E) and nucleophiles are characterized by the solvent-dependent nucleophilicity parameter N and sensitivity parameter s_{N} allows one to predict absolute rate constants with an accuracy of factor 10-100 in a reactivity range of more than forty orders of magnitude. More than 1100 nucleophiles and almost 300 electrophiles have been parameterized in this way.² Equation (1) fails when very bulky reagents are involved, and we have repeatedly mentioned that eq. (1) cannot be applied to multicenter processes.

Recent work has shown, however, that eq. (1) does not only provide rate constants for stepwise cycloadditions via zwitterionic intermediates, but also for concerted cycloadditions with highly unsymmetrical transition states. Cycloadditions in which both new bonds are significantly advanced in the transition state proceed faster than calculated by eq. (1), and the ratio $k_{\text{exp}}/k_{\text{calcd}}$ can be used for deriving the energy of concert $\Delta G^{\ddagger}_{\text{concert}}$.



Applications to Diels-Alder reactions and 1,3-dipolar cycloadditions will be discussed.³

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Invited 3



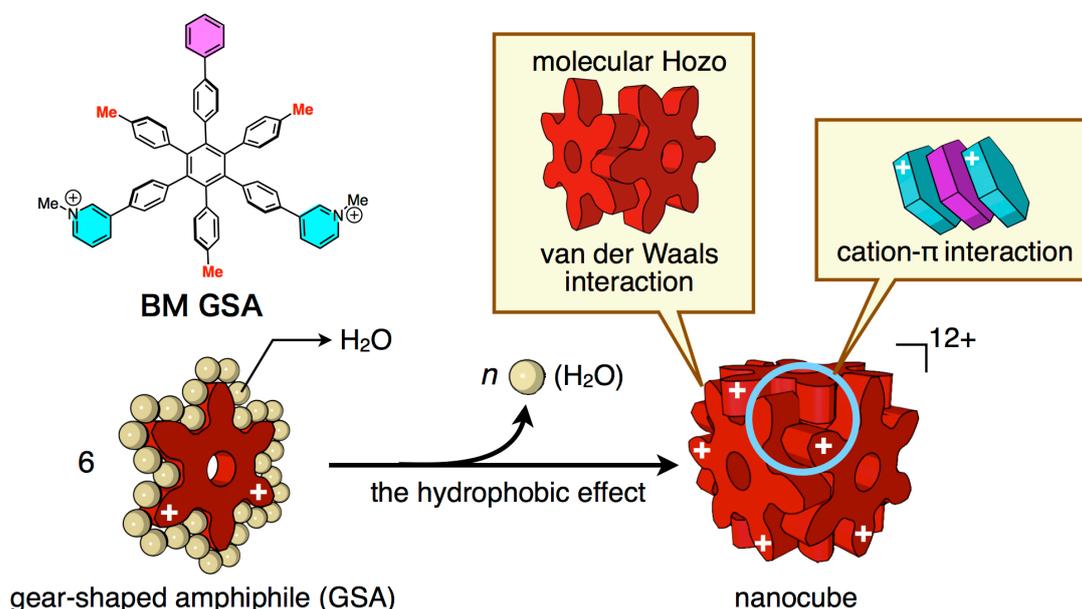
Nanocube: Hyperthermostable Discrete Self-Assemblies in Water

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Like hyperthermophilic proteins, thermally stable supramolecular assemblies, nanocube, composed of six amphiphilic molecules with an indented hydrophobic surface using only weak intermolecular interactions (van der Waals (vdW) and cation- π interactions and the hydrophobic effect) in water were developed based on a concept of molecular Hozo.¹ The decomposition temperature of one of the nanocubes is over 150 °C, which is higher than that of the highest ever hyperthermophilic protein (PhCutA1). Study on the relation between the structure of the component and the stability of the assemblies indicates that the hyperthermostability is realized only if the contributions from all the three weak interactions come together. The importance of vdW interactions in the stability of the nanocubes is clarified by a novel method for the semi-quantitative evaluation of molecular meshing in molecular complexes and assemblies (SAVPR: surface analysis with varying probe radius).² It was found that the components in the nanocubes more tightly mesh each other than usual host-guest complexes and that the contribution of vdW interactions in molecular complexes and assemblies is not negligible for designing stable molecular complexes in water.



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Invited 4

**A Magic Wand to Control Molecular Structure**

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For many molecules, besides the low-energy conformers that are easily accessible to experiment, high-energy forms exist whose population is negligible (or are not populated at all) in most of the usual experimental conditions. Till very recently, the identification and characterization of these high-energy conformers was done only theoretically. Using a simple analogy, the exploration of the molecular conformational landscapes was confined to the Lowlands, while the Highlands were terra incognita, whose inhabitants were never seen.



The recent development of experimental techniques based on the selective in situ generation of high-energy conformers, by selective vibrational excitation (using near-infrared light) of the easily accessible lower-energy conformers, opened a way for journeying to the molecular conformational Highlands. These expeditions have allowed observation of a plethora of novel molecular structures, some of them exhibiting rather unusual properties.

In this talk, the attendees will be invited to make an excursion on molecular landscapes, learn how the expedition can be prepared, enjoy the contact with the “highlanders” and see how they behave. Several molecular systems will be addressed, ranging from simple molecules exhibiting only two conformers to complex multi-dimensional systems that embrace a larger number of conformers.

Acknowledgements

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Invited 5



Physical Interpretation of the Substituent Effect – the Quantum Chemistry Approach

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Substituent effects are most frequently considered by the use of similarity models with the Hammett or Hammett like substituent constants as quantitative descriptors. This kind of approach is very fruitful but it does not allow to describe electron donating/attracting properties of substituents in other situations than those present in reference reactions. Moreover, the general term “substituent effect” can be applied to different kinds of intramolecular interactions in X-R-Y systems: (i) the impact of substituent X on the properties of a fixed group Y, known as a classical understanding of the substituent effect,¹ (ii) the effect of X on the properties of transmitting moiety R, (iii) interrelations between some properties of Y due to the influence of the distant substituent X, and (iv) influence of the fixed group Y or -R-Y on the properties of substituent X, named as the reverse substituent effect.² A classical view on the substituent effect is associated with an empiric approach presented by Hammett.¹ An application of the quantum chemistry modeling allows to find descriptors which are characterized by clear physical meaning and are able to reveal all aspect of the substituent effect. The following quantum chemistry descriptors can be used for this purpose: (i) cSAR(X or Y) describing atomic charges at CX or CY parts of molecules, (ii) SESE, the energetic consequences of interactions between X and Y in X-R-Y systems and (iii) sEDA and pEDA – population of electrons at sigma and pi orbitals of planar systems (or their fragments). In addition, the Y group is also characterized by its structural parameters, whereas the transmitting moiety – by aromaticity index HOMA.

Quantum chemistry modeling by means of charge of substituent active region (cSAR) allows to estimate electron donating/attracting properties for any X substituent in any substituted pi-electron systems. Then, by comparison with cSAR(X) in the reference reaction, mentioned above, allows to transfer cSAR(X) values to the “language” of well-known substituent constants.³ This is allowed because cSAR(X) values are well correlated with the substituent constants.

Therefore, the substituent effect descriptors based on quantum chemistry modeling are able to present more detailed information on physical aspects of the problem.

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Invited 6



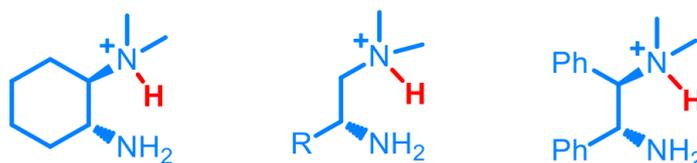
Stereo-ionic Interaction of Protonated Amines in Asymmetric Catalysis

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Non-covalent interactions are ubiquitously utilized in enzymes and chemical catalysis in order to achieve exquisite control of reaction selectivity. In this regard, ion-pairing with charged species or intermediates has become an enabling and powerful approach for enantioselective catalysis. Due to the often weak and non-directional nature of these ionic reactions, to delineate the origin and basis for catalysis and enantioselective control remains extremely challenging. Inspired by Nature, we have developed bio-inspired chiral primary amine catalysts as both functional and mechanistic enzyme mimics,¹ showing unprecedented scopes in fundamental transformations of carbonyls.² One of the general feature of this catalyst is the essential protonated diamine-motif for effective catalytic turnover and stereocontrol. By joint efforts of experimental and computational studies, we have investigated the stereocontrol origins of this type of chiral protonated amines. Distinctive from the typical ion pairing with tetraalkylated ammonium in phase transfer catalysis, the protonated amines show both stabilizing charged H-bonding and destabilizing steric and charge-repulsion effect. This talk will focus on the stereo-ionic interactions with our protonated chiral amine catalysts.



H-bonding and steric/charge repulsion

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Toward Computational Molecular Technology of Complex Chemical Reaction Systems: Applications of Red Moon Methodology

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Recent development of new experimental measurement techniques have made us notice how significant we consider chemistry by the number of molecules, not the amount of substance in mole, leading to the increasing important role of computational chemistry as a molecular science. On the other hand, when we try to treat computational chemically diffusion and chemical reactions in "molecular aggregation states" where a large number of atoms and molecules are gathered in condensation, such fact that these phenomena occur only

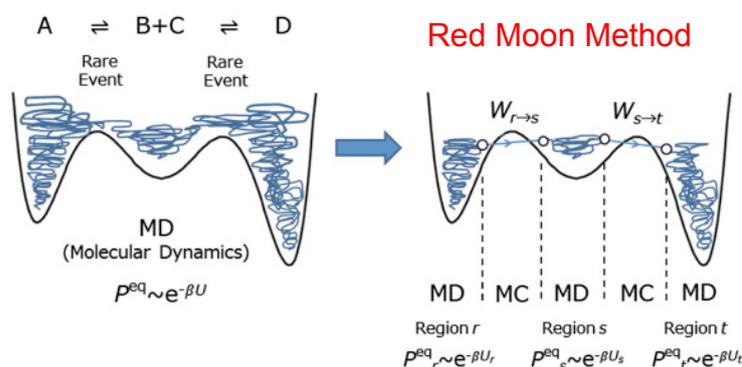


Figure 1. Schematic representation of Red Moon method [1].

very rarely has made it restrictive or sometime impossible to deal with them by the first principles methods of computational chemistry. Even with traditional classical molecular simulations, it is really difficult to determine the long-term properties and stereochemical characteristics. Under the circumstances, we have recently developed Red Moon Method, a new efficient and practical 'atomistic' simulation method combining Monte Carlo (MC) and molecular dynamics (MD) method with a Rare Event-Driving Mechanism, for large-scale chemical reaction systems (Figure 1)¹ and applied successfully to analyze several materials important and valuable in next-generation industrial development^{2,3}.

In this talk, several applications of Red Moon Method are shown from the practical viewpoint of molecular controlling of complex chemical reactions, stereochemistry and aggregate structures^{2,3}. In particular, we take a novel olefin polymerization catalyst (pyridylamide)Hf(IV) complex (I), which is activated by a cocatalyst B(C₆F₅)₃ to form a cationic active species^{4,5} and explain the role of the counteranion in the reaction mechanism of propylene polymerization⁵. Finally, I would like to discuss the microscopic mechanism of chain transfer polymerization of I and ZnEt₂ in solvent toluene, which is clarified by applying Red Moon simulation to the present system⁶.

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Invited 8



Position Matters: Amide Neighbouring Group Participation Facilitates the Rate of Phenylalanine Oxidation in Peptides

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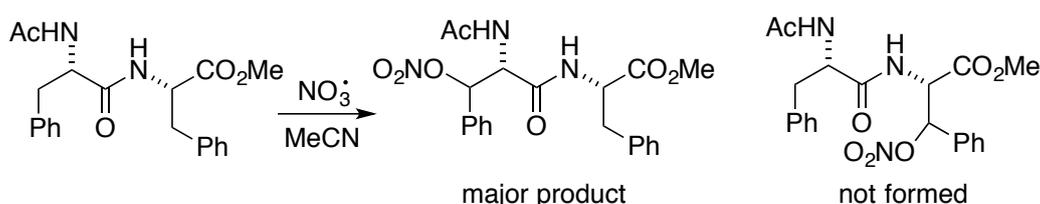
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Nature uses proteins as medium for long-distance electron transfer (ET) to carry out redox reactions in distant areas and compartments. These processes are triggered by a multistep charge hopping reaction, using the side chains of tyrosine, tryptophan, cysteine and methionine as relay amino acids, which have oxidation potentials in peptides of around 1 V vs. NHE. Recently, Lovley,¹ and Reguera² proposed that phenylalanine acts as a relay amino acid in extracellular electron transfer (EET), where electrons migrate over several hundreds of Å from the respiration site at the inner cell membrane to oxidising metal cations outside the cell. In *Shewanella oneidensis* such EET can use pili, which are aggregates of small proteins that carry phenylalanine and tyrosine as possible stepping-stones. However, since the oxidation potential of alkylated phenyl groups is about 2 V vs. NHE, this suggestion is surprising, and the question arises, whether the oxidation of phenylalanine is influenced by the peptide environment.

We have performed a series of experimental and computational studies,³ where we demonstrate that the positive charge of the phenyl radical cation in phenylalanine is efficiently stabilised by adjacent amide groups. As a consequence, phenylalanine cannot only catalyse ET as a relay amino acid, but can also be regioselectively and irreversibly oxidised (Scheme 1). These processes resemble the peptide backbone effect that turns methionine into a powerful relay amino acid and a target for oxidative stress.⁴



Scheme 1. Selective NO_3^\bullet induced oxidation of the N-terminal phenylalanine residue in dipeptide AcNH-Phe-Phe-OMe.

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Precious Metal Catalysis in Allene Chemistry: From Divergent Systems to Heterobimetallic Catalysis

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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. We have studied this divergent reactivity in the transition metal-catalysed reactions of allenes and nucleophiles. Remarkably, the Pt-catalysed dihydroalkoxylation and bisindolylolation of allenes,¹ give acetals or bisindolyl alkanes as products with double addition of the nucleophile (alcohols or indoles) to the less substituted double bond of the allene, and complete saturation of the second double bond, in contrast to the Au(I)-catalysed hydroazidation of allenes that gives allyl azides as the only products of the reaction.²

We have expanded the divergent reactivity encountered with platinum catalysts to the cyclisation of bisallenes in the presence of alcohols and water as nucleophiles³ and to the cyclisation of indolylallenes in the presence of an external nucleophile, such as indoles.⁴

Using a POC approach for the study of these new reactions, we have uncovered details on the different coordination of platinum and gold with allenes and the different reactivity of key intermediates that begins to explain the divergences observed in reactions with the two metals.⁵ Information from these studies have allowed the design of a Pt-Au heterobimetallic system, much more efficient and general catalysts for the cyclisation of indolylallenes in the presence of external nucleophiles, where the scope has been expanded to other heteroarylallenic systems and nitrogen nucleophiles not reactive under single catalyst strategies.⁶ A novel mode of hybrid homo-heterogenous catalysis has also been unveiled in this heterobimetallic system,⁷ opening the questions of the true identity of the catalysts involved in reactions using precious metal catalysis in single and bimetallic strategies.

A summary of the exciting journey from the divergent reactivity encountered in our allene chemistry to the development of the new heterobimetallic system will be discussed in this presentation.

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Reactive and Selective Supramolecular Artificial Enzymes for Phosphate Transfer Reactions

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Enzymes are a source of inspiration for the development of supramolecular catalytic systems consisting of macromolecules, such as Pillararenes, polymers and surfactants. The most important challenges in supramolecular catalysis are increasing reaction rates and selectivities by proper selection of host receptor and functionality.

Phosphate diester hydrolysis in the presence of pillar[5]arene (P5IMD) matrix with anchored imidazoles was strongly accelerated, by a factor of 10^4 at neutral pH in comparison with bulk water. The reaction proceeds via nucleophilic attack of imidazole on the host:guest complex with expulsion of the leaving group placed outside the pillararene cavity. Geometrical restrictions preclude nucleophilic attack with expulsion of the leaving group docked inside the cavity. These spatiotemporal arrangements promote an increase in selectivity, which reaches 10^2 -fold higher than in bulk water. Formation of non-productive host:guest supramolecular complexes, with the best leaving group being docked into the cavity, allows to consider P5IMD as an example of highly efficient and selective artificial enzyme.

Phosphate transfer reactions for diester and triester were also catalyzed by a supramolecular polymer/surfactant complex comprised of a poly(acrylic acid) derivative with imidazole groups attached to the polymer by amide bonds (PAIM), and the cationic surfactant (CTAB). Supramolecular complex formation, at concentrations below the respective critical micellar concentration provide convenient hydrophobic pockets for the reactants close to the multiple catalytic centers, where imidazole and carboxylate groups act as nucleophiles for the degradation of a model phosphate ester, delivering a highly efficient performance of the supramolecular catalysts. For phosphate triester the catalytic effects are on the order of thousands for nucleophilic catalysis and are higher by 2 orders of magnitude for the supramolecular polymer/surfactant complex at pH 9. The catalytic efficiency for phosphate diester was 10^2 -fold higher than for the triester due to a better binding of the substrate into the catalytic supramolecular system.

Our kinetic results are consistent with spatiotemporal concepts where the reagents are in a position favorable to promote the phosphate transfer reaction. Thus, it becomes relevant to evaluate this theory using model molecules, in which catalytic groups and reactive groups can be organized with specific geometries in space.¹ Simpler models can be used to understand the catalytic profile of enzymes and facilitate the design of supramolecular nanoreactors.

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Invited 11



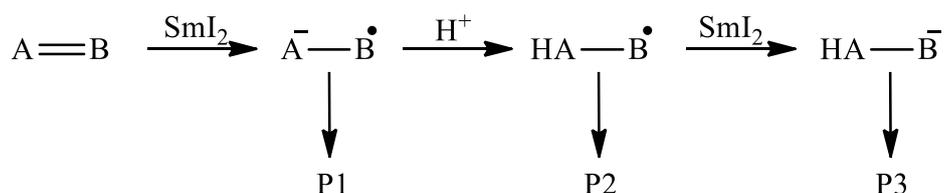
Reaction Mechanism Diagnostic Tool for the Reaction of SmI_2

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SmI_2 is a very convenient and versatile reducing agent. Its versatility stems from the fact that, following the electron transfer step, three different products (P1 – P3) can be generated during the reduction of electrophilic double bonds ($\text{C}=\text{O}$; $\text{C}=\text{C}$, $\text{C}=\text{N}$ etc.), as shown in the scheme below. This is in contradistinction to metal hydride reduction, for example, where only P3 is generated.



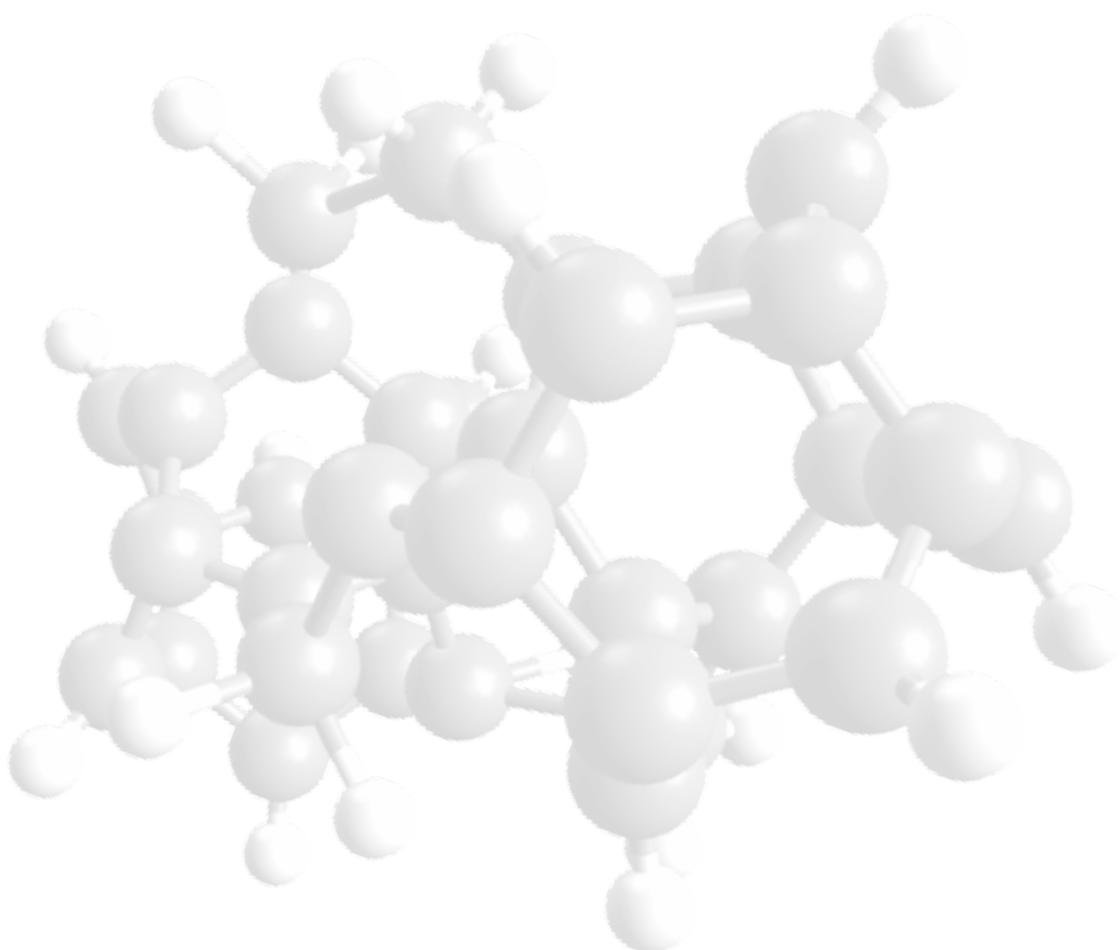
We have shown that an educated choice of the ligand allows us to channel the reaction to the desired product.¹⁻⁶ However, for this to occur, one has to first posit a mechanistic pathway for the reaction and, only then, tailor the ligand type and its concentration accordingly. Thus, in general, the understanding of the reaction mechanism is crucial in planning SmI_2 reactions.

This work presents a newly developed diagnostic tool which takes advantage of the fact that, in some cases, the coordination of the ligands to the SmI_2 results in an increase of the SmI_2 reduction potential. Examination of the ligand effect on the reaction kinetics, in conjunction with its effect on the reduction potential of SmI_2 , enables one to diagnose some very important mechanistic features. These include: the identity of the rate determining step; the nature of the electron transfer step, namely, whether it is an inner sphere or outer sphere electron transfer reaction; and other important mechanistic parameters.

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Oral Presentations



Ring Inversion Kinetics of Photoexcited Chiral [4*n*]Annulene Derivatives: Energetic Impact of Baird Aromaticity

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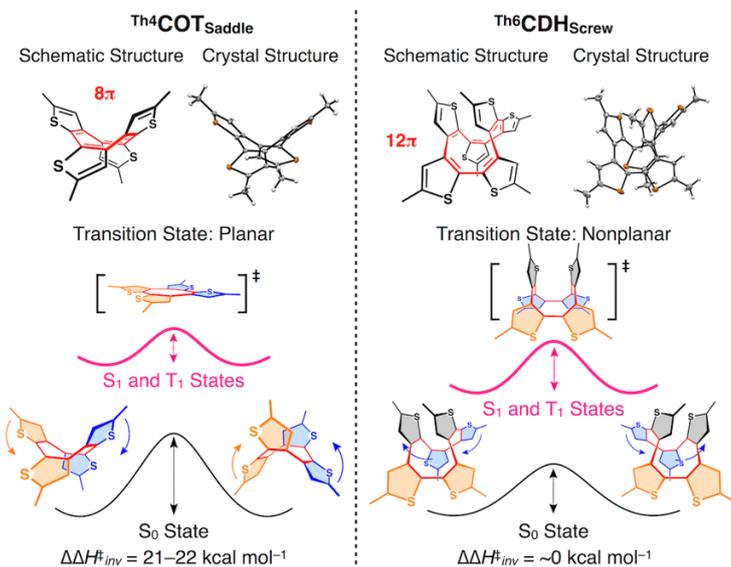
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Aromaticity is one of the most important concepts in organic chemistry that can explain the stability of planar conformations found in some specific cyclic π -conjugated molecules. In the electronic ground state, such molecules with $4n+2$ π -electrons prefer to be planar (Hückel's rule¹) because the resulting electronic conjugation leads to an energetic stabilization. The stabilization effect by Hückel aromaticity is estimated to be 29 kcal/mol based on heats of formation.² On the other hand, in the electronic excited state, it is known that cyclic π -conjugated molecules with $4n$ π -electrons prefer to be planar (Baird's rule³). However, the energetics of the Baird aromaticity has been elusive.

Here we report, by using the ring inversion kinetics of chiral thiophene-fused [4*n*]annulenes, the first experimental evaluation of the energetic impact of Baird aromaticity.⁴ We utilized $\text{Th}^4\text{COT}_{\text{Saddle}}$ and $\text{Th}^6\text{CDH}_{\text{Screw}}$ which has [8] and [12]annulene core, respectively. These compounds can be optically resolved by chiral HPLC. The enantiomerically separated $\text{Th}^4\text{COT}_{\text{Saddle}}$ can maintain its optical activity at room temperature but undergo racemization upon photo irradiation due to photo stabilization of the planar transition state (TS) of the ring inversion. On the other hand, the racemization profile of $\text{Th}^6\text{CDH}_{\text{Screw}}$, whose TS conformation is non-planar, was intact to photo irradiation. These observations can be well explained by Baird's rule. Through the investigations of CD intensity decay profile at various temperatures, the activation enthalpy of the ring inversion of $\text{Th}^4\text{COT}_{\text{Saddle}}$ under photo irradiation was 21–22 kcal/mol lower than that under dark. This value corresponds to the energetic impact of Baird aromaticity. These results contribute not only to the understanding of basic organic chemistry but also for the progress of organic photochemistry and related materials science.



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Quenching of Triplet and Singlet Excited States by Carbon Dioxide

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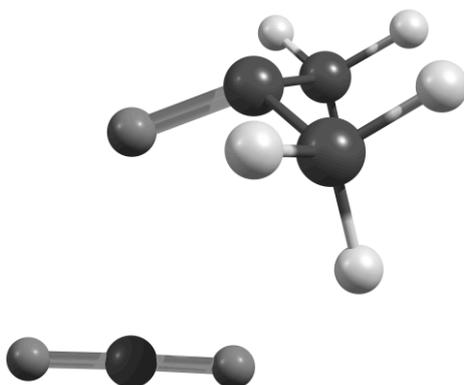
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Quenching of excited states of ketones and other chromophores usually occurs either via energy transfer, by photochemical reaction, such as hydrogen abstraction, or by electron transfer. In some cases, exciplex formation has also been observed, such as, e.g., between ketone triplet excited states and electron rich arenes, or between azoalkane singlet excited states and tertiary amines.^{1,2}

In this contribution, we will present evidence, both from ns time-resolved laser flash photolysis measurements and from ab initio and DFT calculations, that triplet excited states of ketones and other chromophores are quenched by the extremely unreactive molecule CO₂. We will also include a discussion on the nature of the exciplexes formed, with CO₂, as well as with other quenchers.



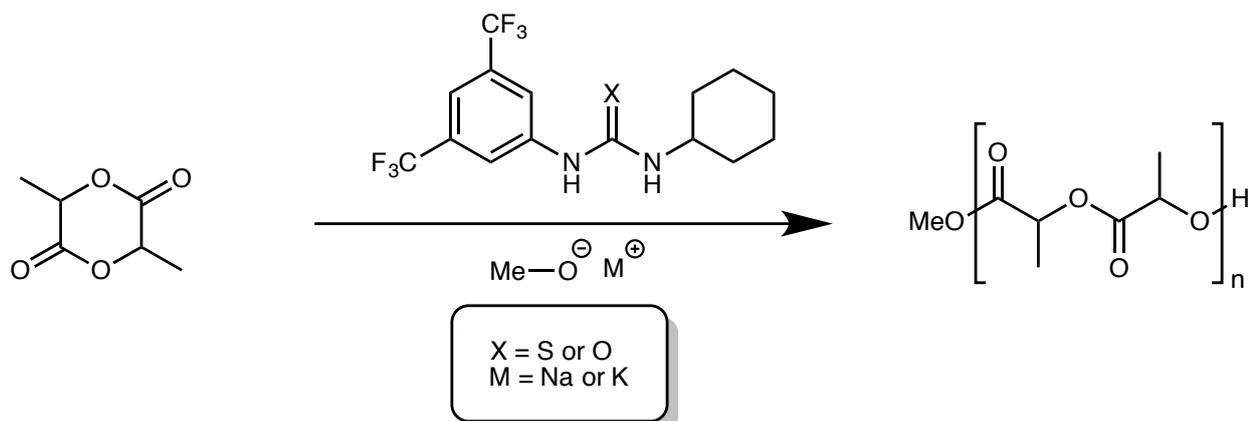
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Oral 3

Theoretical Studies on Ring-Opening Polymerizations by Alkoxides and (Thio)ureasG. O. Jones,^a B. Lin,^a X. Zhang,^b J. L. Hedrick^a and R. M. Waymouth^b^aIBM Research - Almaden, San Jose, CA, USA^bStanford University, Stanford, CA, USA

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The ring-opening polymerization of lactides is a highly sought-after strategy for the generation of functional, biorenewable plastics. We have identified modular catalytic systems comprised of alkoxides and thioureas or ureas that can achieve fast and selective ring-opening polymerizations of lactide.^{1,2} This presentation will describe computational studies that have been performed on lactide ring-opening by these catalytic systems which reveal insights into the mechanism and energetics of lactide polymerizations.

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Aromatic Additivity in Three Dimensions

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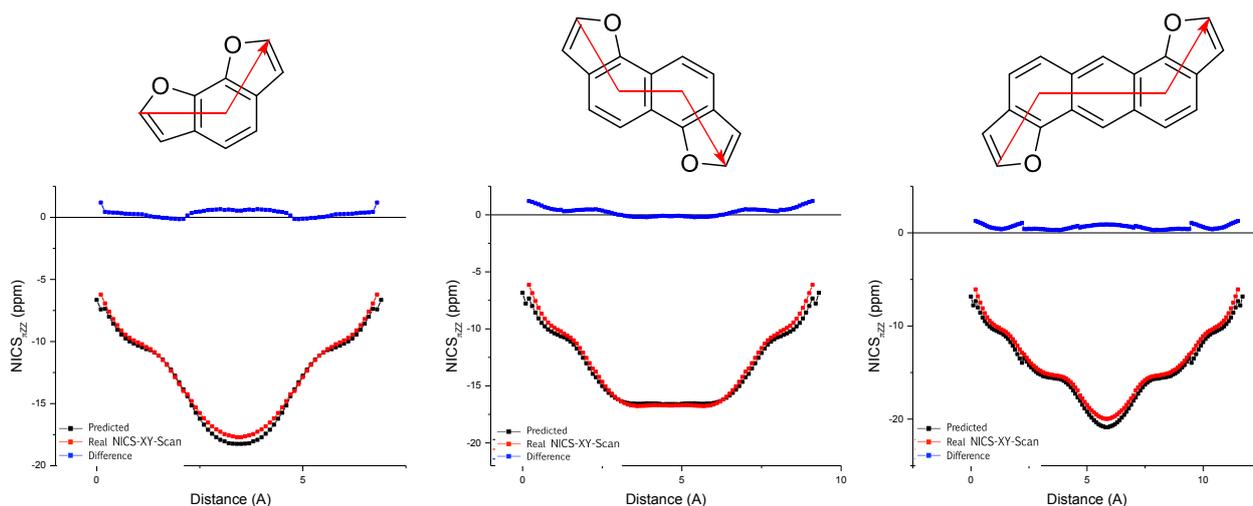
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Aromaticity is a fundamental property, and one that is key to understanding the reactivity and behavior of a wide range of compounds, from simple reagents to complex materials. Magnetic criteria are the most commonly used to evaluate and compare aromaticity, among which the NICS-based methodologies are the most popular.¹

Several years ago, we introduced the NICS-XY-Scan,² which enables identification of local and global ring currents within polycyclic aromatic hydrocarbons. In the intervening years, this methodology has rapidly gained popularity, and has been used extensively for the characterization of a wide range of compounds. Very recently, we showed that the same NICS-XY-Scans can be used in a novel way, as building blocks within an additivity scheme.³ This new application enables prediction of the aromatic profiles of polyacene systems, at a fraction of the computational cost. The additivity scheme was shown to work in 1- and 2-dimensional systems, paving the way for investigation of very large and complex chain-like and graphene-based systems.

We now report that the additivity scheme has been expanded to include heteroatom-containing compounds and anti-aromatic moieties. Furthermore, we have successfully applied the methodology to 3-dimensional structures, which are quite challenging to treat with existing computational methods. These developments render the technique useful for predicting the aromatic profiles of a wide range of aromatic systems of various functionalities. Specifically, this enables access to large structures such as conducting aromatic oligomers and light-harvesting compounds.



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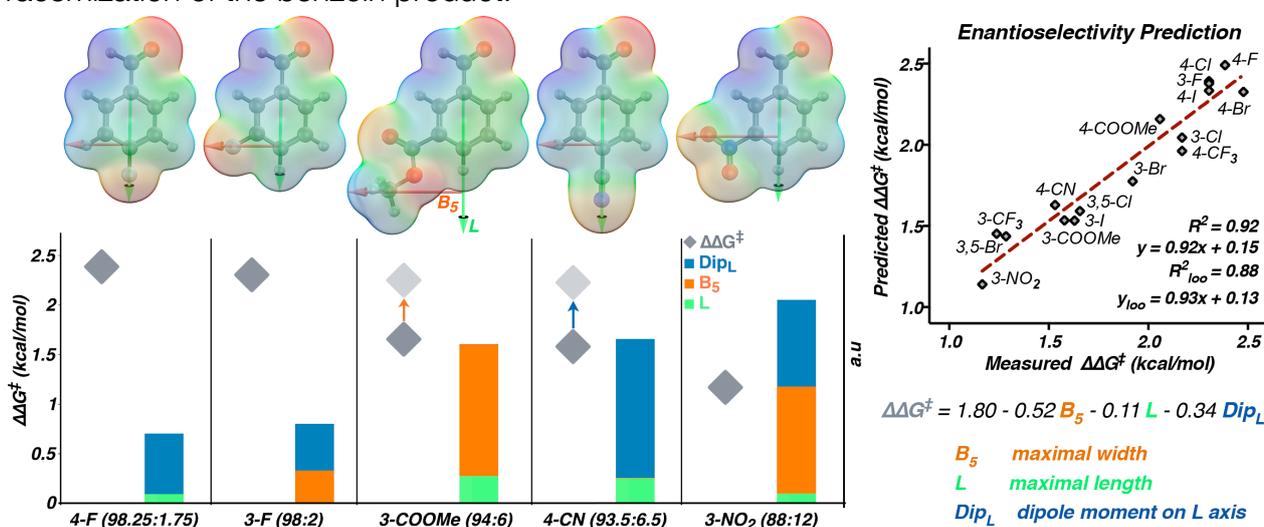
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Physical Organic Principles for Controlling the Secondary Sphere in Organocatalysis

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Inspired by the fundamental effect of secondary-sphere non-covalent interactions on enzymatic catalysis, metal-mediated processes and transition-metal chemistry, our group seeks to offer an approach for the facile in-situ modification and mechanistic interrogation of secondary-sphere interactions in organocatalysis. As a proof-of-concept, we modified the secondary-sphere of N-heterocyclic carbenes (NHCs) using boronic acids (BAs) under reaction conditions and tested their reactivity and selectivity in the benzoin reaction. This in-situ modification afforded unprecedented enantioselectivity in the case of challenging electron-withdrawing substrates. Furthermore, in contrast to the reaction with the catalyst alone, the enantioselectivity is highly reproducible in the presence of BAs. We used mathematical modelling techniques to uncover the structural origin of enantioselectivity,¹⁻⁵ suggesting two possible reasons for its erosion in this system. This strategy allowed us to propose two different methods for improving selectivity. Our mechanistic studies indicate that BAs play a dual role—increasing the reactions' enantioselectivity and also inhibiting the racemization of the benzoin product.



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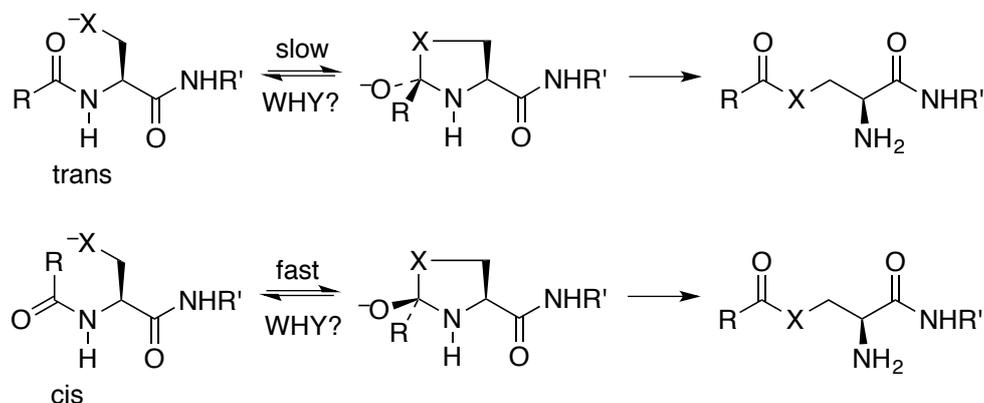
Approach Control. Stereoelectronic Origin of Geometric Constraints on N-to-S and N-to-O Acyl Shifts in Peptides

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Intramolecular N-to-S or N-to-O acyl shifts in peptides are of fundamental and practical importance, as they constitute the first step in protein splicing and can be used for the synthesis of thioester-modified peptides required for native chemical ligation. It has been stated that the nucleophile must be positioned anti to the carbonyl oxygen, as in a cis amide,¹ whose greater reactivity is attributed to its lower stability, relative to trans.² Despite the importance of such reactions, an understanding of this geometric restriction remains obscure. Both acyl shifts are classified as allowed 5-exo-trig,³ so Baldwin's Rules do not distinguish them.



It is proposed that the requirement for positioning the nucleophile is a stereoelectronic effect that arises from the ease of approach of the nucleophile to a carbonyl group. The explanation based on ground-state destabilization is rejected, because it violates the Curtin-Hammett Principle.

DFT(B3LYP)/6-311++G(d,p) calculations on model amides, CH₃CONHCH₂CH₂X⁻ (X = O, S, Se), support this stereoelectronic explanation and indicate a significant decrease, not only in the activation energy for a cis amide but also in its transition-state energy. However, the approach of the nucleophile must be anti not only to the carbonyl oxygen but also to the nitrogen. The direction of approach is expressed by a new, modified Bürgi-Dunitz angle. These data shed light on the mechanisms of acyl shifts in peptides, and they explain why a cis peptide might be required for protein splicing. The further implications for acyl shifts in homoserine and homocysteine peptides and for aldol condensations are also considered.

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A Kinetic Pathway for Protein Folding *in vivo*

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In this presentation two theories of the protein folding process are confronted. One theory relies on the thermodynamic hypothesis¹ according to which the native state corresponds to the minimum of the free energy in normal cellular conditions. In this view, folding reproducibility is assured by the supposition that most of the protein sequences found in living cells do indeed possess a well-defined global free energy minimum. The second theory relies on the kinetic hypothesis which assumes that most proteins have many, equally stable, kinetic traps and that the native state is just one of those kinetic traps^{2,3}. In this perspective, protein folding is a kinetic process and folding reproducibility follows from two requirements: one is that the initial conformation of the protein must be always the same, and another is that the pathway followed by the protein to reach its native state must also be always the same, as first proposed by Levinthal⁴.

These two theories lead to very different protocols for determining the native state of a protein in a computer. Indeed, according to the thermodynamic hypothesis, given a primary sequence it is necessary to search through the enormous conformational space the corresponding protein can access, to find the average conformation that minimizes its free energy. In spite of all the progress made concerning methods to accelerate conformational coverage and computer speed, in most cases, the thermodynamic protocols fail to predict the native states of proteins with sufficient accuracy for practical applications. On the other hand, according to the kinetic hypothesis, in order to determine the native structure in a computer, we need to know the initial conformation and the conformational trajectory from that initial conformation to the native state, effectively covering a much smaller part of the conformational space of each protein. Recently, a particular kinetic pathway has been proposed^{2,3} which is designated as VES KM for reasons that will become clear during the presentation. The VES KM assumes that the nascent chain of all proteins is helical and that the first and defining step of the protein folding pathway is the bending of that initial helix at a site that is specific for each sequence.

Molecular dynamical simulations, on a small all-alpha protein, following the VES KM protocol, will be shown which indicate that the VES KM can overcome the barriers faced by the thermodynamic hypothesis and allow for a more accurate prediction of protein native structure from sequence.

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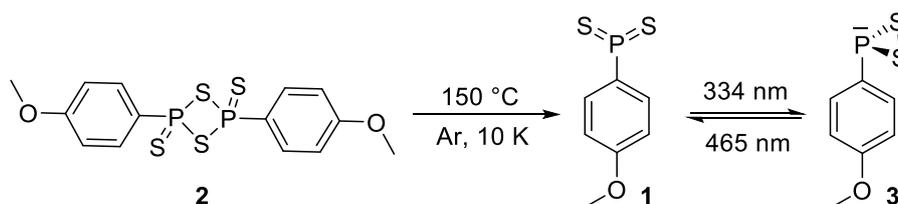
Unravelling Lawesson's Reagent – The Structure of Monomeric (4-Methoxyphenyl)phosphine Disulfide

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The talk reports the synthesis, IR as well as UV/Vis spectroscopic characterization of elusive 4-methoxy-phenylphosphine disulfide (1), isolated in an argon matrix at 10 K for the first time (Scheme 1).¹ This hitherto unreported molecule has been postulated as the key intermediate derived from Lawesson's reagent (2) that is extremely useful in sulfur transfer reactions.^{2,3} Structure 1 proved to be highly photolabile and irradiation with light of $\lambda = 334$ nm led to rearrangement to the hitherto unknown cyclic isomer 3-(4-methoxyphenyl)-1,2,3-dithiaphosphirane (3),¹ which represents the first three-membered organophosphorus-chalcogen ring incorporating a phosphorus atom in the oxidation state +3.⁴ Structure 3 rearranges back to 1 upon irradiation at $\lambda = 465$ nm. The structures and IR spectra of 1 and 3, and their deuterated isotopologues (d_3 -1 and d_3 -3) were unambiguously assigned through matching of experimental and DFT computations at B3LYP/6-311++G(3df, 3pd) level of theory.



Scheme 1. 4-Methoxy-phenylphosphine disulfide (1) generated from Lawesson's reagent 2 via pyrolysis and trapping in an argon matrix. Subsequent photochemistry to 3-(4-methoxyphenyl)-1,2,3-dithiaphosphirane (3).

We also examined the nature of the phosphorus-sulfur bonds in 1 and how this relates to its reactivity, which often invokes some ylide-type resonance form (1a) (Figure 1). Our bonding analysis finds no indications for ylide- or biradical-type species and the structure of 1 is best depicted with two nearly equal P=S double bonds.

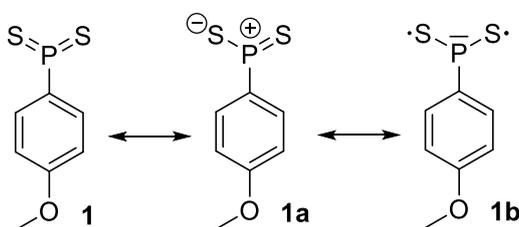


Figure 1. Resonance structure for 1.

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Computational Study of Substituent Effects on Gas-Phase Stabilities of Amino(phenylboranyl)methyl Anions

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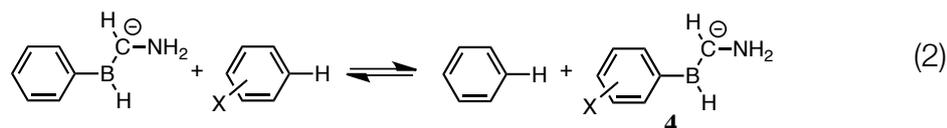
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Substituent effects on the stabilities of anions of aromatic compounds are well described by the extended Yukawa-Tsuno Eq. 1.¹

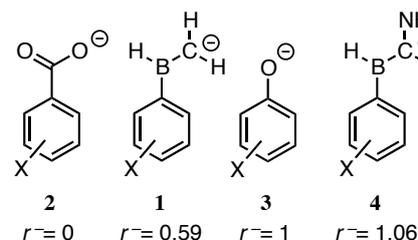
$$-\Delta E_X = \rho(\sigma^0 + r^-\Delta\bar{\sigma}_R^- + s\Delta\bar{\sigma}_S) \quad (1)$$

The normal substituent constant (s^0) measures the basic electron-donating or electron-withdrawing capabilities of all ring substituents. The resonance and saturation substituent constants ($\Delta\bar{\sigma}_R^-$ and $\Delta\bar{\sigma}_S$) were both defined by $s^- - s^0$ and measure the capability of the through-resonance and saturation effects, respectively. Resultant r^- and s values reveal the degree of the through-resonance and saturation effects in a given system, respectively.

Recently, we analyzed the substituent effects on the gas-phase stabilities of phenylboranymethyl anions (1) and obtained the r^- value of 0.59.² A canonical form in which the negative charge is delocalized on the benzene ring cannot be drawn for 1 similarly to benzoate anions (2) that is the s^0 -reference system. However, a large through-resonance effect was observed in 1, which is ca. 60% of that of phenoxide anion (3) of the s^- -reference system. To discuss the inducement mechanism of the through-resonance effect operating in 1 in detail, we computationally determined the substituent effect on the gas-phase stabilities of amino(phenylboranyl)methyl anions (4) using an isodesmic reaction 2 and analyzed them with Eq. 1 in this study.



An excellent linear correlation was obtained with the r value of 18.06, the r^- value of 1.06, and the s value of 0.61, with the correlation coefficient R of 0.999. The r^- value of 4 is significantly increased by introducing an NH_2 group to the anionic center and become even larger than that of 3, indicating the substantial through-resonance effect. NBO analyses revealed the orbital interaction between the p orbital of the B–C bond in the side chain and the p^* orbital of the benzene p -electron system in 4 of which the interaction energy is larger than that of 1. It has become apparent that the through-resonance effects in both 1 and 4 operate through the overlap of such the p - p^* orbitals.



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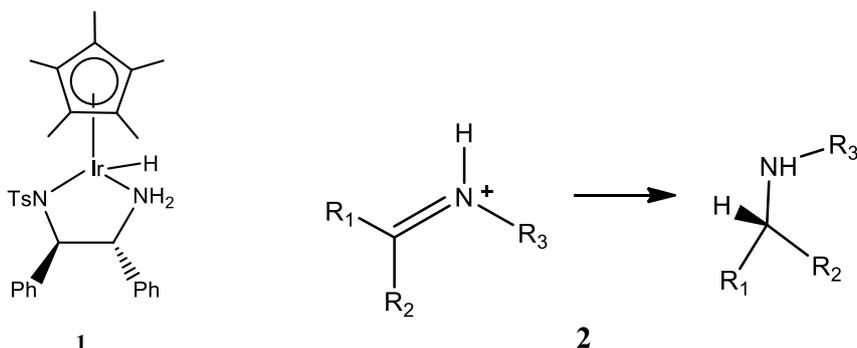
The Kinetics and Mechanism of Organo-Iridium-Catalysed Reactions

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The iridium complex of pentamethylcyclopentadiene and (S,S)-1,2-diphenyl-N'-tosylethane-1,2-diamine (**1**) 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.



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

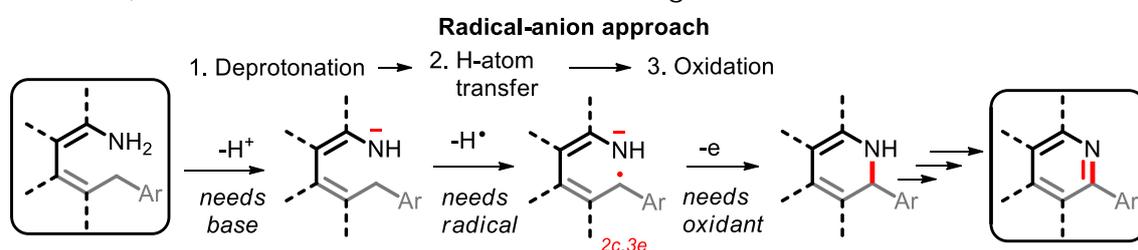
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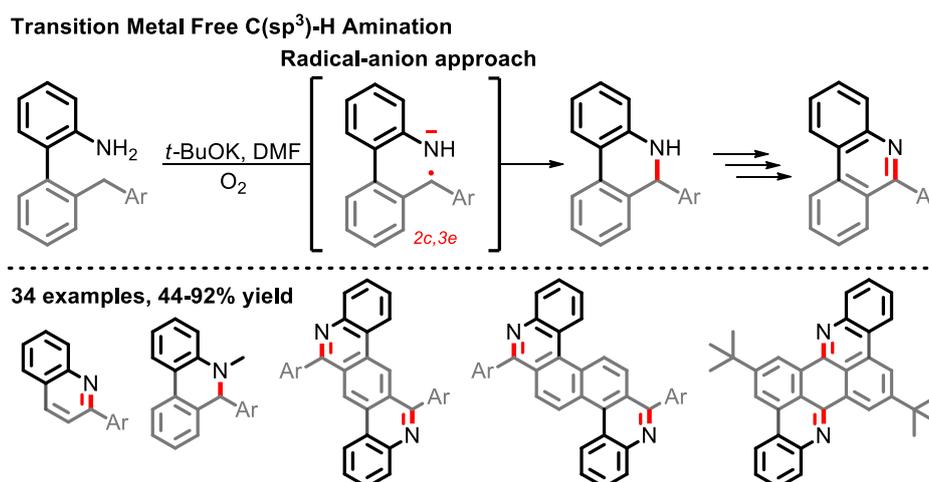
Coupling N-H Deprotonation, C-H Activation And Oxidation: Metal-Free C(sp³)-H Aminations with Unprotected Anilines

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An intramolecular oxidative C(sp³)-H amination from unprotected anilines and C(sp³)-H bonds readily occurs under mild conditions using *t*-BuOK, molecular oxygen and N,N-dimethylformamide (DMF). Success of this process, which requires mildly acidic N-H bonds and an activated C(sp³)-H bond (BDE = < 85 kcal/mol), stems from synergy between basic, radical and oxidizing species working together to promote a coordinated sequence of deprotonation; H-atom transfer and oxidation that forges a new C-N bond.



This process is applicable for the synthesis of a wide variety of N-heterocycles, ranging from small molecules to extended aromatics without the need for transition-metals or strong oxidants. Computational results reveal the mechanistic details and energy landscape for the sequence of individual steps that comprise this reaction cascade. The importance of base in this process stems from the much greater acidity of transition state and product for the 2c,3e C-N bond formation relative to the reactant. In this scenario, selective deprotonation provides the driving force for the process.



The process opens a quick access to the previously unknown classes of extended N-heterocycles.

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Oral 12

Desulfurization Route of Carbons Modified with SO₂. Polymerization of the Sulfur Allotropes Intermediates

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The desulfurization of carbons modified with SO₂ was studied as a dispersion in boiling cyclohexane. The reaction was followed with a diode array spectrophotometer, using modified activated carbon, 0.66 S% (mAC) and graphene oxide, 2.92 S% (mGO). For mAC there was a burst of a sulfur species identified as S₂ by the UV spectrum (λ_{\max} 215 nm, plateau at 250-270 nm), that showed a second-order decay of absorbance with $k_2 = 1.82 \times 10^2 \text{ M}^{-1} \text{ min}^{-1}$. The UV spectrum of the product showed λ_{\min} 212-215 nm, shoulder at 227-230 nm, which was postulated to correspond to S₄. No other reaction was observed within 60 min. However, mGO showed a zero-order decay up to 18 min with λ_{\min} 210, followed by a second-order increase of absorbance with $k_2 = 90.2 \text{ M}^{-1} \text{ min}^{-1}$ where the product showed a double maximum at λ 260-285 typical of S₈. These results are consistent with a mechanism of consecutive dimerizations of S₂ and S₄, which are both thermodynamically favorable, and with the desulfurization mechanism that have been previously postulated.^{1,2}

The desulfurization route presents a unique occasion to study the elusive sulfur allotropes, diatomic and tetrasulfur, in solution and at low temperature.

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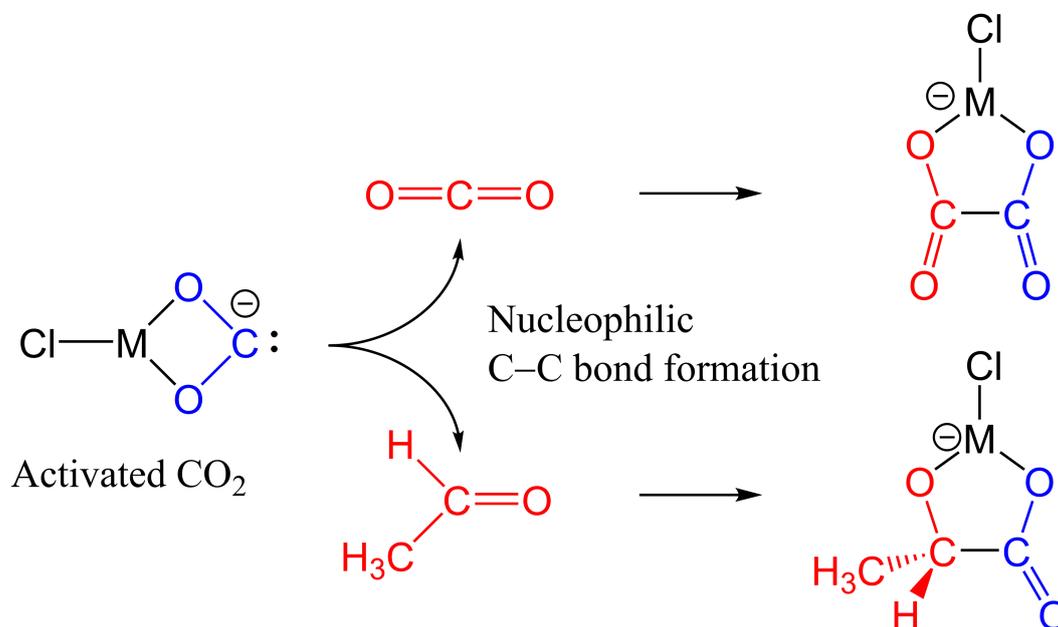
C–C Bond Formation of Mg and Zn Activated Carbon Dioxide

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Gas phase activation of CO₂ by chloride tagged metal atoms, CIM⁻ (M = Mg, Zn), has been investigated by mass spectrometry and high-level quantum chemistry. Both metals activate CO₂ with significant bending of the CO₂ moiety to form complexes with the general formula [CIM,CO₂]⁻. The structure of the metal-CO₂ complex depends on the method of formation, and the energy landscapes and reaction dynamics have been probed by collisional induced dissociation and thermal ion molecule reactions with isotopically labelled species. Having established these structural relationships, the gas phase reactivity of [CIM(κ²-O₂C)]⁻ with acetaldehyde (here considered a carbohydrate mimic) was then studied. Formation of lactate and enolate-pyruvate complexes are observed, showing that CO₂ fixation by C–C bond formation takes place. For M = Zn, even formation of free pyruvate (C₃H₃O₃⁻) is observed. Implications of the observed CO₂ reactivity to electrochemical conversion of carbon dioxide, and to biochemical and artificial photosynthesis is briefly discussed. Detailed potential energy diagrams obtained by the quantum chemical calculations offer models consistent with experimental observation.



Regioselectivity and Reaction Mechanism on Tricyanovinylolation of Pyrrole Derivatives

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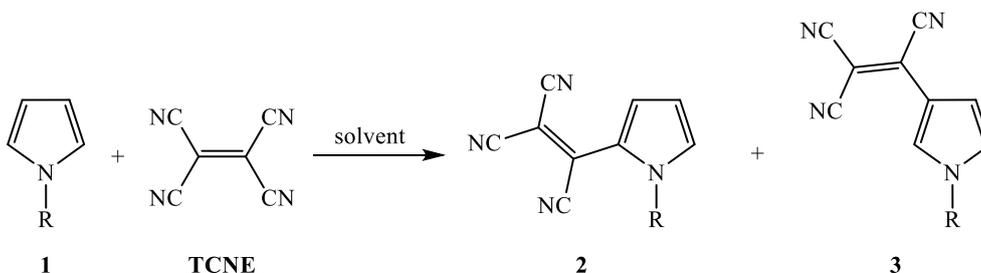
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Regioselectivities of tricyanovinylolation reaction of pyrroles have been investigated experimentally and theoretically. It has been reported that the regioselectivity of substitution reaction of pyrroles with tetracyanoethylene was frequently influenced by substitution on the nitrogen atom of the pyrrole ring,¹ and our experimental results also showed that reactivities and selectivities of this reaction were significantly affected by solvent species. Reaction mechanism analysis by molecular orbital calculation suggested that this reaction proceeded via stable intermediate, which was actually observed experimentally.



Scheme 1. Tricyanoethenylation of pyrroles.

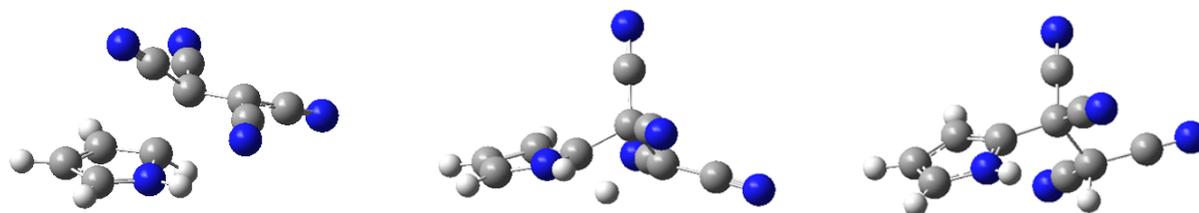


Figure 1. Reaction mechanism of C-C bond forming step in tricyanoethenylation of pyrrole with tetracyanoethylene optimized by cam-B3LYP/6-31+G(d) level calculation.

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Chemical Modification of g-C₃N₄ by β -Cyclodextrin for Enhanced H₂ Photocatalytic Generation

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Production of solar fuels (H₂) by water splitting using optical semiconductors requires a clear separation of the oxidation and reduction channels to achieve real significant performances.¹ The polymeric graphitic carbon nitride, g-C₃N₄ (CN) is a chemically stable, metal free wide bandgap semiconductor (2.7 eV), which we have used in the H₂ photocatalytic production.² However, the path to new synthetic routes endowing CN with better photocatalytic activity is still a challenge.

β -Cyclodextrin (β -CD) is a cyclic oligosaccharide that contains a hydrophobic inner cavity and a hydrophilic exterior containing -OH groups, which can condensate to form H-bonds with the precursors of CN, or be incorporated between the layers³ of CN, inducing therefore physical chemical modifications on electronic structure of the semiconductor.

In this work we report the synthesis, characterization and application of a CN photocatalyst modified with β -CD (hereafter designed as β -CD/CN) for the photocatalytic H₂ generation. The electronic spectrum of β -CD/CN shows a significant improvement of the light absorption in visible region as compared with pure CN. Furthermore, the bandgap energy of CN is somehow narrowed after modification with β -CD, suggesting a change on the interfacial structure of β -CD/CN as compared to CN. The photocatalytic performance of β -CD/CN and CN was assessed on H₂ generation, after 6 h of visible light irradiation ($\lambda > 400$ nm) of aqueous suspensions in presence of EDTA as sacrificial electron donor and Pt as co-catalyst. Under these conditions, β -CD/CN enhanced H₂ production by a factor of almost 5. This higher performance is attributed to the improved separation and mobility of the photogenerated charge carriers of β -CD/CN, as evidenced by steady-state and time-resolved luminescence studies.

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Beta Keto Acids: Structure, Reactivity, and Formation as Elusive Intermediates in Heterogeneous Catalysis

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Keto acids are best-known as intermediates formed in living organisms by food metabolism. Their decarboxylation in solutions and in catalysis by enzymes has been extensively studied by both experimental and computational methods.¹⁻³

Far less studied is the formation of beta keto acids as intermediates and their subsequent decarboxylation in the mechanism of high-temperature catalytic transformation of carboxylic acids into ketones on surface of metal oxides. Half life time of beta keto acids, counted by hours at mammal's body temperatures, is shortened to milliseconds and microseconds in a typical catalytic reactor operating at temperatures 300-450 °C.

Four compounds representing alkyl substituted acetoacetic acids which could form during catalytic decarboxylative cross-ketonization of a mixture of acetic and isobutyric acids have been synthesized and isolated in a solid form. Molecular structures of all acids were characterized by single crystal x-ray diffraction method. Reaction rates of their decarboxylation in solution were measured and correlated with the bond distances of the breaking C-C bond found by x-ray diffraction. The experimental order of reactivity based on alkyl substituents does not support the concerted mechanism of decarboxylation which has a different order of reactivity by DFT computations.⁴

Current investigation is a part of our broader research on the mechanism of the catalytic decarboxylative ketonization of carboxylic acids, in which we study adsorption and enolization of carboxylic acids on surface of zirconium and titanium oxides, their Claisen-like condensation, dehydration, and decarboxylation by both experimental and DFT computational methods.

When the temperature dependence of the decarboxylation rates in aqueous solutions is extrapolated to the typical temperatures of the vapor phase catalytic process, it can be concluded that the decarboxylation is not the rate limiting step of the decarboxylative ketonization mechanism.

Formation of beta keto acids via Claisen-like condensation of vapor phase carboxylic acids on surface of metal oxide catalysts is predicted by DFT computations to be the rate limiting step.⁴ Unlike esters, carboxylic acids do not form C-C bond by condensation in solutions. It will be explained how such condensation becomes possible in heterogeneous catalysis on surface of metal oxides. Experimental data obtained by physical chemistry methods on the most important steps will be provided in support of the DFT computational mechanism.

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Predicting Racemisation Risk to Avoid Pointless Stereoselective Syntheses

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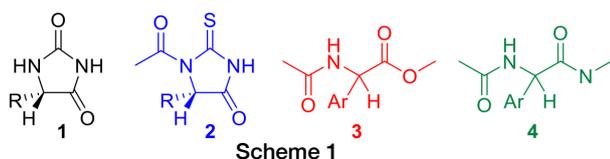
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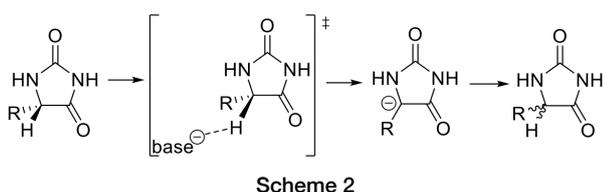
Enantiomers can show significant differences in key pharmaceutical properties, including inhibition of cytochrome P450s and blocking of the hERG channel.¹ It is therefore of interest to administer the correct enantiomer (or epimer) of drugs. The thalidomide disaster has resulted in strong awareness of the importance of chirality in drug development and to development of enantioselective syntheses.

Unfortunately, several types of stereogenic centres (including in thalidomide) racemise under physiological conditions. A detailed understanding of racemisation processes and a method to quantitatively predict racemisation risk are therefore required to avoid the synthesis and use of potentially pointless stereocentres.



We studied the kinetics and mechanism of racemisation of 1-4, carrying stereogenic centres involving a C-H bond, in aqueous solutions (H₂O and D₂O) using techniques

including ¹H NMR, circular dichroism, and mass spectroscopy as well as optical rotation. For 1, the ratio of the rate constant for racemisation and the rate constant for H/D exchange ($k_{rac}/k_{H/D}$) of 1.3, the primary KIE of 3.5, the solvent KIE of 1.0, general-base catalysis with a Brønsted β of 0.6, the activation parameters, and isotopic labelling experiments are all in agreement with an S_E1 mechanism (Scheme 2). Racemisation kinetics for 2 & 3 are more complicated because of concurrent hydrolysis processes but these reactions similarly proceed by the S_E2 mechanism.



We then predicted deprotonation energies using DFT and using a group contribution model. The racemisation rate constants for our compounds, together with



Figure 1

rate constants for additional compounds taken from the literature, correlate usefully with the predicted deprotonation energies. This correlation allows quantitative predictions of racemisation risk² which can be used to keep stereocentres safe by design (Figure 1).

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Chiral Intertwined Spirals and Chiroptical Properties - Dictated by Cylinder Helicity

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The presence of anomalous chirality in a roll of graphitic carbon sheets has been recognized since the discovery of carbon nanotubes (CNT). Exploration of the properties arising from cylinder chirality is expected to expand the scope of tubular entities in the future. By studying molecular fragments of helical CNT molecule, [4]cyclo-2,8-chrysenylene ([4]CC),¹ we herein revealed interesting properties that arise from this chirality.²

The chirality of nanoscale cylinders resulted in chirality of larger dimensions in the form of a double-helix assembly in crystalline state (Fig. 1a). (P)-(12,8)-[4]CC afforded M-type double helix in the space group of $P6_5$, and (M)-(12,8)-[4]CC afforded P-type double helix in the space group of $P6_1$. Furthermore, fluorescence measurements for a solution sample showed highly efficient emission with the quantum yield of 80%, and the emission was circularly polarized luminescence (CPL, Figure 1b). Cylinder chirality in solution gave the dissymmetry factor (g_{lum} value) of +0.152 for (M)-(12,8)-[4]CC and -0.152 for (P)-(12,8)-[4]CC, and this unprecedented value smashed world records of g_{lum} value of organic molecules for the first time in a half century. Theoretical investigations by TDDFT methods revealed the pivotal role of cylindrical shapes in enhancing magnetic dipole transition moments and minimizing electric dipole transition moments to yield extreme rotatory strength.

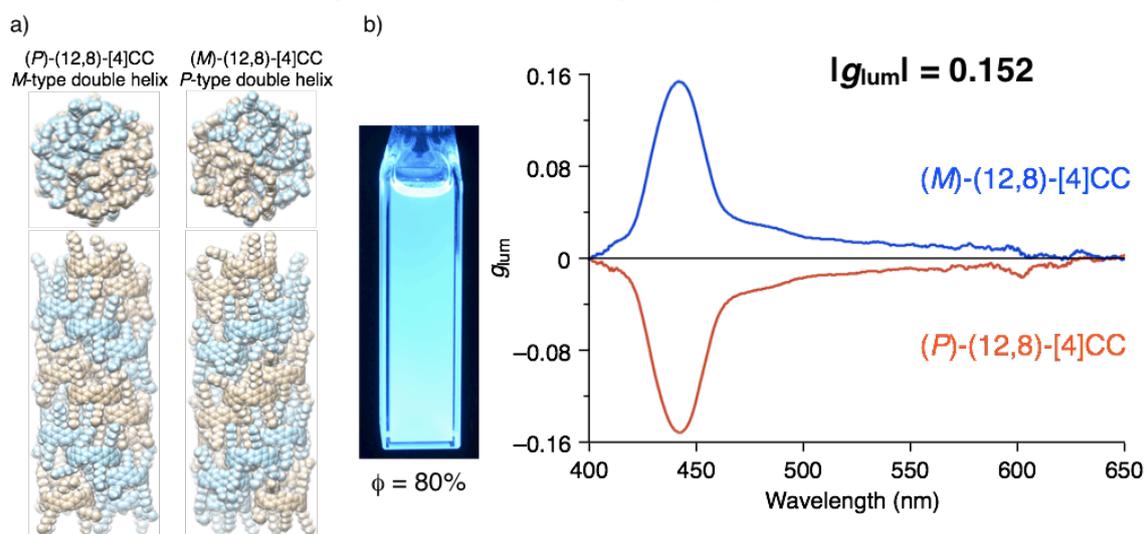


Figure 1. (a) Crystal packing structure of [4]CC and (b) optical properties in solution state.

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Molecular Recognition of Cations by Enantiopure Cryptophanes

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Water-soluble cryptophanes bearing phenol substituents exhibit high affinities for alkali cations such as $M^+ = K^+, Rb^+$ and Cs^+ . The thallium cation (Tl^+) is also very well-recognized with even higher association constants under the same experimental conditions.¹⁻⁴ These complexes have been thoroughly studied by ^{133}Cs and ^{205}Tl NMR spectroscopy as well as chiroptical techniques such as Electronic (ECD) and Vibrational Circular Dichroism (VCD). For instance, NMR spectroscopy revealed the presence of strongly high field shifted signals for both the $^{133}Cs@cryptophanes$ and the $^{205}Tl@cryptophanes$ complexes. An unusual behavior of the NMR spectra with the temperature has also been observed for several complexes. In addition, thanks to the synthesis of the enantiopure cryptophanes, Synchrotron Radiation Circular Dichroism (SRCD) and VCD spectroscopy have been used to reveal the conformational changes upon complexation.

Isothermal titration calorimetry (ITC) was found to be a powerful technique to quantify the interaction between the molecular host and the different cations in water. In addition, based on a model developed by D. Eggers that takes into account water molecules as a third partner we show that the desolvation free energy is extremely favorable for these systems ($\Delta G_{solv} < 0$).⁵

In conclusion, a thorough study of the $M^+@cryptophane$ complexes sheds light on the different parameters that lead to the efficient complexation of cationic species by the cryptophane derivatives. Our results show for the first time that water-molecules play a crucial role in the stabilization of these complexes.

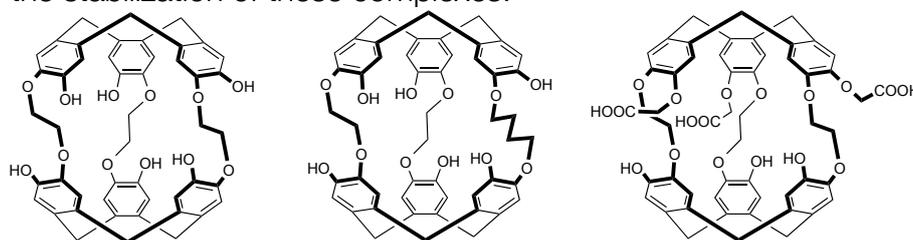


Figure 1: Structure of cryptophanes with good affinity for M^+ cations ($M^+ = Rb^+, Cs^+, Tl^+$).

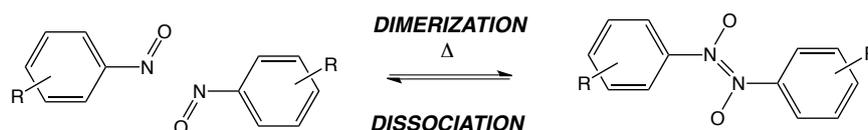
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Reaction Mechanisms in Crystalline Molecular Solids and their General Importance in Physical Organic Chemistry: A Case Study

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Using the dimerization-dissociation of aromatic C-nitroso compounds as a molecular model (Scheme) we have opened the discussion about the possible conceptualization of the reaction mechanisms in the molecular crystals. By detailed studies of the thermodynamics and kinetics of these thermally induced reactions occurring in crystalline solids we have found that the most important parameter which modify the chemical reactivity is activation entropy. Variation in activation entropy that could be caused by softening of the reactive zone within the crystal can in most cases compensate the changes in the enthalpy of activation, keeping the rate coefficient (and the free energy of activation) within the same range of values under different conditions. Since similar idea appeared also in studying thermodynamics and kinetics of the enzyme catalysis, investigations of the solid-state reaction mechanisms by using convenient models could be of more general importance in physical organic chemistry.



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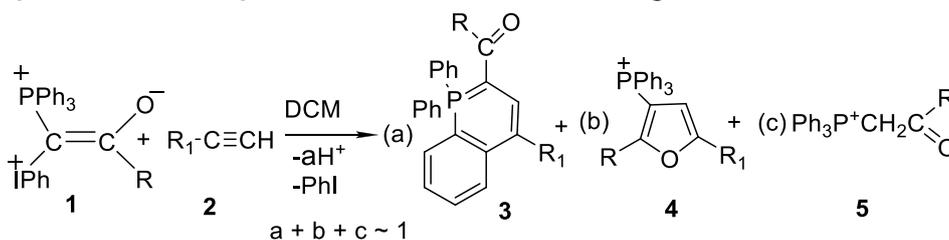
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Aggregation-Induced Chemical Reaction: Annulation of Acetylenes with Mixed Phosphonium-Iodonium Ylides

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Recently, it has been found that the reaction between mixed phosphonium-iodonium ylides (**1**) and acetylenes (**2**) affording two types of heterocyclic compounds, λ^5 -phosphinolines (**3**) and substituted furan derivative (**4**) (Scheme, the counter ion BF_4^- is omitted for simplicity), proceeds only in DCM at the ylide concentrations exceeding 0.01 M.¹



The reaction occurs with an induction time (4–20 min) and then develops in several minutes. This reaction is very simple, one-pot, metal-free method for the synthesis of different P-containing heterocycles by variation of the ylide and acetylene structures.² The ratio of the products **3** and **4** for ylide **1** depends on the ionization potential of the acetylene: the lower ionization potential, the higher yield of **4**. The ratio of the yields **3** : **4** for **1** ($R = \text{Ph}$) is 50 : traces, 40 : 40, and traces : 80 for phenylacetylene, 4-ethynylanisole, 9-ethynylphenanthrene, respectively.

It has been shown that the critical concentration of the ylide necessary for the formation of heterocycles coincides with a drastic increase in the size of the ylide aggregates in DCM, the diameter of which attain 900 nm at $[1] \geq 0.01 \text{ M}$.³ This implies that self-aggregation of ylides play the most important role for the annulation. The radicals generated in these aggregates either under the action of light or in the electron transfer between **1** and **2** are in close proximity to each other. This results in the fast formation of **4** in the radical pair and precursors of **3** in reactions of the radicals with **2**. The participation of radicals is confirmed by direct observation of relatively stable radicals by EPR⁴ and CIDNP effect in the ^1H and ^{31}P NMR spectra, negative for **3** and **4** and positive for **5**, observed in the course of the reaction. The independent formation of **3** and **4** via different mechanisms, acid catalysis, and the possibility to govern the direction of the reaction will be discussed.

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From Single-Electron Processes to Multielectron Handling and Storage at the Molecular Level: Designing Super-Electrophores for the Next Generation of Prototypes of Photochemical Molecular Devices for Man-Made Photosynthesis?

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As part of our continuing research program devoted to Artificial Photosynthesis,¹ which relies on multi-photon and multi-electron processes, we have recently revisited the physical chemistry, and especially the electrochemistry of pyridinium derivatives as multielectron acceptors.²

Here we report on design and rich electrochemistry of two classes of super-electrophores that share the common feature of being able to undergo a two-electron reduction in a single step. The functioning of these super-electrophores relies on the intriguing phenomenon of “potential inversion” that can be implemented in different ways, actually corresponding to two different electrochemical paradigms. On the one hand, there are polyaryl-substituted pyridiniums referred to as branched “Expanded Pyridiniums” (EPs), that are multifunctional platforms featuring good electrophoric properties and also effective chromophoric and luminophoric activities.^{2–4} On the other hand, there are specifically assembled multi-electrophoric compounds, referred to as “Structronic Assemblies” (SAs), characterized by their electrochemical hysteresis, that allow the storage of electrons in the form chemical bonds used as electron reservoirs.⁵

Special emphasis is herein placed on the rationalization of electrophoric properties and the mechanisms that explain the unusual electrochemical behavior of these two classes (EPs & SAs) of super-electrophores. These studies combine various experimental methods (crystallography, NMR, electrochemistry as well as in-situ UV-vis. and IR spectro-electrochemistry) with theoretical modeling. Finally, the manner by which these types of super-electrophores (EPs & SAs) could be used within the framework of research devoted to man-made photosynthesis, will be evoked.

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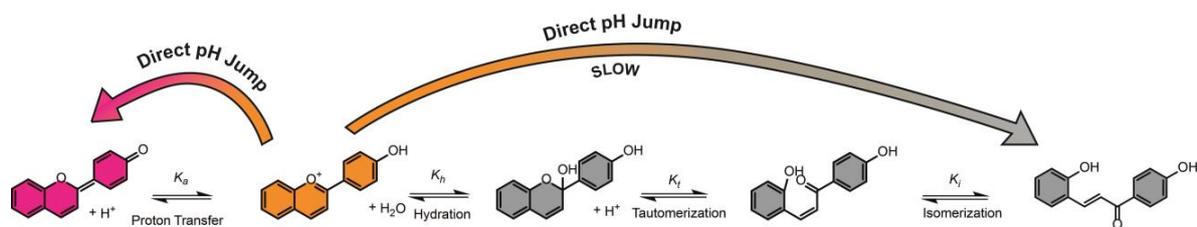
Stimuli-Responsive Supramolecular Systems Based on Bio-Inspired Molecular Switches

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Flavylium compounds comprise a family of both synthetic and natural dyes which include anthocyanins, the pigments responsible for most of the beautiful blue and red colors found in flowers and fruits. Independently of being natural or synthetic, flavylium compounds share the same intricate network of reversible chemical reactions (Scheme 1). The flavylium cation is only stable at acidic pH values. A pH jump to less acidic or neutral conditions gives rise to the sequential and reversible formation of different species, as exemplified in Scheme 1, and whose mole fraction distribution depends on the different substituents connected to the flavylium skeleton. In many synthetic compounds, the trans-chalcone is the main species present at the equilibrium under neutral slightly acidic conditions. Owing to the photochemical properties of this species and the reversible nature of the reaction network, the system can be reverted to the cationic species by light irradiation or reacidification. These features account for the multistate and multi-stimuli chromogenic properties of flavylium compounds. In this presentation, the kinetics, thermodynamic and photochemical properties of these compounds will be discussed and some examples of stimuli-responsive supramolecular systems based on flavylium cations will be introduced to demonstrate the great potential of this class of molecules in supramolecular chemistry and self-assembly.¹⁻⁶



Scheme 1 – Flavylium network of reversible chemical reactions.

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A Supramolecular Strategy to High-Quality Covalent Organic Frameworks

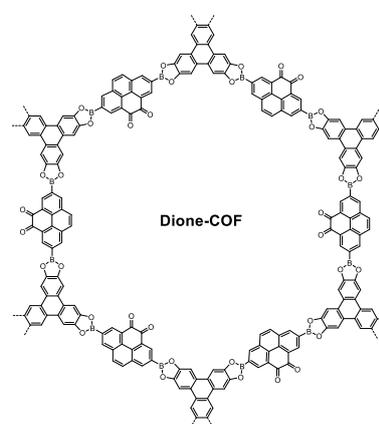
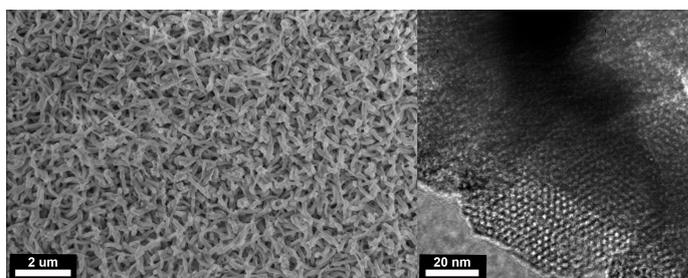
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Nanoporous 2D covalent organic frameworks (COFs)¹ are crystalline materials formed by the self-assembly of organic building blocks that assemble into sheets, which undergo stacking interactions, forming a porous structure. Due to their structural versatility, large specific surface area, and low density, COFs show great promise for a wide variety of applications, such as catalysis, gas storage, adsorption, and optoelectronics. Aromatic interactions play a central role in the formation, stability, and layer alignment of 2D COFs.² Despite the importance of these interactions in both formation and properties of 2D COFs, few experimental studies have been dedicated to their optimization.

Herein, we present a supramolecular strategy based on dipole moments to obtain highly crystalline and porous covalent organic frameworks.⁴ As a proof-of-principle, we have prepared Dione-COF based on pyrene-4,5-dione and hexahydroxytriphenylene. The strong dipole moment of the pyrene dione building block is proposed to favor columnar stacking within the pore wall and the obtained material features high crystallinity and surface area. Additionally, post-synthetic modification of the dione moieties was performed successfully. Overall, the supramolecular strategy for COF formation combined with post-synthetic modification of the constituting building blocks is a powerful approach to give access to more diverse and versatile COFs.



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Organic Fluorophores in Confined Environment: Properties and Applications

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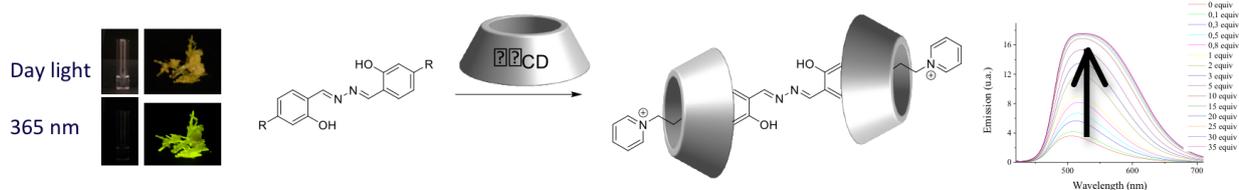
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All-organic luminescent dyes have attracted much attention for biological imaging, due to their ease of use, and because they are easily modified to fine-tune their properties. Unfortunately, they usually present a high sensitivity to their environment, and can lose their emission properties upon aggregation or interaction with their surroundings. Interestingly, some fluorophores present the opposite effect, and exhibit an enhanced emission intensity in confined environments.¹ These modifications of emission properties can be advantageous to detect a change in the environment of the dye.

A series of organic dyes based on a double hemi-salen core has been prepared and characterized (See figure below). They are almost non emissive in dilute solution, but become highly fluorescent when they are in the crystalline state, in a phenomenon known as Aggregation-Induced Emission Enhancement.¹ This observation has been rationalized through the study of their crystal structures. The emission wavelength of the dyes has been fine-tuned by modifying the substituents.

To broaden the scope of application of these fluorophores, water soluble derivatives have been prepared, presenting the same photophysical properties. Their interaction with cyclodextrins and DNA has been studied: upon formation of inclusion complex or interaction with DNA, the emission intensity is enhanced, in a way similar to when the dyes crystallize. These preliminary results illustrate the potential of these fluorophores for applications such as biological imaging and supramolecular detection of macromolecules.



Acknowledgements

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Hetero-Bambusurils

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Synthetic anion carriers are essential for studying natural ion transporters and channels and for useful applications, such as treatment of channelopathies, supramolecular architecture, anion sensing and catalysis. Considering the rich host-guest chemistry of the glycoluril-based cavitands, we anticipated that replacement of the oxygen atoms in bambusurils (BUs) by other heteroatoms, such as sulfur or nitrogen, would feature new binding properties along with attractive opportunities and novel applications. Recently, we described calculations of the molecular electrostatic potential of various glycoluril and bambusuril analogs, which predicted that heteroatom replacements would significantly alter their electrostatic surface, leading to a general trend of anion affinity: $X = S > O > NH$.¹ Furthermore, this study envisaged that protonated aza-bambusurils would bind multiple anions and could function as synthetic anion channels.

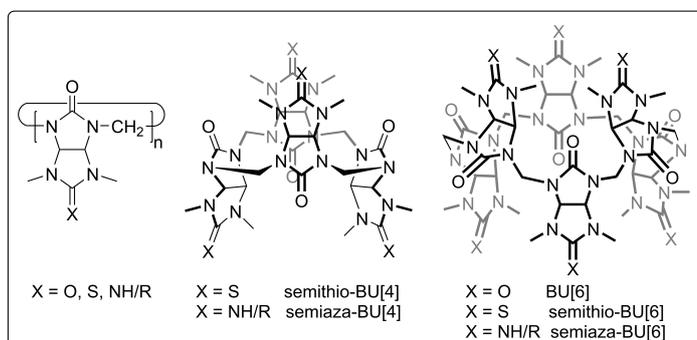
In this talk, I will present our experimental results with semithio- and semiaza-bambusurils,^{2,3} which confirmed those predictions, including synthesis, crystallography, thermogravimetry and calorimetry. By converting a semithio-bambus[6]uril into the corresponding semiaza-bambusuril we are able to switch a single anion receptor into a potential anion channel, which simultaneously accommodates three anions linearly positioned within the cavity along the main symmetry axis. The quaternary complexes of semiaza-BU[6]s demonstrate a notable capacity of overcoming the strong electrostatic repulsion among three anions held together at a significantly small distance, as short as 4 Å. It is noteworthy that exactly the same inter-anionic distance of 4 Å was reported for adjacent chloride binding sites in the crystal structures of two mutant *E. coli* ClC chloride channels.

Additionally, we show that although all bambusuril analogs are excellent anion binders, only the sulfur analog is also an effective anion transporter, capable of polarizing lipid membranes through selective anion uniport.⁴ This property, which reflects significant differences in the lipophilic character of the bambusuril analogs, may lead to therapeutic applications, such as treatment of channelopathies.

Another aspect of the semithio-BUs, namely, their ability to bind anions in their interiors and coordinate metal ions at their sulfur edged portals, is also highlighted.

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Influence of Dielectric Environment upon Isotope Effects on Glycoside Heterolysis: Computational Evaluation and Atomic Hessian Analysis

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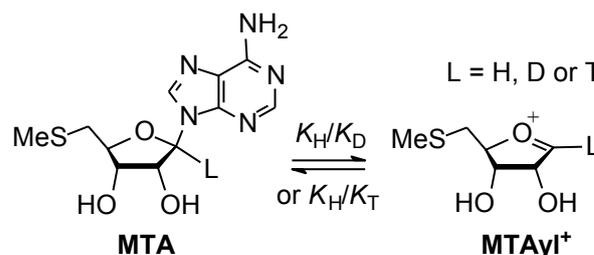
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Kinetic isotope effects (KIEs) are a powerful experimental tool for transition-state (TS) analysis of mechanisms of reactions in chemistry and biochemistry, provided that their values may be meaningfully interpreted. It is often assumed that trends in KIEs may be related to structural changes in TSs understood in terms of geometries and bond orders, but recent computational studies have suggested that changes in the electrostatic environment of a TS may be significant.¹⁻³ B3LYP/aug-cc-PVDZ/PCM calculations with a molecule-shaped UFF cavity show equilibrium IEs for heterolysis of the N-glycosidic bond in 5'-methylthioadenosine (MTA) in water ($\epsilon = 80$) to vary significantly as the dielectric constant for the MTAYl cation varies in the range $2 < \epsilon < 10$ usually considered to represent the environment of an enzyme active site. Interpretation of experimental KIEs for the reaction catalysed by MTA nucleosidase,⁴ should include consideration of the electrostatic environment of the TS and intermediate as well as the geometrical changes that accompany bond breaking and rehybridisation at the anomeric centre.



Remarkably, there is a near-perfect linear correlation between EIEs calculated from the full Hessian (involving all the atoms of MTA and MTAYl⁺) and an “atomic” Hessian (involving only atom L at the anomeric centre) over the range of dielectric constants. Essentially all the variation is captured by the influence of the dielectric upon the isotopically substituted atom alone. The atomic-Hessian EIE can be factorized into contributions from the three degrees of freedom of this atom, and logarithms of these factors plotted against $1 - 1/\epsilon$ (proportional to the electrostatic free energy in the Born model of solvation) illustrate a novel type of free-energy relationship which is linear for the stretching component but distinctly non-linear for the bending components. The vibrational frequencies and their isotopic shifts for motions transverse to the direction of covalent attachment of atom L to the rest of the molecule depend on specific characteristics of the cavity shape that we do not yet understand. This serves as a warning against use of implicit solvation models for calculations of isotope effects. A far better (but albeit more demanding) approach is to consider explicitly at least those parts of the first solvation shell that make direct contact with the site of isotopic substitution.

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New Studies of Interactions and Bond Formation in *Peri*-Naphthalenes

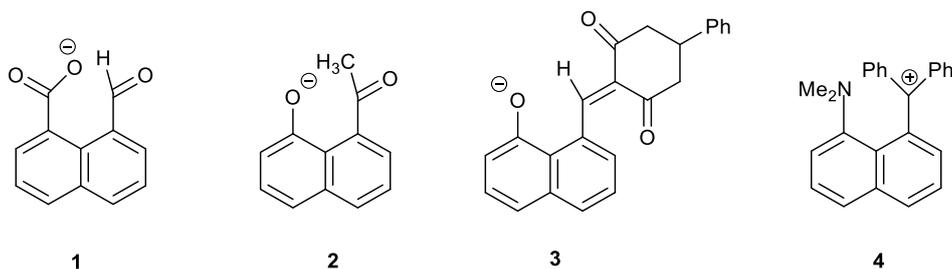
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We have been studying the interaction between pairs of electrophilic and nucleophilic groups located in the peri-positions of the naphthalene skeleton, as models for the different stages of bond formation, with particular interest in N-C bonds, with studies made by X-ray crystallography and charge density measurements and by solid state NMR.¹

Here we will report our new structural results on the interactions and bond formation between oxyanions and electrophilic centres. Of particular interest are the two modes of interaction between a carboxylate group and an aldehyde group in anion **1** in a series of salts with inorganic or organic cations. We will also report our first results where a naphthoate anion is the nucleophilic species, as in the tetramethylguanidinium salt of anion **2**, and how the interaction changes into bond formation when the ketone is replaced by a polarised alkene as in **3**.

New strategies to observe N---C interactions in the 1.60-2.40 Å region will be discussed including the molecular structure of the species where a dimethylamino group is positioned next to a carbocation centre as in **4**.



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On the Way from Understanding of Basic Principles to Rational Design of Reaction Conditions for Palladium Catalysed C–H Activation Reactions

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Knowledge of the exact structures of reactants, catalytic species and reaction intermediates has a crucial importance for understanding chemical reactions. However, identification of key species as well as their function in complex reaction mixtures could be very arduous. In recent work we are trying to explore in detail influence of carboxylic acids added to the palladium(II) acetate in C–H activation and functionalization reactions. The obtained findings could be used for rational design of reaction conditions.

Addition of carboxylic acids to the mixture of palladium acetate and substrate causes several effects; formation of precatalyst by substitution of acetates for carboxylates^{1,2} that changes the reactivity of palladium; protonation of substrate that makes it more or less available for C–H activation; finally, presence of stronger or weaker bases significantly changes the reaction profile of C–H activation.³ All these effects are explored experimentally as well as by theoretical calculations.

Our results open way to more rational optimisation of reaction conditions, milder reaction conditions and tuning the reactivity of substrates containing different directing groups.

Acknowledgements

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Interaction of Formic Acid with Nitrous Oxide and Carbon Monoxide

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Formic acid (FA, HCOOH), nitrous oxide (N₂O) and carbon monoxide (CO) participate in atmospheric chemistry, where noncovalent interactions play an important role. These molecules have also been detected in interstellar molecular clouds and are relevant to studies of prebiotic species in astrochemistry.¹⁻³

The complexes of FA with N₂O and CO were studied experimentally and computationally. The structure, energetics, and vibrational properties of the complexes were calculated at the M06-2X, MP2(full), and CCSD(T)-F12a levels of theory. Several structures of the trans-FA...N₂O and trans-FA...CO complexes were identified by infrared spectroscopy in cryogenic matrices. Higher-energy cis-FA...N₂O and cis-FA...CO complexes structures were prepared by vibrational excitation of the trans-FA conformer in the complex structures.⁴⁻⁶ The cis-FA...N₂O and cis-FA...CO complex structures decay back to the trans-FA...N₂O and trans-FA...CO complex structures by H atom tunneling.⁷ The lifetimes of the cis complex structures in the cryogenic matrices are longer than that of cis-FA monomer. This difference is explained in terms of the calculated barrier heights of these species.

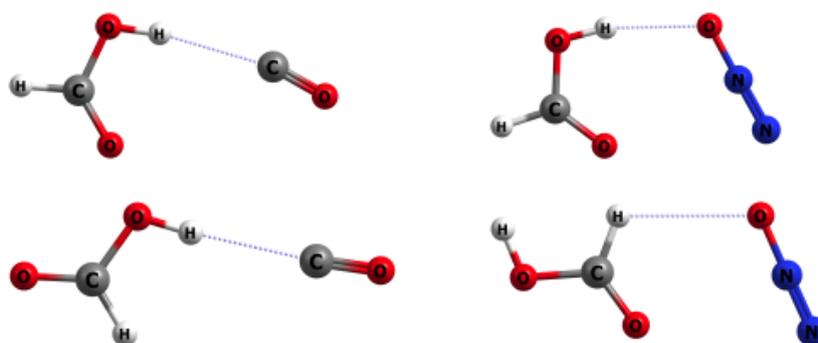


Figure 1 – Structures of trans and cis complexes of FA with CO and N₂O.

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Spontaneous and Photochemically Induced Reactions of Triplet 2-Formyl-Phenylnitrene in Low-Temperature Matrix

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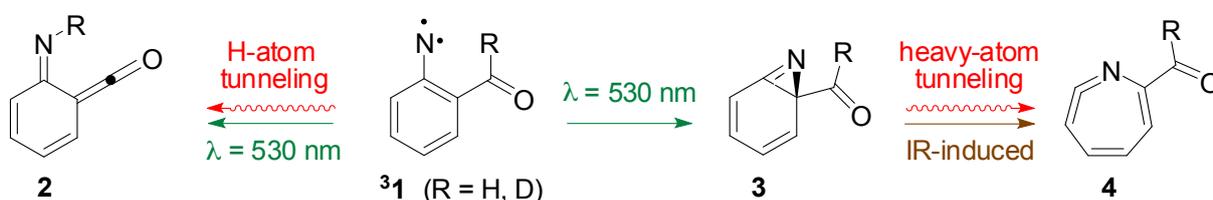
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Two isotopologues of triplet 2-formyl phenylnitrene (³1, Scheme 1), the formyl-protium (R=H) and its formyl-deuterated (R=D) analogue, were generated in cryogenic inert (Ar, Kr, Xe) matrices by UV-photolysis of respective 2-formyl-phenylazides.¹ The resulting phenylnitrene (³1) was characterized by IR, UV-vis, and EPR spectroscopies.¹



Scheme 1. Photochemical and spontaneous reactions of triplet 2-formyl phenylnitrene ³1.

The H-analogue of ³1 spontaneously rearranges to singlet 6-imino-2,4-cyclohexadien-1-one (2) in dark, at 10 K (Scheme 1) on the time scale of hours, while the D-substituted triplet ³1 was found to be stable against spontaneous decay under similar conditions.¹ The distinctive behavior of the two isotopologues indicates that decay of (³1, R=H) occurs by the tunneling mechanism.

Irradiation of 2-formyl phenylnitrene ³1 with visible (λ=530 nm) light results in its photo-transformation into imino-ketene 2, as well as into benzazirine 3.² Interestingly, we found that benzazirine 3 spontaneously rearranges, on the time scale of days, into cyclic ketenimine 4 (Scheme 1), at 10 K in dark (despite an estimated activation barrier of 7.5 kcal mol⁻¹). The experimental and theoretical data (IR spectra, kinetic profiles, potential energy surfaces) will be discussed. The rate constants without and with tunneling (using canonical variational transition state theory, and small curvature tunneling, respectively) were computed and confirmed that the observed spontaneous transformation of 3 into 4 can only occur by heavy atom tunneling.²

Acknowledgements

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Size-Induced Chemoselectivity in Esterification Reactions

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The directed use of London dispersion forces in chemo-, regio- or stereoselective transformations represents a key objective in current organic synthesis research.¹ We have now studied the reaction of carboxylic acid chlorides with secondary alcohols carrying flexible alkyl or rigid aryl substituents in the presence and the absence of rigid, planar pyridine-based catalysts. Relative reaction rates have been studied as a function of substrate substituent pattern, solvent choice and temperature. While reaction rates depend only moderately on the carboxylic acid substituents, large rate differences are observed for changes in the alcohol substrates. From this as well as spectroscopic data for transient intermediates of the catalytic cycle, an effective transition state model has been derived, where attractive interactions between alcohol side chains and catalysts lead to large rate accelerations.²

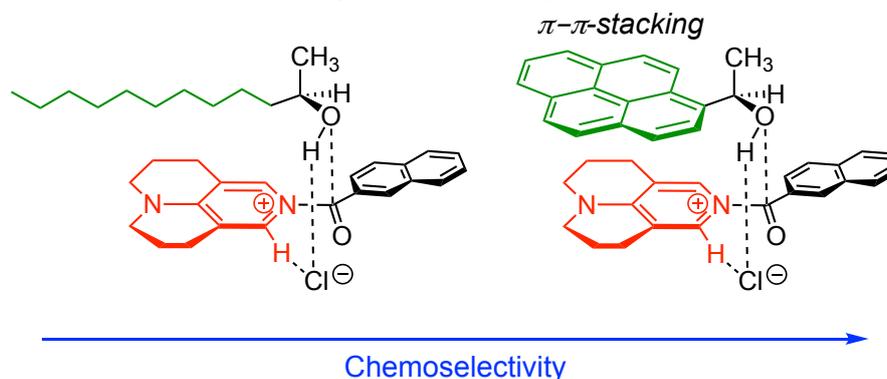


Figure 1: Transition state models for the acylation of conformationally flexible and preorganized alcohol substrates.

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A New Approach to Detect Short-Lived Radicals: Application to Atmospherically-Relevant Radicals

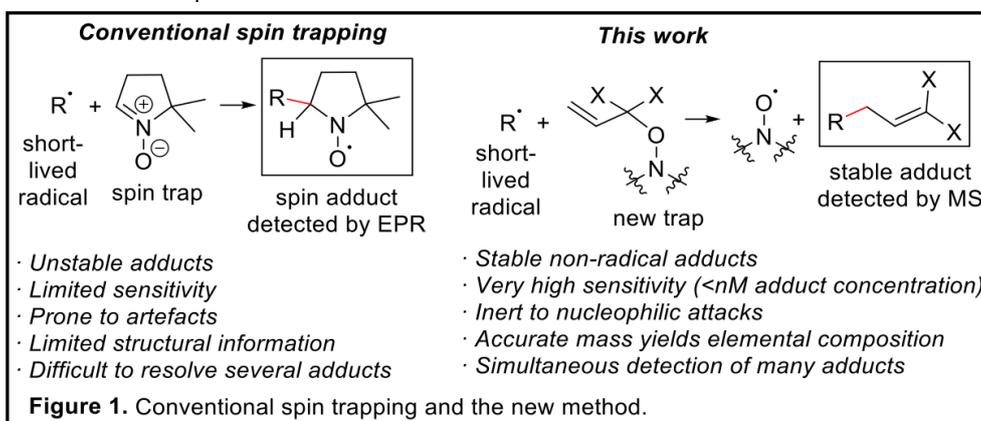
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Spin traps have been used for detection of short-lived radicals by EPR since 1960s. There are however some disadvantages to using spin traps (Figure 1). In this work, we develop a new type of radical traps which eliminate a stable nitroxide upon reaction with short-lived radicals. The stable adducts are detected by mass spectrometry (MS). MS has already been used with conventional spin adducts^{1,2}.



The new traps have been applied to the radical detection in the gas phase (e.g., oxidation of alkanes, Figure 2). 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.

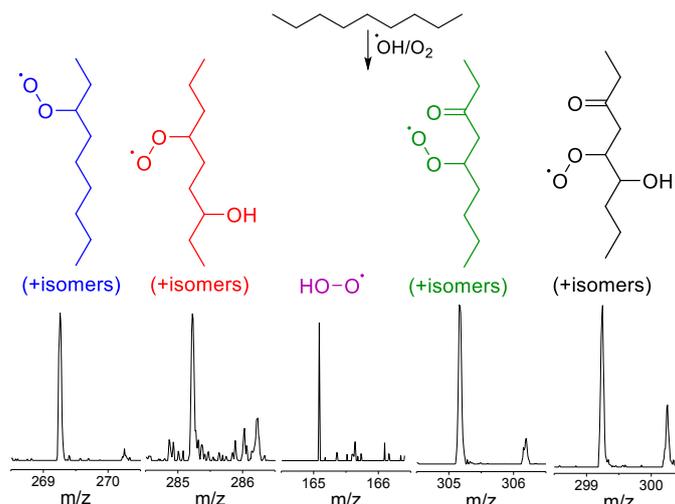


Figure 2. Trapping radicals in nonane oxidation.

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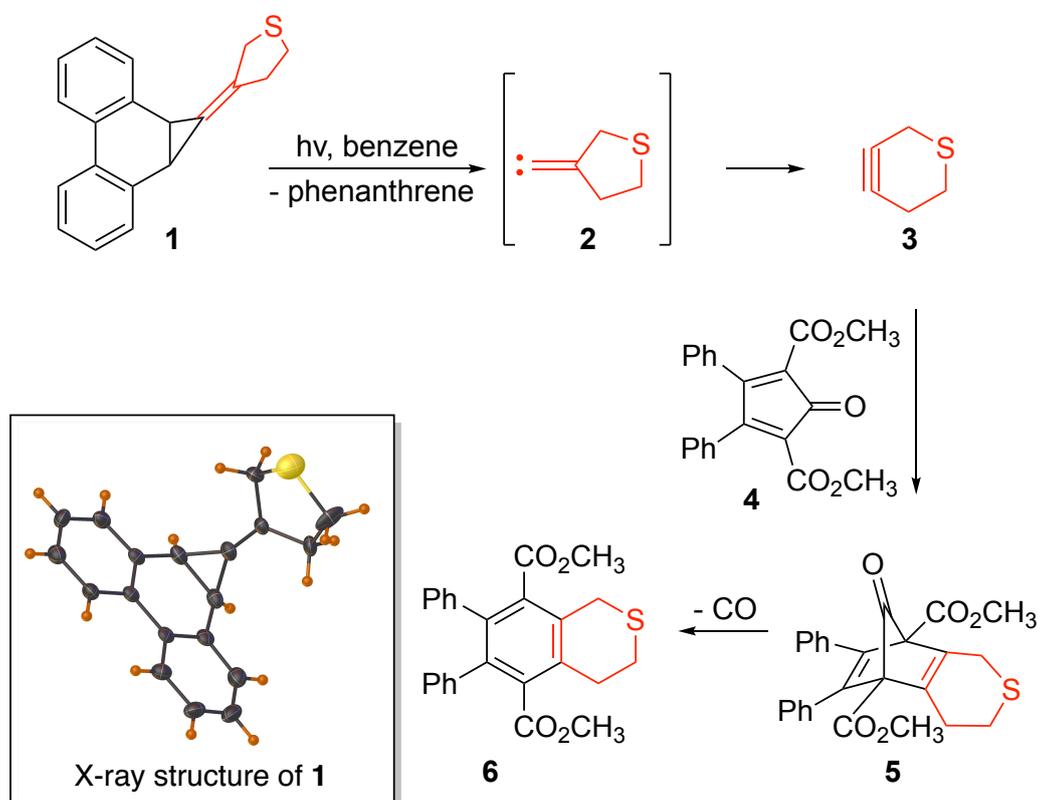
Generation and Trapping of 3-Thiacyclohexyne

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Previous work in our laboratory has shown that methylenecyclopropanes based on the phenanthrene system are photochemical sources of alkylidenecarbenes¹ and strained cycloalkynes.² In continuation of this work, we herein report the first photochemical generation of 3-thiacyclohexyne (3) from the cyclopropanated phenanthrene precursor (1), via the putative alkylidenecarbene (2). *In situ* trapping of 3 was accomplished using the dienone (4) which eventually led to the adduct 6, presumably after the loss of CO from the initially formed Diels-Alder product 5. Results of computational studies on the carbene 2 and its rearrangement into the strained heterocyclic alkyne 3 are also presented.



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In Search for Truly Green Photocatalysts

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Environmental pollution is currently one of the greatest challenges, and photocatalysis is a promising efficient decontamination alternative. In some cases, what are now considered as residues may be valorized profiting from photocatalysis. Finally, a number of relevant industrial manufacturing processes may also be improved making use of photocatalysis.

Among different available photocatalysts, nanosized particles of some oxides, such as TiO₂, have shown great advantages. However, photocatalysis is much more efficient in suspension, and the subsequent need for filtration reduces its efficiency by increasing the energy cost of the process... To reduce costs and improve separation, thin films of photocatalyst can be deposited onto particles that may be easily filtered out or separated from solution. For this, the sol-gel (SGM)¹ and liquid phase deposition (LPD) methods² have been frequently chosen. To improve the binding of the catalyst to the surface, different pre-treatments have been used, trying to increase surface microroughness to favor adhesion and prevent abrasion of the films.

We have used different photocatalytic approaches to the degradation of important and common water pollutants, including kinetic, thermodynamic and analytical aspects. We have explored homogeneous and heterogeneous methods, generated thin films, doped the structure of a photocatalyst to make it more effective, tried to profit from potential synergies of composite structures, etc. Here, we briefly discuss some of the obtained results, as well as some of the advantages and disadvantages of each method.

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Reactivity of the Atmospherically Important Hydrofluoropolyethers Towards OH: A Cost-Effective Implementation of Multiconformer Transition State Theory

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The adverse environmental impact of CFC release into the atmosphere^{1,2} has led to an international effort to replace them with acceptable alternatives. The Montreal Protocol led to the phase out of CFCs in industrialized countries because of their elevated ozone depletion and global warming potentials (ODP and GWP). Development of suitable replacements with lower tropospheric lifetimes became urgent, with HCFCs firstly selected as alternatives mainly on the basis of their higher reactivity towards OH radicals. However, HCFCs still had non-zero ODP and were also found to have a high GWP. Development of environmentally friendly second-generation replacements based on fluorocarbon derivatives thus became an urgent priority, with HFCs and PFCs appearing as a preferred choice. However, they were targeted by the Kyoto Protocol because of their high GWP. Renewed and increasingly important efforts to design and develop useful alternatives were then put into practice, with hydrofluoropolyethers (HFPEs) appearing as promising third-generation replacements because of their zero ODP and even lower GWP.

Here, we will provide a detailed insight behind the computational strategies involved in predicting the reactivity of different HFPEs with the general formula $R-(OCF_2CF_2)_p(OCF_2)_q-OR$ ($R=CF_2H, CH_3, CH_2CH_3, CH_2CH_2CH_3, CH(CH_3)_2$) towards the OH radical. We will focus on all $p=0, q=1$ cases and also on the $p=1, q=0$ case for $R=CH_3$. The quality of our cost-effective approach³ to the calculation of these rate constants through multiconformer transition state theory⁴ will be assessed by comparison with two experimental rate constants: $p=0, q=1$ with $R=CF_2H$ ⁵ and $p=1, q=0$ with $R=CH_3$ ⁶, since there are no reported theoretical results. Our objective is to start unveiling the theoretical aspects of the unestablished atmospheric chemistry of HFPEs, particularly the effect of changing the R group on the reactivity. Hopefully, the gained theoretical knowledge will serve as an important tool to boost the design and development of new greener CFC alternatives.

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Chemical Functionalization of Nanographene

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Graphene is a carbon allotrope structurally characterized by its sp^2 -bonded carbon layer. Graphene has several important features including mechanical strength, high carrier mobility, and zero-band gap. Opening the band gap of graphene has achieved by cutting of graphene by oxidants or strong acids, offering nanometer-sized graphene, graphene quantum dots (GQDs). GQDs have photoluminescence properties in UV-to-visible region due to quantum size and edge effects. GQDs often display blue- and yellow-light-emission, while those displaying white-light-emission are limited so far.

Recently, our group developed GQD (GQD-1) carrying 4-propynyloxybenzyl groups at the periphery (Figure 1).¹⁻³ GQD-1 is soluble in organic solvents such as dichloromethane and chloroform and can be chemically modified with organic functional groups by the Cu(I)-catalyzed Huisgen cycloaddition in organic solvents. We found that GQDs modified with the Fréchet's dendritic wedges display white-light-emission.

In this presentation, we will report the synthesis of chemically modified GQDs and their physical properties.

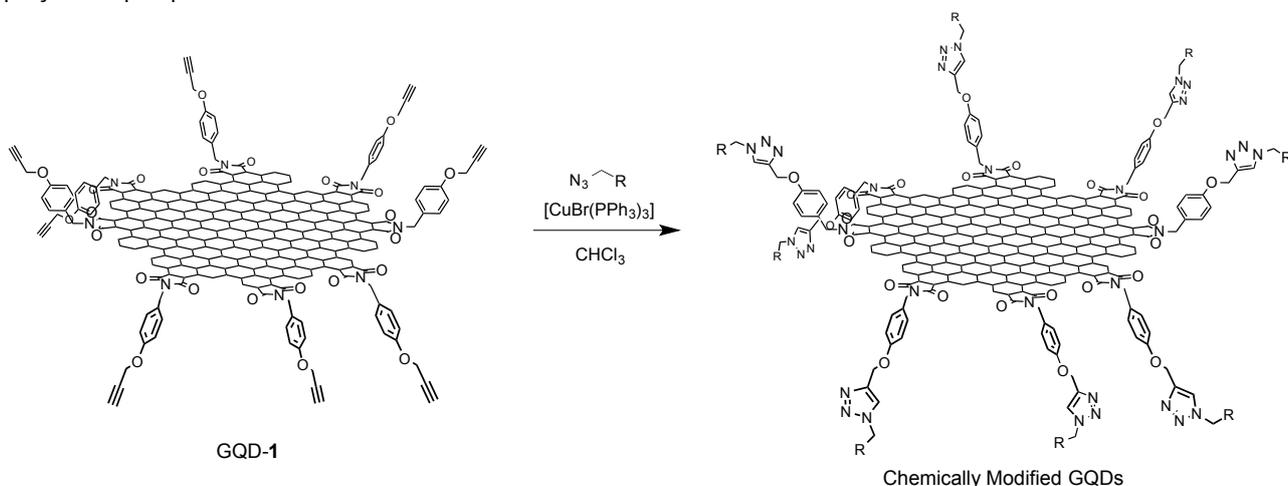


Figure 1

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Solvatochromic Donor-Acceptor Covalent Organic Frameworks

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Covalent organic frameworks (COFs) formed by connecting multidentate organic building blocks through covalent bonds provide a platform for designing multifunctional porous materials with atomic precision.

As they are promising materials for applications in optoelectronics, they would benefit from a maximum degree of long-range order within the framework, which has remained a major challenge. We have developed synthetic concepts to allow consecutive COF sheets to lock in position during crystal growth, and thus minimize the occurrence of stacking faults and dislocations.^{1,2} Hereby, the threedimensional conformation of the molecular building units is used to generate well-defined periodic docking sites, which guide the attachment of successive building blocks that, in turn, promote long-range order during COF formation. Applying this design concept we have constructed large-pore COFs with periodically ordered donor-acceptor motifs.^{3,4}

Most recently we have realized the first COFs that change their electronic structure reversibly depending on the surrounding atmosphere.⁵ These COFs can act as solid-state supramolecular solvatochromic sensors that show a strong colour change when exposed to humidity or solvent vapours, dependent on the vapour concentration and the solvent polarity. The excellent accessibility of the pores in vertically oriented films results in ultrafast response times below 200 ms, outperforming commercial humidity sensors by more than an order of magnitude. Employing a solvatochromic COF film as a vapour-sensitive light filter, we constructed a fast humidity sensor with full reversibility and stability over at least 4000 cycles. Considering their immense chemical diversity and modular design, COFs with fine-tuned solvatochromic properties could broaden the range of possible applications for these materials in sensing and optoelectronics.

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Metallo-Supramolecular Polyelectrolytes: From Growth Kinetics to Electrochromic Properties

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Recently, metallo-polymers (MEPE) have attracted considerable attention due to their promising properties for numerous technological applications. The metal ion-induced self-assembly of polytopic ligands results in macromolecular equilibrium structures that can adapt to external stimuli. Ditopic terpyridines and related ligands are often used due to strong metal ion binding and the pseudo-octahedral coordination geometry that in case of rigid ligands results in charged rigid-rod type macromolecules. With suitable counter ions MEPEs are soluble in water, presumably due to colloidal stabilization. The metal ions add interesting value-adding features, such as electrochemical, reactive, magnetic properties but they also offer unusual structural and dynamical aspects to the resulting polymers. In contrast to discrete metal complexes metallo-polymers can in principle be processed like polymers, which is an advantage for device fabrication. However, little is known about the polymer physics of these systems such as growth kinetics, size distribution, concentration dependence of structure. The presentation will address fundamental aspects of metallo-polymer growth and kinetics and will highlight possible applications including electrochromics.

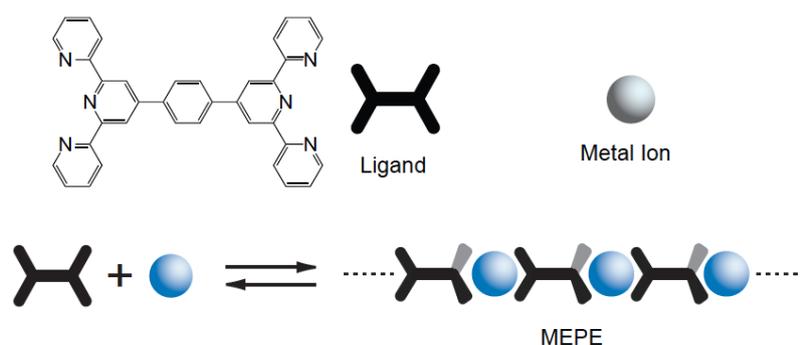


Figure 1. Metall-ion induced self-assembly of ditopic ligands based on terpyridines and related metal ion receptors results in spontaneous formation of equilibrium polymers.

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Metal-Organic Cages: Expanding the Toolbox of Stimuli-Responsive Behaviour

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Metal-organic cages function as molecular containers as there is the potential to encapsulate guest molecules with high affinity and selectivity within their well-defined cavities. Molecular networks can be constructed from stimuli-responsive cages¹⁻⁴ whose properties (e.g. guest uptake/release) are altered in response to an external signal. In order to design networks approaching the complexity and functionality exhibited by signalling pathways in biological systems, it is necessary to expand the toolbox of stimuli-responsive behaviour. Herein we report new strategies to control guest uptake/release within metal-organic cages, such as the transformation of a high-spin Fe^{II}L₄ cage to its low-spin analogue induced by subcomponent exchange.⁴ In a two cage system this transformation is exploited to switch guest release upon addition of a second chemical stimulus (Figure 1).

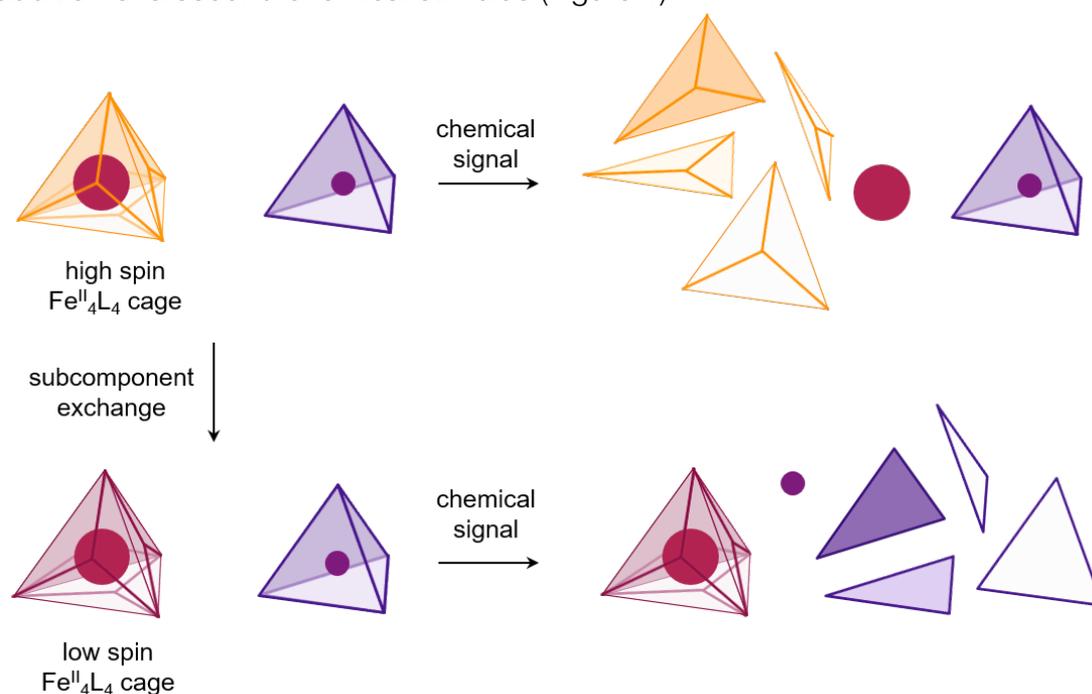


Figure 1. Transformation from a high- to low-spin cage induced by subcomponent exchange switches guest release upon addition of a second chemical stimulus.

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Advances in Cellulose Dissolution and Regeneration: From Scattering and Rheology to a New NMR Approach (With Some Controversial Thoughts in Between)

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As the major carbohydrate produced by plant biosynthesis, cellulose occupies a prominent place as a 'green' polymer for the production of innovative and sustainable materials. Unlike other polymers, cellulose is not meltable and therefore most of its applications rely on an efficient dissolution step followed by shaping processes where the properties of the regenerated material are strongly dependent on how well cellulose is dissolved and organized in solution.¹ Cellulose is insoluble in water but can be dissolved in acidic or alkaline conditions, given the proper conditions. However, work in developing new solvents for cellulose has been following a "trial and error" empirical character.² In the first part of this talk some basic fundamentals will be reviewed together with current perspectives. Our recent work emphasizes the role of cellulose charge and the concomitant ion entropy effects, as well as hydrophobic interactions.² On the second part, a new NMR methodology - Polarization Transfer Solid State NMR (PT ssNMR) - is introduced as a promising technique regarding an efficient and robust characterization of the solution state of cellulose. With this method it is possible to identify the liquid and solid fractions of cellulose, the degradation products, cellulose polymorphs, etc..^{3,4} Finally, combining static light and small angle X-ray scattering we will also probe the effect of cellulose aggregation on solution rheology.⁵

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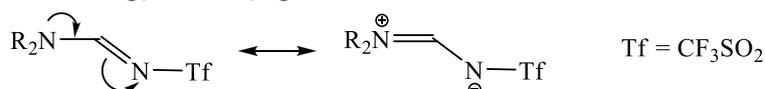
Structural, Electronic and Mechanistic Features of Unsaturated Triflamides

B. Shainyan

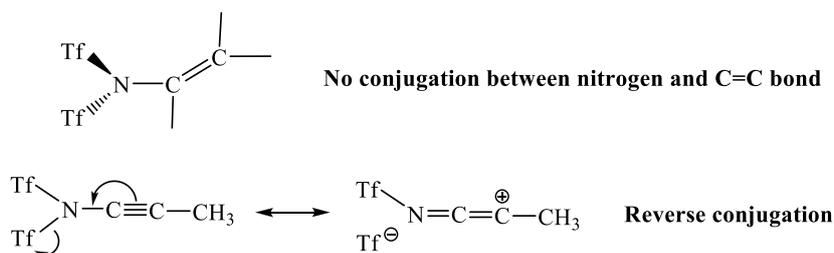
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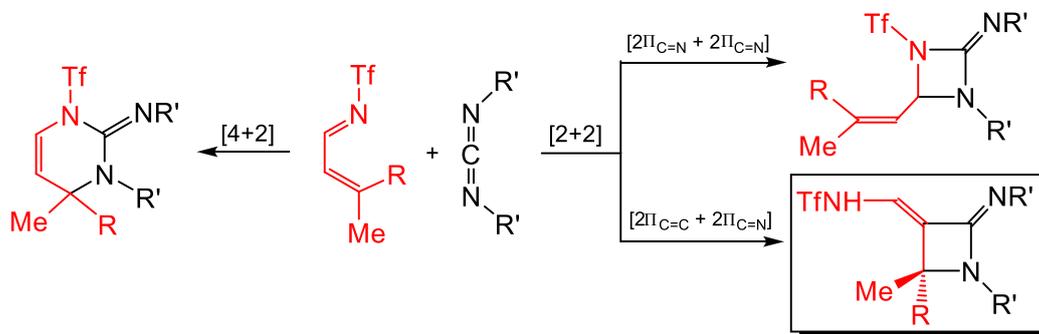
Structural: N-Triflylamidines $\text{TfN}=\text{CHNR}_2$ and N-triflyl guanidines $\text{TfN}=\text{C}(\text{NHR})_2$ revealed an unusual structural feature: from the X-ray analysis, the formally single C–N bonds in their molecules turned out to be shorter than the formally double C=N bonds indicating a very strong conjugation in the N=C–N triad.^{1,2} Theoretical calculations and NBO analysis were applied to evaluate the energy of conjugation.



Electronic: Theoretical analysis of spatial and electronic structure of N-propenyltriflamides showed the absence of conjugation between the nitrogen atom and the C=C bond because of orthogonal arrangement. In N-propynyltriflamides, unlike in ynamines, the conjugation is directed from the triple bond to the nitrogen atom, whose p-orbital is practically vacant due to strong electronwithdrawing effect of two triflyl groups.³



Mechanistic: Exclusive $[2\pi_{\text{C}=\text{C}} + 2\pi_{\text{C}=\text{N}}]$ cyclization of N-alkenyldenetriflamides with carbodiimides was verified by theoretical calculations, which showed that $[2\pi_{\text{C}=\text{C}} + 2\pi_{\text{C}=\text{N}}]$ cyclization has $\Delta G^\circ > 0$ and, hence, is thermodynamically forbidden, and the $[4+2]$ route is unfavorable due to a small content of the s-cis conformer of azadiene.⁴



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The Conundrum of the $C_4H_7^+$ Cation Dedicated to George A. Olah

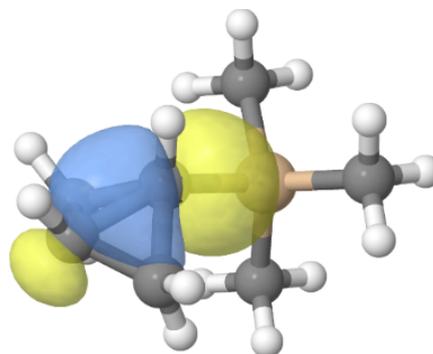
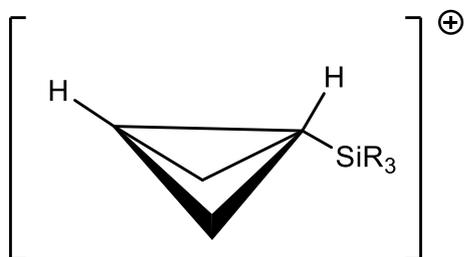
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Nobel Laureate George A. Olah passed away March 8, 2017 at the age of 89. George Olah was a true legend in the field of chemistry. His pioneering research created an entire new field of chemistry of considerable theoretical and practical importance. 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 Bicyclobutonium $C_4H_7^+$ and related cations.



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How to Cope with Change? The Effects of Dynamic Environments on Out-of-Equilibrium Chemical Reaction Networks: Behaviour Diversification and Early Warning Signals

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Out-of-equilibrium systems chemistry promises to transform our current chemical systems and inanimate materials into life-like systems. Yet, the governing principles guiding the behaviour of these systems in dynamically changing environments have been overlooked and are unknown. Here, we demonstrate that the coupling of a small out-of-equilibrium chemical reaction network (Figure 1A)¹⁻⁴ to its temperature environment can enrich its functional output as the network is capable of harnessing a dynamic temperature forcing to produce new emergent properties of increasing complexity (Figure 1B). Our results show new pathways to diversifying out-of-equilibrium behaviour of chemical reaction networks without the need to change the underlying network structure or composition. Through measuring the Arrhenius dependence of reactions in the network we are able to model the effect of temperature which reveals that chemical reaction networks are capable of sensing their proximity to a collapse transition and present characteristic Early Warning Signals prior to failure (Figure 1A).

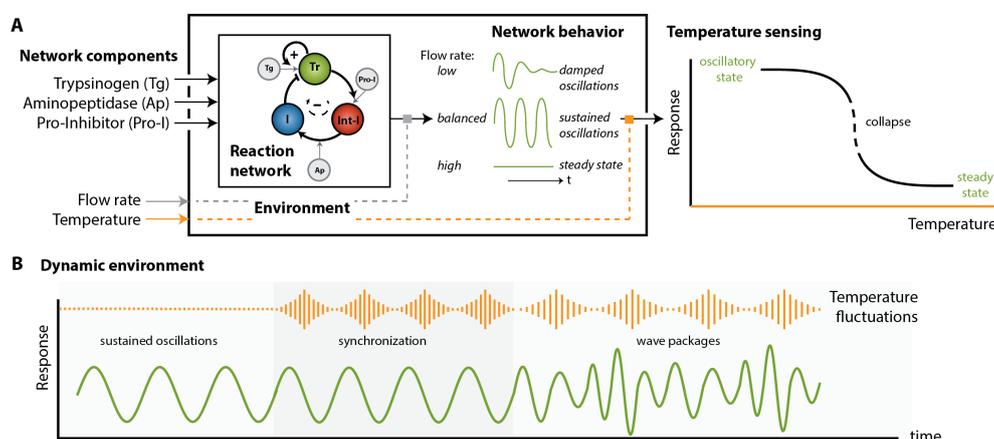


Figure 1. A) The Trypsin oscillator network is kept out-of-equilibrium in a Continuous Stirred Flow Reactor. The behaviour of the network is affected by its environment, namely temperature and flow rate, and shows oscillations only within a certain temperature range, outside of which the oscillations dampen to a steady state. The network is capable of sensing this transition in behaviour. B) In the presence of a dynamic environment the behaviour of the network increases in complexity and is able to synchronise to a sinusoidal temperature forcing and generate a new wave packet behaviour.

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ADH1A - Catalysed ATP Hydrolysis is Coupled to Ethanol Dehydrogenation by Energy Transfer

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Recently we explored the mechanism of light transport within the inverted retina, where the light enters Müller cell endfeet at the inner limiting membrane of the retina, meeting intermediate filaments (IFs) that fill larger part of the interior of these glial cells. These IFs traverse the entire length of Müller cells, following uninterrupted into neighboring cones, and going inside these up to the opsin-containing photosensitive membrane¹. These electronic microscopy results led us to propose that IFs transport light to the photosensitive membrane, in the form of excitons (excited states), as the small diameter of the IF bundles inside the cone cells precludes propagation of photons. This explains the high-contrast vision achieved in the inverted retina, which can't be adequately accounted for either by the classic optics or the Müller-cell light-guide hypothesis. We present further evidence that confirms our ideas, produced both in our group and elsewhere².

These results brought us to a hypothesis on the more ubiquitous role of excitons in live systems. In particular, we explored excitons interacting with human ADH1A alcohol dehydrogenase enzyme, both immobilized on solid support with embedded Co nanofilm excitonic conductor³, and in solution. Excitons were produced by enzyme molecules that hydrolyzed ATP producing ADP, and transmitted to other enzyme molecules where the enzymatic reaction took place, transforming ethanol into the acetaldehyde (AA) product. Alternatively, excitons were produced by either visible photons absorbed by the Co nanofilm, or by ultraviolet photons absorbed by the ADH1A-NAD complex, generating AA with higher than unity quantum yields in both cases.

These results show that the enzymatic function is controlled by the possibility to dump energy from the transient state at the ATP-binding site, either to the substrate-binding site on the same enzyme molecule in vivo, or to the Co nanofilm in our experiments. On the other hand, the enzymatic function at the substrate-binding site is controlled by the energy received either from the ATP-binding site in vivo, or from the Co nanofilm in our experiments. We also infer that excitons propagate within the protein molecule along the polypeptide backbone. We present additional experimental data in favor of our theory.

The present results justify a new look at the cellular morphology and function, due to the possibility of excitonic energy transfer within and between the cells, at the structure and function of enzymes, controlled by energy exchange, and also at the evolutionary role of enzymes that can operate on sunlight without requiring ATP.

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In-Cage Reaction of Intermediates Generated in the Photosolvolysis of 3-Substituted 2-benzyloxy-naphthalene

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Photosolvolysis of 2-benzyloxy-naphthalenes (1) in methanol undergo cleavage of NaphO-CH₂Ph bond to afford benzyl methyl ether (2), benzyl alcohol (3), benzaldehyde (4), and benzyl benzoate (5) as products derived from benzyl moiety. The first product was obtained by the nucleophilic addition of methanol to benzyl cation, while the other products are considered resulted from the reaction of benzyl radical with O₂ in solution. Over 90% homolytic products were obtained in the photosolvolysis under aerobic condition, while the evacuation of O₂ from solution diminished the homolytic products and increased the yield of 2 up to 38% in accord with the retardation of photosolvolysis rate (Table 1). These effects of O₂ in solution indicate that photosolvolysis of 1a exhibits concurrent heterolysis and homolysis of ether bond, and the radical intermediates return to substrate if they were not trapped by O₂ in solution. The heterolytic / homolytic product ratio was also affected by the substituent at 3-position, and increased with electron donating substituent such as -OH (1b), -OMe (1c), -NH₂ (1d), and -NMe₂ (1e) (Table 2). The product distribution as well as the rate of photosolvolysis of 1c, on the other hand, were little affected by the evacuation of O₂ from solution, suggesting that less homolytic intermediates were involved in the photosolvolysis of 1c. Trapping of benzyl cation or radical generated in the photosolvolysis of 1c was carried out in the presence of N₃⁻ or TEMPO, respectively, however, ended in failure. The results indicate that the photosolvolyses of 1 afford their intermediates as geminate pairs, which react within the cage of solvent. To clarify the in-cage reactions of heterolytic intermediates, photosolvolysis product derived from naphthoxide moiety was investigated in the photosolvolysis of 1c. It was revealed that 3-OMe-2-OH-naphthalenes with benzyl substituent at naphthalene ring were obtained besides of 3-OMe-2-OH-naphthalene.

Table 1. Effect of O₂ in Solution on Yields of Photosolvolysis Product of 1a in MeOH

Cond.	Irrad.	Conv.	2	3	4	5	6
Aerobic	90 min	46.7%	5.6%	67.8%	-	26.6%	-
Degassed	15 h	54.5%	37.7%	3.3%	-	-	15.5%

Table 2. Yields of Photosolvolysis Product of 1 in MeOH

X	Irrad.	Conv.	2	3	4	5	6
H	90 min	46.7%	5.6%	67.8%	-	26.6%	-
OH	75 min	58.6%	64.2%	4.3%	3.9%	-	-
OMe	20 min	47.7%	54.0%	4.3%	9.0%	-	-
NH ₂	15 min	61.8%	45.7%	9.2%	8.6%	-	-
NMe ₂	10 min	53.7%	59.8%	4.75%	3.18%	5.59%	-

Broad-Spectrum Azole-Based Molecules: From Strong Ligands in Coordination Chemistry to Organocatalysts

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Small organic molecules continue to occupy a privileged space on the development of crucial areas for the welfare of the humanity, such as medicinal chemistry and catalysis. From the huge number of small organic compounds known currently, there are some restricted families that are distinctive, proving to be effective when applied to different problems. Within this limited group we highlight three heterocyclic compounds namely, tetrazole, (iso)thiazole and thiadiazole.

These five-membered ring heterocycles are very important building blocks in organic synthesis and are widely used in coordination chemistry as ligands. Such kind of azole-type compounds can coordinate through the nitrogen or sulphur electron-donating atoms in the ring, acting as multidentate robust units able to participate in distinct coordination modes with metal ions. Frequently, metal-complexes comprising these ligands reveal superior catalytic activity even in harsher chemical environments (e.g. in presence of strong oxidants or reductants). As multifunctional molecules and attending to their physico-chemical properties, tetrazole, thiazole and thiadiazole derivatives, may interact by itself with numerous chemical systems others than metal ions, by establishing a wide range of intramolecular interactions. For that reason, many of these molecules proved to be excellent organocatalysts in several reactions. The most remarkable example is (S)-5-(pyrrolidin-2-yl)-1H-tetrazole (proline isoster) which has emerged as a singular organocatalyst to mediate a variety of useful asymmetric reactions, including aldol, Michael, Mannich, α -amination reactions and so forth.^{1,2}

Novel catalytic systems for the anaerobic oxidation of benzyl and secondary alcohols, using a tetrazole-amino-saccharin organocatalyst or Cu(II) and Co(II) tetrazole-saccharinate complexes, have been recently established by us and will be presented in this communication.^{3,4}

Acknowledgements: This work was partially supported by the Foundation for Science and Technology (FCT), Portugal, (UID/QUI/00100/2013 and "Investigador 2013" [IF/01270/2013/CP1163/CT0007] programs). L.F. and M.N.K. express gratitude to FCT for the post-doc fellowship (SFRH/BPD/99851/2014) and working contract, respectively. B.G.M.R. is grateful to FCT for the PhD fellowship (SFRH/BD/52370/2013; CATSUS PhD program PD/00248/2012).

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Task-Specific Ionic Liquids for CO₂ Capture and Catalytic Conversion in fuels

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Carbon capture and sequestration (CCS) is currently under scrutiny at large pilot-plant level as a mitigation strategy for the CO₂ emission problems and global warming.

The present work describes the development of alternative technologies for CO₂ capture and further conversion to value-added products.

Two different approaches will be discussed:

- i) an alternative, competitive and reversible CO₂ capture system using bioinspired ionic liquids and salts based on aminoacids, monosaccharides, di- and polysaccharides in the presence of organic superbases (e.g. Tetramethylguanidine, TMG and DBU);¹⁻⁴
- ii) the use of ruthenium nanoparticles, produced in situ and stabilized in suitable fluorinated ionic liquid media, to produce methane (at least 88% of conversion) from CO₂ by hydrogenation reaction.⁵

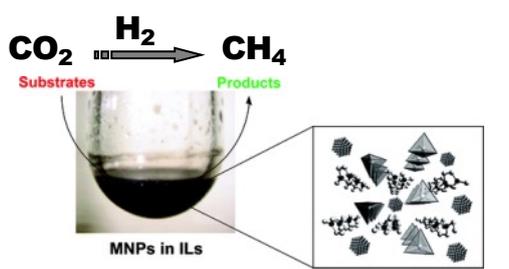


Figure 1- Carbon Dioxide catalytic conversion in methane by hydrogenation reactions in the presence of Ru nanoparticles/ionic liquid systems.

The capability of task-specific ionic liquids (ILs) to absorb CO₂ both physically and chemically opens-up the possibility of simultaneous capture and conversion CO₂ into desired products. This type of technology seems to be promising for future applications in sustainable nanocatalysis and energy fields.

Acknowledgements: This work was supported by the Associate Laboratory for Green Chemistry- LAQV which is financed by national funds from FCT/MCTES (UID/QUI/50006/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01-0145-FEDER - 007265). Also, we thank to the project “SunStorage - Harvesting and storage of solar energy”, with reference POCI-01- 0145-FEDER- 016387 and by national funds (PTDC/QEQ-QFI/1971/2014), trough FCT - Fundação para a Ciência e a Tecnologia.

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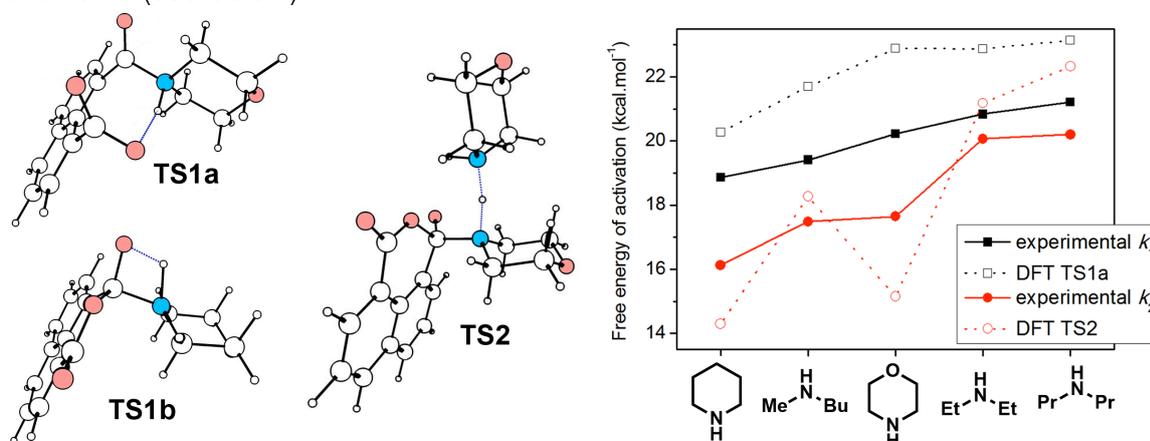
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Aminolysis of 1,8-Naphthalic Anhydrides in Aprotic Solvents Involves Two Reaction Paths

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We have recently shown that in a system possessing an otherwise unactivated amide positioned between two carboxyls, the model amide is cleaved at an enzyme-like rate due to the concerted action of two carboxylic moieties in proper geometries, at distances less than the diameter of water.¹ In order to fully understand the system we report some results on the reverse reaction, consistent with previous findings. Aminolysis of naphthalic anhydride (NAn) and its 4-nitro, 4-bromo-, 4-amino, 2- and 4-carboxy derivatives with secondary amines showed to be first and second order with respect to amine. The kinetic data could be fitted using the quadratic equation $k_{\text{obs}} = k_1[\text{amine}] + k_2[\text{amine}]^2$, where k_1 and k_2 are the rate constants for the reaction involving one (path i) or two amines (path ii), respectively. Substituent effects indicate that both reaction paths are accelerated by electron-withdrawing groups, while solvent effects suggest charge development in the TS, with observed decreases in reaction rates in less polar solvents. For both paths the reaction of NAn with amines in DMSO follows the order piperidine > N-methylbutylamine > morpholine > diethylamine > dipropylamine, indicating that the reactivity is related to both the steric bulkiness and basicity of the nucleophile. Interestingly, $\log k$ vs the nucleophilicity parameter N is linear for k_1 only. This result is consistent with the hypothesis that in path ii one of the amines acts as a general base catalyst. The mechanism of NAn aminolysis was also studied by DFT calculations. For path i, a concerted transition state (TS1a) with proton transfer to the leaving group was 12 kcal.mol⁻¹ lower in energy compared to a stepwise mechanism (TS1b), with proton transfer to the carbonyl oxygen and formation of a tetrahedral intermediate. For path ii, a mechanism involving the attack of the amine with general base catalysis by a second amine was found (TS2). The good agreement between experimental and theoretical DG^\ddagger support the proposed mechanisms (see below).



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Thiophenediyl-bridged Macrocages as Crystalline Molecular Dipolar Rotors

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Much attention has been focused on the chemistry of artificial molecular rotors.¹ We have reported macrocage molecules with a bridged phenylene 1a-1c as molecular rotors in a crystalline state, because the phenylene encased by three alkyl spokes can rotate rapidly inside a crystal.² Recently, we have reported a macrocage molecule with a bridged thiophene-diyl (2a,2b) or selenophene-diyl (3a,3b) as a molecular rotor in a crystalline state.³ In this presentation, similarity and dissimilarity of the properties among crystalline molecular rotors are discussed.

Structures of the molecules inside a single crystals were determined by X-ray crystallography (eg. Figure 1b). There are sufficient space for the rotors for rotation inside the cages. Rotation of the rotor inside crystalline states can be observed by solid-state ²H NMR spectroscopy using derivatives of which aromatic moieties were labeled with deuterium atoms. The thermal rotation of the rotor is accelerated with increasing temperature confirmed by solid-state NMR, the activation energies for the rotation are dependent on the size of the cages.

In the case of the thiophene-diyl or selenophene-diyl bridged derivatives, observation of intermolecular dipole–dipole interactions in a crystalline state are expected due to dipole moments of the hetero ring. Actually, crystal structures of these compounds at low temperature showed that the hetero rings were oriented diametrically opposite each other to cancel out the polarization. However at high temperature the crystal structures exhibited that the rings were randomly oriented between the two sites with exchange, indicating intermolecular dipole–dipole interactions were disturbed by thermal noise.

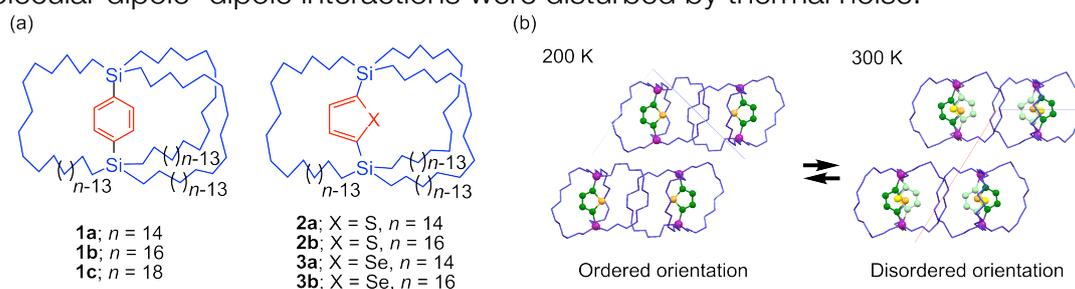


Figure 1. (a) Structural formulas of molecular rotors and (b) temperature dependent crystal structures of 2a.

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Light-Induced Release of Guests from Host-Guest Complexes in Water

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The idea of using light to remotely control supramolecular assemblies is very attractive for the design of functional systems with applications as intelligent soft materials, in delivery, sensing/monitoring or for the demonstration of chemical communication. Our recent focus has been on cucurbiturils (CBs) and their host-guest complexes, enabling the working in water under conditions that assimilate bio-relevant situations.¹ This has been integrated with the design of light-responsive systems, (a) by implementing photochemical reactivity with the guest² or (b) by employing phototriggers that change equilibrium conditions of the host-guest complexes, e.g., change of pH or generation of competitor guests.³⁻⁵ In this presentation two systems that exemplify the two strategies will be highlighted. Thus, the templated [4+4] photocycloaddition of anthracenes in a homoternary complex with cucurbit[8]uril will be discussed in the context of strategy (a).² Strategy (b) will be illustrated by the release of guests from their complexes with cucurbit[7]uril by means of the light-induced generation of a competitor (see Figure 1).³⁻⁵

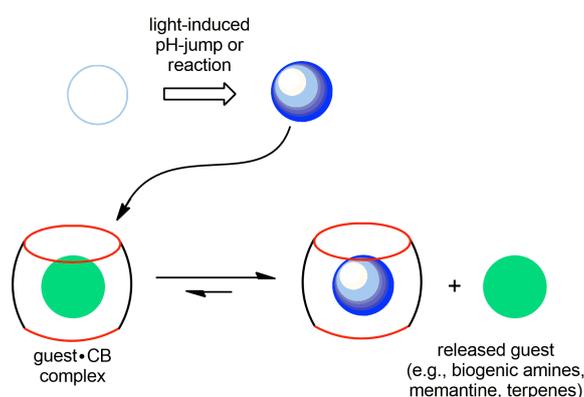


Figure 1. General presentation of strategy (b); see text.

Acknowledgement. The work was supported by the Spanish MINECO (CTQ2014-54729-G2-1-P), ERDF, the Junta de Andalucía (P12-FQM-2140), and the Associated Laboratory for Sustainable Chemistry-Clean Processes and Technologies-LAQV [FCT/MEC (UID/QUI/50006/2013) and ERDF (POCI-01-0145-FEDER-007265)]. N.B. thanks the Portuguese FCT for the award of a postdoctoral grant (SFRH/BPD/84805/2012).

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Light-Controlled Molecular Encapsulation

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The encapsulation and controlled release of small molecules has attracted persistent attention across both academic and industrial research interests and has been applied to a range of fields including separation and purification, sensing, solubilization and stabilization of reactive ingredients, stimuli responsive materials and capture of hazardous substances.¹ There also exist biological analogues including visual transduction, which is initiated by the photoisomerization of retinal in the integral membrane protein, Bacteriorhodopsin, resulting in the extracellular release of a proton.²

The design of light controlled molecular encapsulation host/guest systems requires that either the host or guest has two stable, readily photo-accessible states, which differ in their binding strengths by orders of magnitude. Systems which rely on the photo-switching of the guest have been well documented³ but have a relatively limited scope of applicability, as they require specially designed guest molecules. Macrocyclic hosts incorporating a photoswitchable element would, however, facilitate the uptake and release of a wider range of guest species and hence have greater versatility. However, they also suffer from undesirable drawbacks, including cumbersome synthesis and hindered photoisomerization on account of ring strain and molecular crowding.⁴

Here, we report our work on strategies to impart photoswitchable properties to molecular hosts, which are capable of uptake and photo-stimulated release of a range of guest species by drawing upon the well-known E/Z photoisomerization of azobenzene. In the first case we design an azobenzene ancillary first guest for the macrocycle cucurbit[8]uril (CB[8]), which is capable of incorporating a second guest within its cavity. Photoisomerisation between the E and Z states of the azobenzene results in the selective inclusion and expulsion of a range of small molecules from the CB[8] cavity. In the second case we incorporate two azobenzene units within the backbone of a flexible macrocycle. Four imidazolium units provide hydrogen bonding recognition potential for guests with appropriate hydrogen bonding acceptors, which may be regulated by alternative exposure to ultra violet and visible light.

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Tuning Particle Diameter and Morphology of Hybrid Mesoporous Silica Nanoparticles and Application to Controlled Drug Release

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Mesoporous silica nanoparticles (MSNs) have received considerable attention due to their excellent biocompatibility, high surface areas, large pore volumes, high loading capacity, uniform and tunable pore sizes, and versatile surface functionalization.¹

The most common processes to synthesize MSNs use either ammonium bases and co-solvents, or hydroxide base in aqueous media, leading to diameters that are usually larger than 100 nm.² For MSNs with diameter under 100 nm, only a few works can be found, usually by changing the silica source/surfactant ratio, temperature, or by introducing silicate hydrolysis retardant agents – essentially with a low degree of control over the properties of the obtained MSNs.²

Here, we describe the preparation of MSNs with precisely controlled diameters under 100 nm, under mild synthesis conditions.³ The synthesis is performed using a sol-gel method, in an aqueous medium, with TEOS as silica source, an ionic surfactant as template, without ammonium bases or co-solvents, at constant temperature. We are able to control the particle diameters from 20 to 80 nm with low size dispersity, by varying the pH and/or the ionic strength. The dimension and shape (alligned vs. wormhole) of the pore system can also be controlled, in this case by varying the ionic strength of the reaction mixture. Additionally, the morphology of the particles is tuned by varying the reaction temperature.

Additionally, we have used this low size MSNs as nanocontainers, with the external surface selectively modified with a temperature-responsive biocompatible copolymer to control cargo release. The nanoparticles feature either a polymer brush or a gel-like responsive shell, produced by grafting from RAFT polymerization of PEG-acrylate macromonomers. Our proof-of-concept system shows that by modulating the temperature, it is possible to achieve a pumping regime that increases the release rate in a controlled way.⁴

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Influence of Molecular Symmetry on the Entropy of Pure Phases

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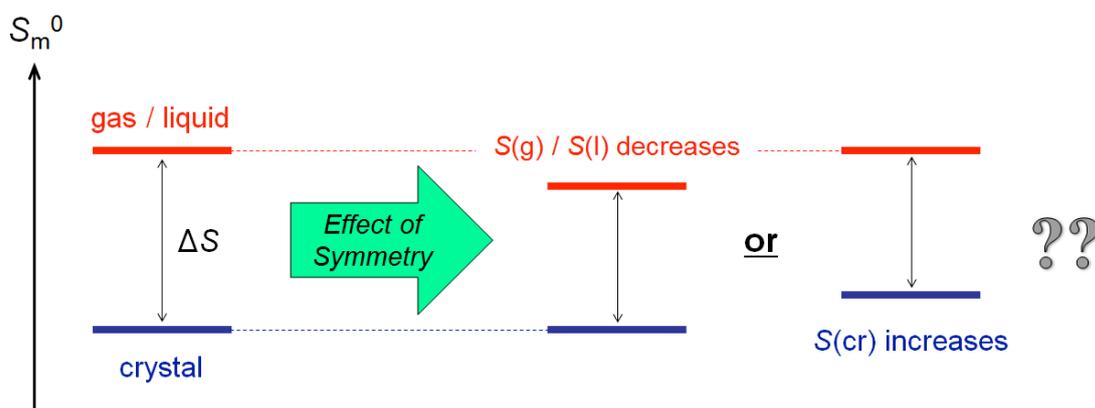
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Molecular symmetry has a notorious influence on the entropy of compounds.¹⁻³ For example, it impacts on phase equilibria, being known that symmetrical compounds generally have higher melting points and lower volatility. However, the question of in which phases of matter does symmetry affects entropy has never been thoroughly discussed. Does symmetry increase the entropy of the solid or does it decrease the entropy of liquid and gas phases? Herein, through careful analysis of some relevant experimental evidence, we propose an answer to this question. The results and rationale constitute compelling evidence that, at least for relatively large polyatomic molecules, the influence of molecular symmetry is chiefly reflected on the entropy of the crystal phase. Symmetry increases the number of equivalent ways to allocate the molecule in the crystal lattice and this increases the residual entropy of the solid by $R \cdot \ln(\sigma_{\text{sym}})$, where σ_{sym} is the molecular symmetry number. Moreover, by indicating that symmetry has no meaningful effect on rotational entropy, these findings challenge the applicability of the Pauli exclusion principle concerning the rotation of large molecules. We solve this problem by suggesting that symmetrical molecules will spontaneously regain rotational entropy if they are able to break symmetry through energetically low-demanding vibrational motions.



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Development of Novel Autoreactive and Ecological Monocomponent Adhesives

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Microcapsules, one of the controlled release techniques, have been used in many fields, such as food, medicine, environmental and biological engineering, cosmetics and coatings. Microcapsules are spherical particles (micro containers) of size in the tens or hundreds of μm that contain an active liquid or solid agent encapsulated by a natural or a polymeric membrane. The encapsulation can be used to protect active agents from oxidation, shield an irritating smell, prevent the evaporation of volatile compounds and reduce the toxicity of certain active substances.¹

Nowadays, the most reactive encapsulations are performed in batch processes to produce microcapsules, ranging from 10–500 μm , in high quantity. However, besides the advantage of batch processes for high throughput production, these techniques traditionally do not provide precise control over the resulting capsule size, dispersity and morphological properties.²

In recent years, polyurethane materials have been widely used in various fields. Polyurethane microcapsules, a polyurethane product, are receiving increasing attention for their high thermal and mechanical stabilities, corrosion resistance, biocompatibility, and low cost. Due to these properties, polyurethane microcapsules have been widely applied. Isocyanates, including toluene diisocyanate (TDI), methylene diphenyl isocyanate (MDI), and isophorone diisocyanate (IPDI), are common precursors for preparing polyurethane microcapsules. Interfacial polymerization is a convenient technique for the rapid production of polyurethane microcapsules under mild conditions of pressure and temperature. The polyurethane microcapsules are fabricated by forming droplets of an oil phase containing an isocyanate in an aqueous phase containing a polyalcohol, or a polyamine. The isocyanate groups are in contact with the OH, or NH groups at the oil–water interfaces and quickly react, forming a solid polyurethane, or polyurea shell around the oil droplets.^{1,3} Several methodologies have been described for the construction of size controlling spheres with a narrow size distribution.⁴ Since microfluidic emulsification was reported by Thorsen et al.⁵ similar approaches were used for the fabrication of monodisperse water-in-oil (W/O), oil-in-water (O/W) emulsions, and bubbles. Microfluidic devices show remarkable success in allowing precise size control.⁶

In this work, we report a microfluidic approach, including 3d-printed T-junctions, to fabricate monodisperse isocyanate microcapsules with lipophilic cores and polyurethane shells. These microcapsules are generated in a microcapillary microfluidic device we designed using monodisperse O/W emulsion, with high potential application in aeronautic and automobile industries.

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Recent Insights Into the Biological Activities of Polyoxometalates

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Polyoxometalates (POMs) are an emerging class of inorganic metal oxides that have been studied in various fields with applications in catalysis, prevention of corrosion, smart glasses and macromolecular crystallography. Furthermore, POMs and POM-based hybrid and nanocomposite structures are gaining more and more attention from the field of medicine due to their antidiabetic, antibacterial and anticancer activities^{1,2}. In the present communication, recent insights as well as pitfalls of biologically active POMs are described¹⁻⁴. In general, POMs are able to inhibit crucial enzymes like phosphatases, ecto-nucleotidases and, as very recently referred, also Ca²⁺-ATPases³. Regarding the latter enzyme and when taking into account only high affinity POMs, exhibiting IC₅₀ inhibition values lower than 16 μM, a correlation between their activity (IC₅₀ value) and their charge density was observed³. Thus, POMs such as K₉(C₂H₈N)₅[H₁₀Se₂W₂₉O₁₀₃] and K₆[α-P₂W₁₈O₆₂]·with a low charge density favored the inhibition of Ca²⁺-ATPase activity indicating that besides electrostatic interactions also steric interactions might play important roles in the successful inhibition of the ATPase. On the other hand, the parameter size could be one aspect affecting the kinetics of cellular uptake, thus preventing large POMs from targeting these P-type ATPases as shown by ex-vivo experiments³. In fact, the mechanism of POMs uptake and their permeation through cellular membrane still need to be clarified. Targeting ATPases could at least partially contribute to the observed biological activity of some POMs. Regarding the antibacterial activity of POMs, it was found that POMs are located at the periphery of the cells, most likely within the inner membrane, indicating that membrane associated enzymes including ion pumps, sialyl- and sulfo-transferases and processes such as respiration (or other redox processes) are the main targets of POMs^{1,2,3}. In that sense, it would be important to clarify the exact mode of interaction of POMs with proteins and thus exploring relevant proteinogenic binding sites as these information will lead to a deeper understanding of the mechanism of inhibition^{3,4}. Furthermore, the biovalidation of the in vitro findings, such as the effects of POMs and POM-based hybrid and nanocomposite structures on apoptosis/necrosis, for example, is missing and therefore further, complex and varied studies are required in a near future.

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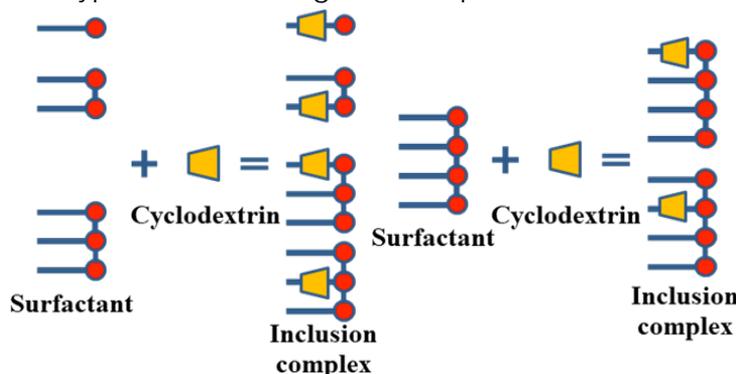
Influence of the Surfactant Degree of Oligomerization on the Formation of Cyclodextrin: Surfactant Inclusion Complexes

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Supramolecular complexation is an attractive strategy to modulate the performance of surfactants, e.g., by host-guest interactions.¹ Here, we investigate the interaction of single-chained, di-, tri-, and tetrameric cationic surfactants with cyclodextrins by conductivity and ¹H NMR measurements, exploring the effect of increasing the number of the surfactant hydrophobic tails on the stability of cyclodextrin:surfactant inclusion complexes. The stoichiometry and the binding equilibrium constants of the different inclusion complexes were elucidated. Under the working conditions, the number of hydrophobic chains was found not to affect stoichiometry and 1:1 inclusion complexes were formed for all the surfactants investigated. The stability of the host-guest complexes decreases from single-chained to dimeric ("gemini") surfactants, the binding following a non-cooperative mechanism. This result may be rationalized by taking into account steric constraints and electrostatic effects as well as the need to overcome the hydrophobic interactions between the chains of the same surfactant molecule. However, a further increase in the number of hydrophobic tails, from two to three to four, results in an increase in the equilibrium binding constant, K_1 . In this case, an increment in the number of chains capable of interaction with the cyclodextrin molecules seems to be the main factor responsible for the increase in K_1 . ROESY spectra show the coexistence of different types of 1:1 host-guest complexes for tri- and tetrameric surfactants.



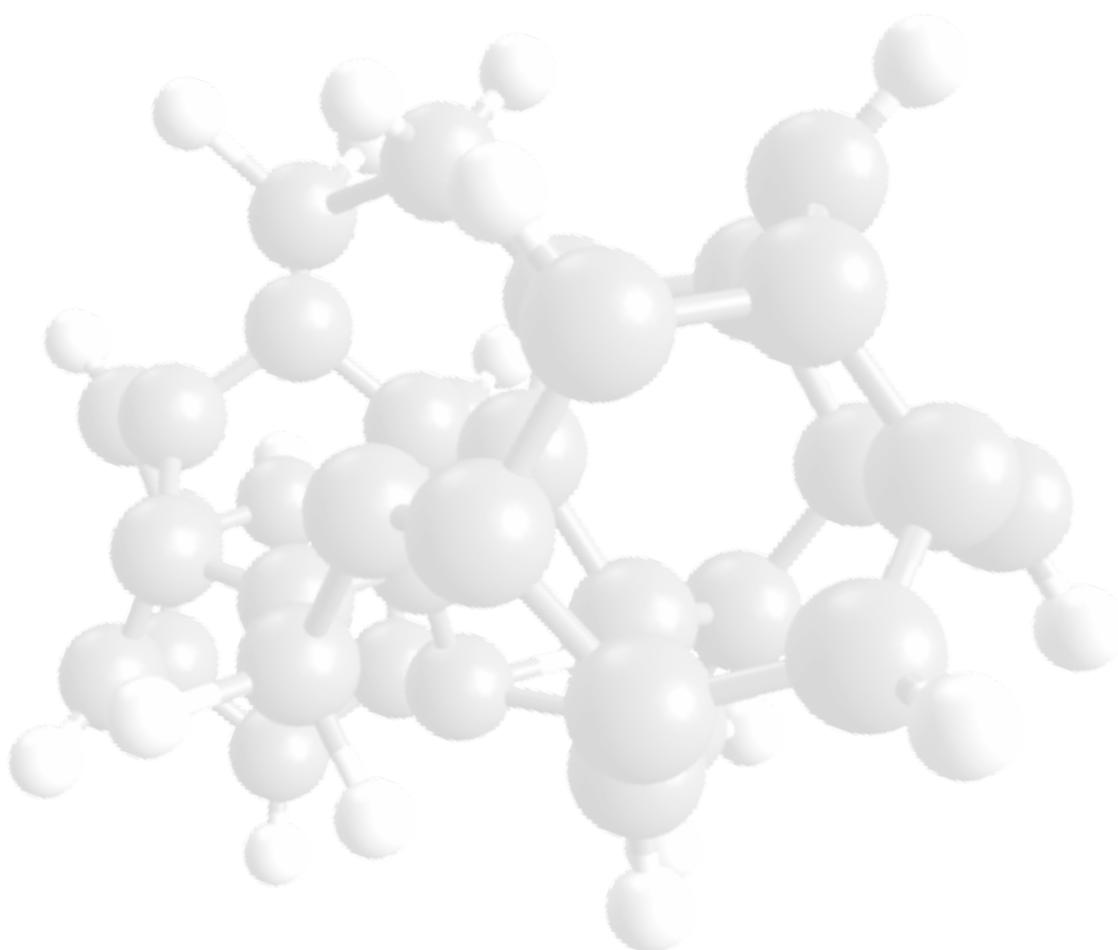
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Poster Presentations

ICPOC 24



Poster 1

Reliable Charge Assessment on Encapsulated Fragment for Endohedral SystemsA.J. Stasyuk,^{a*} M. Solà,^a and A. A. Voityuk^{a,b}^a*Institut de Química Computacional and Departament de Química, Universitat de Girona, C/ Maria Aurèlia Capmany 69, 17003, Girona, Catalonia, Spain*^b*Institució Catalana de Recerca i Estudis Avancats, 08010, Barcelona, Spain*

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Atomic charge is one of most fundamental and generally used concept in chemistry. But, even for simplest diatomic molecule the exact definition can be done only in some ideal cases – for ideal ionic compound there is a complete charge transfer occurring (charges +1 and -1), or for ideal covalent compound where the bonding electron pair is shared equally (charges 0). Focusing our attention on endohedral Cl@B39 borospherene complex¹ (Fig. 1) we have encountered the problem of the reliability of charge determination on central fragment. The population analysis carried out within various schemes demonstrates significantly different distribution of charges.

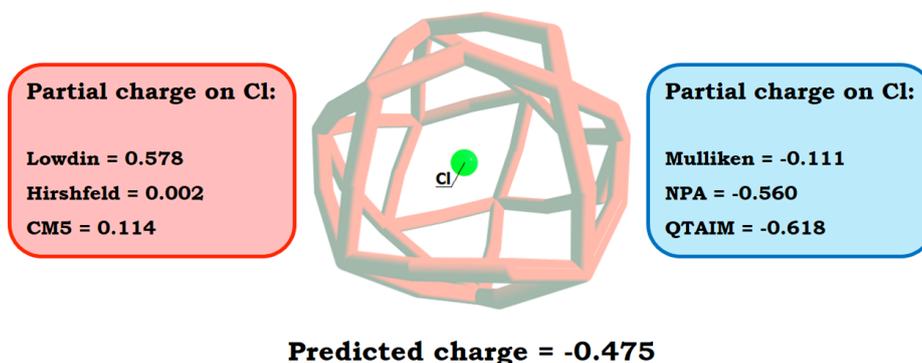


Fig. 1 Graphical representation of endohedral borospherene complex Cl@B39 and charge density analysis performed with Mulliken, Löwdin, Hirshfeld, CM5, QTAIM and Natural Population Analysis schemes.

We have developed a new approach for charge assessment of the encapsulated fragment based on the comparison of the low-lying orbital energies of atoms in central fragment in complex of interest with reference systems. The proposed approach demonstrates excellent performance on endohedral borospherenes X@B39 with encapsulated metal atoms, halogens or small radicals. Moreover, the workability of proposed approach has been demonstrated on the typical fullerene based Sc₃N@Ih-C₈₀ endohedral complex. In view of the physical and computational simplicity, the proposed method can be applied to very large systems. In cases when conventional schemes provide essentially different results, the proposed method could be used as a convenient and robust tool to exclude unreliable data from consideration.

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Poster 2

Biological Activities and Phytochemical Study of *Cistus Salviifolius*Sihem Boubekour^{1,2} and Aicha Hassani¹*Bioactive Products Laboratory and Biomass Enhancement, High School, BP 16308, Kouba, Algiers, Algeria
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In the aim of valuing Algerian flora, we focused in the study of *Cistus salviifolius*. This shrub is distributed everywhere in Algeria, in the tell, in the littoral and in forests. The objective of our work was mainly the identification of chemical compounds, the determination of the total content of phenolic compounds of the alcoholic extract, the estimation of the antibacterial activity of the butanolic extract and the estimation of the anti-inflammatory activity of the aqueous extract.

The preliminary phytochemical tests performed on various extracts (aqueous, alcoholic and etherical) as well as on the plant's powder showed the plant richness in secondary metabolites especially flavonoïds, gallic-tannins and leuco-anthocyanes

The estimation of total phenolic compounds was carried out by UV-vis. Gallic acid was used to estimate the calibration curve. The result obtained was (274,1 milligram gallic acid equivalent per gram of the dried plant).

The study of the antibacterial activity of the *Cistus salviifolius* was by using the discs method. The butanolic extract shows a strong inhibitory activity against all the GRAM+ strains tested.

To evaluate of the anti-inflammatory activity, we check the inhibitive action of the aqueous extract of *Cistus salviifolius* on an oedema caused by the injection of the 1% carraghenin in the leg of a mouse. The aqueous extract shows an anti-inflammatory effect: 2134mg/kg provoked oedema reductions about 29,32% comparing to the anti-inflammatory product CLOFENAL[®] which shows an anti-inflammatory effect more important: 2,5mg/kg provoked oedema reductions which reaches 56,02%, and that at the sixth hour of the experiment.

Keywords: *Cistus salviifolius*, phenolic compound, antibacterial, anti-inflammatory, assay.

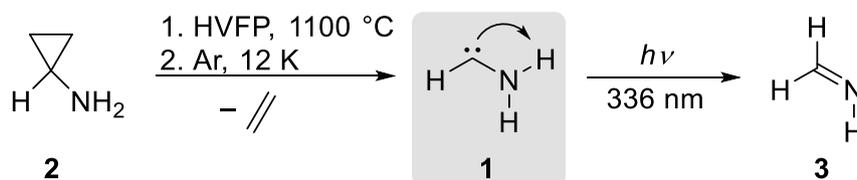
Spectroscopic Evidence for Aminomethylene ($\text{H}-\ddot{\text{C}}-\text{NH}_2$) - The Simplest Amino Carbene

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Carbenes have turned from fleetingly existent laboratory curiosities into commonplace catalysts in organic chemistry. In particular, N-heterocyclic carbenes (NHCs) have found multiple applications and have been studied well.¹ However, the simplest aminocarbene (**1**), aminomethylene $\text{H}-\ddot{\text{C}}-\text{NH}_2$, has not been spectroscopically identified yet.² Here we report the gas phase preparation of **1** by high-vacuum flash pyrolysis (HVFP) of cyclopropylamine (**2**) and subsequent trapping of the pyrolysate in an inert argon matrix at 12 K.³ Aminomethylene was characterized by matching matrix IR and UV/Vis spectroscopic data with high-level ab initio coupled cluster computations. After irradiation of the matrix with UV light **1** rearranges to its isomer methanimine (**3**), formaldimine $\text{H}_2\text{C}=\text{NH}$.



Scheme 1: Generation of aminomethylene (**1**) by high-vacuum flash pyrolysis (HVFP) of cyclopropylamine (**2**) at 1100 °C and subsequent trapping of the pyrolysis products in solid argon at 12 K. After 5 min irradiation of the matrix with a wavelength of 336 nm the carbene rearranges to methanimine (**3**).

Based on our experimental results and computations **1** has a singlet ground state with a reaction barrier of almost 46 kcal mol⁻¹ to **2** so that H-tunneling⁴ to **2** is excluded.

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Poster 4

Insights into the Photochemistry of 5-Aminotetrazole Derivatives; Effect of the Saccharyl Moiety on the Photostability

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An investigation on the chelating capacity of tetrazole-saccharinates, a chemotype with applications in coordination chemistry, revealed that selected N-linked conjugates exhibit strong binding selectivity to copper ions.¹ This property was considered of interest for therapeutic applications, mainly because of the recent findings that link elevated levels of copper to cancer progression.² Despite the promising results observed for these new ligands, the tetrazole ring system is known to undergo easy cleavage, induced thermally or photochemically.^{3,4} It is thus relevant to investigate the photochemistry of tetrazole-saccharinates, as the electron withdrawing saccharyl system, known to be relatively photostable, can be expected to increase the photostability of the tetrazole moiety.

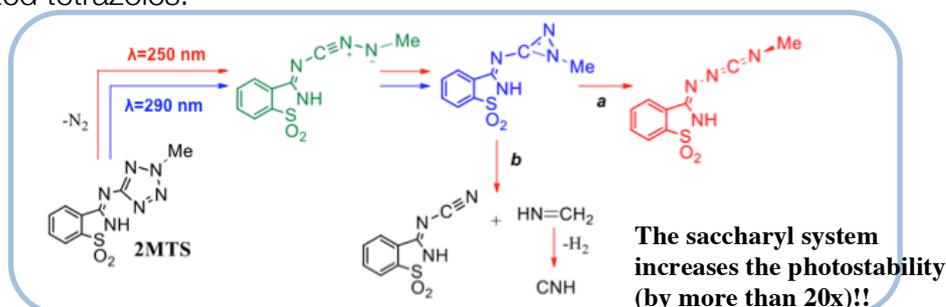
The photochemistry of monomeric N-linked 2-methyltetrazole-saccharinate 2MTS (one of our most promising ligands for the development of selective tools for cancer chemotherapy based on selective copper chelators)¹ isolated in cryogenic inert matrices is compared with that of 2-methyl-5-aminotetrazole 2MT, used as building block for the preparation of the ligand 2MTS. In addition, results obtained from the photochemistry of both isomers, 1MT and 2MT, using similar experimental conditions, enabled the clarification of important mechanistic questions regarding the effects of the ring substitution pattern on the photofragmentation pathways of disubstituted tetrazoles.⁵

2MTS

50% consumed after **2 min.**

nitrile imine

consumed after **60 min.**

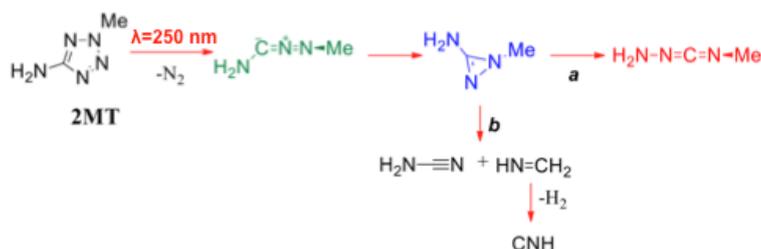


2MT

50% consumed after **2 sec.**

nitrile imine

consumed after **4 min.**



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Different Solvolytic Behavior of Aryl/Alkyl Carbonates, Carboxylates and Phenolates

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Mayr's LFER equation [Eq (1)]¹ has been used to determine heterolytic reactivities of a large number of leaving groups, i.e. nucleofugalities (N_f), in various solvents.¹⁻⁴ The procedure includes the construction of the $\log k$ vs. E_f correlation plot, in which k represents first-order rate constants for solvolysis of a series of substituted benzhydryl substrates with a leaving group of interest, whereas the E_f parameter represents electrofugalities of corresponding benzhydryl electrofuges from the E_f reference scale. Eq (1) defines N_f as the negative intercept on the abscissa (E_f axis).¹

$$\log k (25\text{ }^\circ\text{C}) = s_f(E_f + N_f) \quad (1)$$

Although the goal of this LFER approach is to determine N_f parameters, whose application is described elsewhere,¹ the second nucleofuge-parameter, namely the s_f parameter (the slope of the $\log k$ vs. E_f correlation plot), might also provide useful information concerning the nature of solvolytic transition states. Similarly as the Hammett–Brown ρ^+ parameter, the s_f parameter represents the solvolysis reaction constant that implies the degree of charge separation in TS. Different pattern of variation of the s_f parameters with reactivities of leaving groups in the series of aryl/alkyl carbonates, carboxylates and phenolates, shown by the s_f vs. $\log k$ (dianisylmethyl-LG) correlation, reveals the different degree of charge separation in the transition states that are constituted from a common electrofuge and leaving groups with similar reactivity but different functionalities.³

Correlation of $\log k$ for solvolysis of dianisylmethyl aryl/alkyl carbonates, carboxylates and phenolates with $\log k$ for solvolysis of corresponding benzhydryl derivatives might mimic the reactivity-stability correlation whereas the difference between electrofugality of the common electrofuges in these two series is 6 orders of magnitude.^{3,4} However, this correlation also reveals the separation of data points according to the type of leaving groups and predicts the breakdown of linear relationship between the reactivity of leaving groups of different functionalities and the stability of corresponding free anions.

The both correlations indicate a different impact of the intrinsic barrier on the nucleofugality of different types of leaving groups which might be attributed to the lag in developing electronic stabilizing effects along the heterolysis reaction coordinate.

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Poster 6

The Termolecular Reaction $\text{H} + \text{O}_2 + \text{M} \rightarrow \text{HO}_2 + \text{M}$

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Potential Energy Surfaces (PES) are used to study the rate of elementary reactions and their dynamics, being useful to compute state to state rate constants. Unfortunately in a complex reactive system, many elementary reactions are normally involved and the overall study becomes difficult. The usual approach to study such system is to make use of all the system's available rate constants and build a system of master equations. This procedure is based in the assumption that reactants are in thermal equilibrium. But studies seem to indicate that the number of non-reactive collisions can be small and the energy distribution of the intermediate species may be far from the Boltzmann distribution. MreaDy program (Multi-process Reactions Dynamics), aims to reproduce complex mechanisms, such as the hydrogen combustion, using accurate PES. This is accomplished by defining a global Potential Energy Surface (gPES) for the process in question, integrating various PESs, each one of them representing an elementary reaction that is expected to play a role in the chemical process, and performing reactive classical dynamic calculations on it¹. MReaDy was modified in order to study the pressure dependence of the reaction $\text{H} + \text{O}_2 + \text{M} \rightarrow \text{HO}_2 + \text{M}$. This reaction is one of the main sources of uncertainty when modelling hydrogen combustion chemistry, and being a termolecular reaction, it cannot be studied using normal classical trajectory programs. We start with hydrogen atoms and oxygen molecules, forming by collision excited HO_2^* radicals. We can count how many of the excited HO_2^* radicals are stabilized by collisions at 1500, 2000, and 2500 K and pressures of 10, 20, 30 and 50 atm., and we calculate the formation rate of stable HO_2 radicals. We present preliminary results for this process showing a clear increase of the rate constant with pressure. We are also able to study the rate constants of the different reactions present in the system.

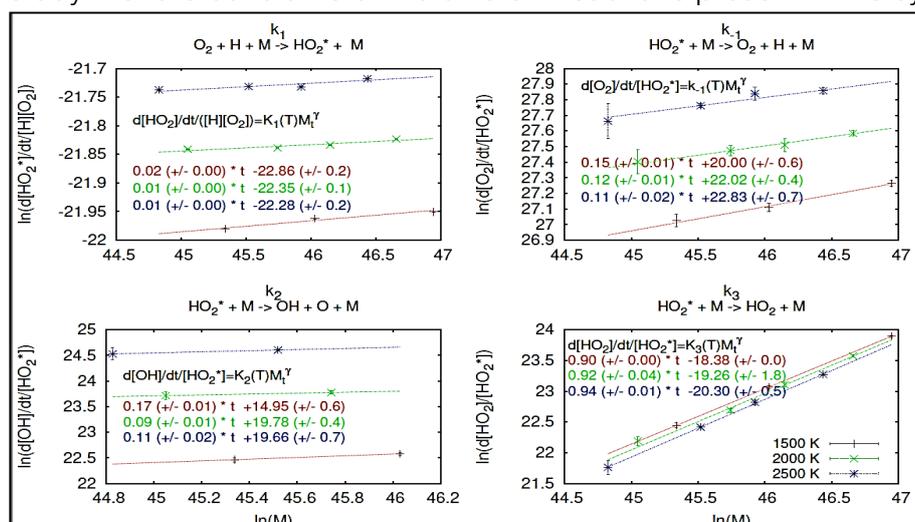


Figure: Obtained reaction rate constants for the reactions present the system.

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Polynomial Coefficients. Application to Spin-Spin Splitting by N Equivalent Nuclei of Spin $I > 1/2$

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It is well known that the NMR intensity pattern of a nucleus that is split by N identical nuclei of spin $1/2$ is an $(N+1)$ -line multiplet with relative intensities given by the binomial coefficients, $C_r^N = N!/(r!(N-r)!)$. The binomial coefficients are conveniently obtained from Pascal's Triangle, where each coefficient is the sum of the two coefficients above it. This is equivalent to the chemist's branching diagram (Fig. 1).

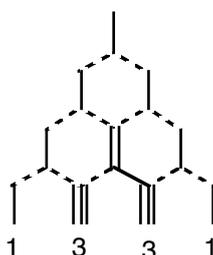


Figure 1. Splitting by three adjacent nuclei of spin $1/2$.

Much less well known is the pattern from splitting by N identical nuclei of spin $I > 1/2$. This was originally presented in terms of sums of multinomial coefficients,¹ but polynomial coefficients I_r^N are more convenient. These describe the number of ways that N objects can be distributed to $2I+1$ boxes. They arise in the polynomial expansion (eq 1) and are conveniently obtained from generalizations of Pascal's Triangle.² For $I > 1/2$ each coefficient is the sum of the $2I+1$ coefficients above it, as illustrated by the branching diagram (Fig. 2). Further examples will be given, including the relative intensities 1:9:45:156:414:882:1554:2304:2907:3139:2907:2304:1554:882:414:156:45: 9:1 for splitting by nine identical nuclei of $I = 1$, as in the ^1H NMR spectrum of $(\text{CD}_3)_3\text{CH}$.

$$\left(\sum_{r=0}^{2I} x^r\right)^N = (1 + x + x^2 + \dots + x^{2I})^N = \sum_{r=0}^{2NI} I_r^N x^r \quad (1)$$

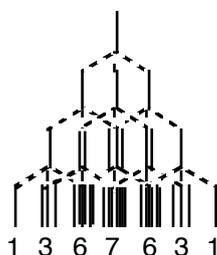


Figure 2. Splitting by three adjacent nuclei of spin 1

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Cyclization of Triplet 2-Formyl-Phenylnitrene to 2,1-Benzisoxazole: A New Heavy-Atom Tunneling Event?

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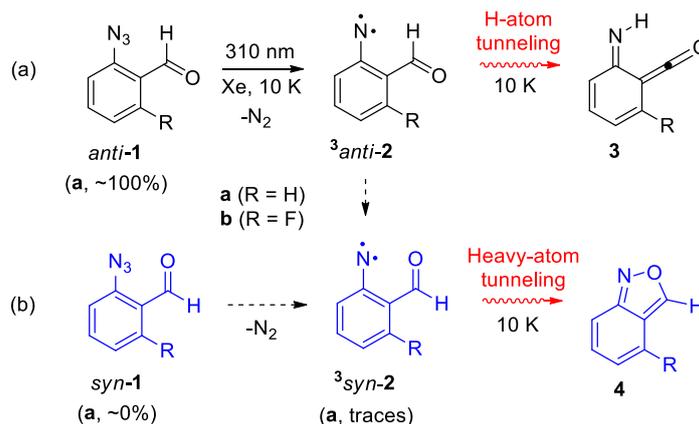
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We have recently described the first direct evidence of a tunneling reaction in the nitrene chemistry.¹ Triplet anti-2-formyl-phenylnitrene 2a (R = H) was found to spontaneously rearrange via H-atom tunneling to imino-ketene 3a in low-temperature matrices (Scheme 1a). A tunneling half-life of ~5 hours was measured in argon and krypton matrices at 10 K but only ~25% conversion after 7 days was observed in xenon matrices.

During new investigations performed in xenon matrices, we have discovered a second spontaneous transformation occurring at a much faster rate. Presumably, the heavy-atom tunneling reaction of triplet syn-2-formyl-phenylnitrene 2a into 2,1-benzisoxazole 4a (Scheme 1b). Nevertheless, only a very small amount of conformer syn-2a is formed during the irradiation of azide 1a, which makes difficult to obtain reliable experimental data.



Scheme 1. (a) H-atom tunneling from triplet nitrene anti-2a to imino-ketene 3a. (b) Heavy-atom tunneling from triplet nitrene syn-2a to 2,1-benzisoxazole 4a. Observations made in Xe matrix at 10 K.

Calculations predict that introducing a fluorine atom adjacent to the aldehyde group in phenylazide should stabilize significantly the conformer syn-1b (R = F) leading to a syn/anti population ratio of ~50 %. This contrasts with the population of syn-1a (R = H) that was estimated and experimentally found to be ~0 %. In this way, we hypothesize that irradiation of 1b would generate nitrene syn-2b in sufficient yield so the existence of heavy-atom tunneling from triplet 2-formyl-phenylnitrene to 2,1-benzisoxazole can be elucidated. These results will also be presented in the current communication.

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Structural Insights Into Non-Covalent Halide Adducts with Tyrosine and 3-Nitrotyrosine Using Ion-Spectroscopy

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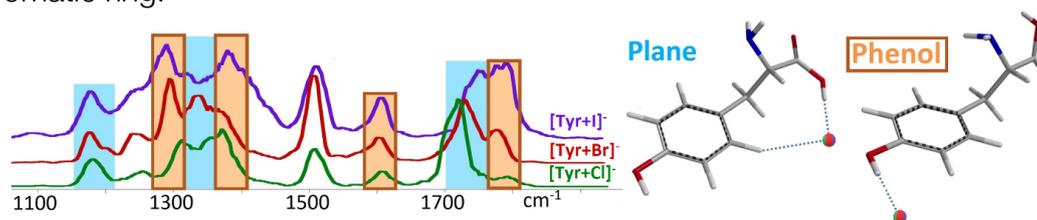
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The interaction between halide ions and aminoacids has been recognized to have an important role in biologically relevant functions such as neuron-signaling, ion transport and drug-receptor recognition.¹ Despite the physiological importance of anion interaction with aminoacids, and the several factors that can influence it, including formation of hydrogen-bonds and ion-dipole effects, fewer information is available on the subject in comparison to the one about metal cation adducts.

In this contribution, we present an investigation on the binding motifs of halide ions with the aromatic aminoacid tyrosine and its derivative 3-nitrotyrosine.² To obtain structural information about the assayed complexes we employed IR multiple-photon dissociation (IRMPD) spectroscopy, a mass spectrometry-based technique which permits to identify vibrational features of mass-isolated ions. In particular, the anionic complexes of either tyrosine or 3-nitrotyrosine with chloride, bromide and iodide were investigated in the fingerprint region of the IR spectrum (1000-2000 cm⁻¹). The IRMPD spectra were compared with the theoretical IR spectra calculated at the B3LYP/6-311++G** level. Thermodynamic parameters were also evaluated using the B3LYP-D3 functional and single point MP2 calculations. Our experiments showed the prevalence of canonical isomers (having intact amino and carboxylic functions) in the sampled gas-phase population and the presence of multiple non-covalent forms. In particular, a diagnostic C=O stretching at ca. 1720 cm⁻¹ was found to discriminate between two main families of isomers, namely the phenol- and plane-bound ones. The tyrosine complexes showed the presence of both isomers with an increasing percentage of the phenol-bound one moving from chloride to iodide, a trend well reproduced by calculated energies at the MP2 level. Regarding the 3-nitrotyrosine complexes, the phenol-bound isomer appeared to be highly disfavored, while the augmented π -acidity favoured the formation of ring-isomers in which the anion is placed above the face of the aromatic ring.



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The Structure and Properties of a Novel Sulphonyl-Bridged Thiadiazolyl-Saccharinate Ligand

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Copper is involved in vital redox processes in the human body and alterations of its normal homeostasis are known to promote toxicity, through induced formation of reactive oxygen species (ROS) that may target essential biological molecules.^{1,2} Thus, effective and selective copper chelators may act as powerful tools for the control of Wilson's disease, or in cancer chemotherapy. Recent studies have shown that some N-linked tetrazole-saccharinates bind selectively to copper, forming complexes that are highly cytotoxic towards cancer cells.³ We now describe the synthesis, monomeric structure, photochemistry and cytotoxicity of a novel sulphonyl-bridged thiadiazolyl-saccharinate (MTSB; Figure 1).⁴

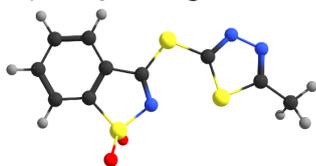


Figure 1. Structure of 3-[(5-methyl-1,3,4-thiadiazol-2-yl) sulphonyl]-1,2-benzothiazole 1,1-dioxide (MTSB).

The structure of MTSB was investigated by matrix-isolation infrared spectroscopy and quantum chemical calculations. Investigation of relevant regions of the potential energy surface and charge density analysis were based on the AIM theory and Wiberg's bond order methods. The crystal structure of MTSB was studied by X-ray and vibrational spectroscopies. Results obtained show the relevance of a central S...N interaction in the structure of MTSB. UV irradiation of matrix-isolated MTSB revealed its high photostability, compared to parent tetrazole-saccharinates. In vitro cytotoxicity assays demonstrated that MTSB is toxic to a range of cancer cell lines but does not show toxicity towards non-tumoral cell, indicating that MTSB could be a promising lead for cancer chemotherapy based on chelating agents.

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Fulvalene: Computationally Tuning Aromaticity and TunnelingE. Solel^a and S. Kozuch^a^a*Department of Chemistry, Ben-Gurion University of the Negev, Beer Sheva, Israel***kozuch@bgu.ac.il*

Fulvalenes are a family of molecules built from two fully-conjugated rings, connected to one another by an exocyclic double bond. Pentafulvalene, having two five-membered rings that are each one electron short of a 6π -electron aromatic system, is non-aromatic and has no dipole moment. We investigated computationally various derivatives of pentafulvalene and found that placing strong electron withdrawing groups on one ring and strong electron donating groups on the second ring can induce significant charge transfer between the rings, and stabilize a zwitterionic structure. This produces one aromatic and one antiaromatic ring in the same molecule. We also found that such derivatives can undergo π -system shifting in the antiaromatic ring via quantum mechanical tunneling even at temperatures very close to 0 K. In addition, triplets of such pentafulvalene derivatives exhibit a charge transfer diradical structure, as the triplet is localized on the positively charged ring. This produces one ring with Hückel $4n+2$ aromaticity, and a second ring that is a 4π -electron triplet system and is aromatic according to Baird's rule. However, in most of the derivatives tested, the Jahn-Teller effect wins over Hund's rule and the singlet is more stable than the triplet. Even so, a right arrangement of the substituents can stabilize the triplet, and thus produce a novel neutral pentafulvalene having two aromatic rings in its ground state.

Anisotropy of the Current Induced Density (ACID) - A New Method for Prediction and Explanation of Diels-Alder Reactions

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Electronic delocalization is one of the most important and basic concepts in chemistry. Unfortunately it is neither a quantum chemical observable nor can it be directly measured. Herges et al. developed the Anisotropy of the Current-Induced Density (ACID) method^{1,2} as an intuitive and generally applicable method for the investigation and visualization of electron delocalization and bond conjugation in molecules in ground, excited and transition states. The ACID approach is a scalar field which is invariant with respect to the relative orientation of the magnetic field and the molecule which can be plotted as an isosurface. The so-called Critical Isosurface Value (CIV), the value at which the isosurface breaks, is indicative of the strength of electron delocalization in a molecule and is an indicator for aromaticity in case of an aromatic compound. Moreover it is possible to separate the π from the σ orbitals, thus enabling the individual investigation of π and σ delocalization. Several examples demonstrate the predictive power and the general applicability of this method.^{1,3,4} A novel utilisation of ACID is the prediction and explanation for the selectivity of Diels-Alder reactions. Within the cycloaddition of a diene to a conjugated system with multiple dienophilic positions, this method can easily predict and explain the experimental regiochemistry. The ACID program can be obtained free of charge from the Herges group.

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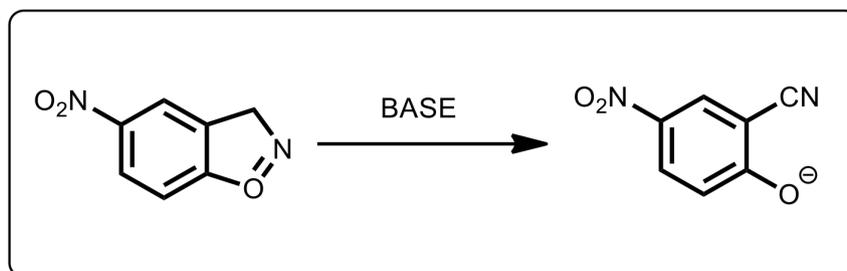
Effects of Binary Solvent Mixtures on Reactivity

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The solvent in which a chemical reaction occurs 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 predicted¹. One particularly attractive approach treats solvent-solute interactions as electrostatic and focuses on hydrogen bond donor (α) or acceptor (β) sites on solvent molecules to create a supramolecular model solvation². This model has been very effective in predicting chemical equilibria³, and now we want to explore whether it is equally effective in predicting reactivity. We are using the Kemp elimination as a probe 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 fitting the observed behaviour to a model based on the binding properties of the mixed solvent, as well as the work correlating hydrogen bond parameters with reactivity in both pure and mixed solvents.

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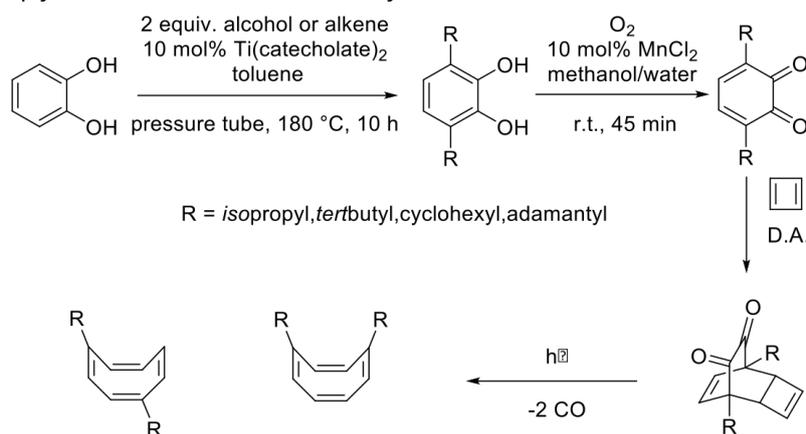
A Synthetical Approach to 1,4-di-Substituted-Cyclooctatetraene Based Dispersion Balances Via 3,6-Substituted Pyrocatechol Derivatives

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Quantum mechanical computations point out the dominance of attractive London dispersion (LD) interactions in molecular association of nonpolar compounds or groups¹ but experiments have casted doubt on the importance of these forces in solution.² Highly functionalized molecular balances bearing many heteroatoms tend to fold due to hydrogen bonding and thus underestimate shorter range van-der-Waals forces.³ Therefore, 1,4-di-substituted-cyclooctatetraenes⁴⁻⁷ were chosen as nonpolar, hydrocarbon-based molecular balances, because LD will dominate their folding equilibria. The equilibrium constants will be determined in a variety of solvents to determine to what degree solvation attenuates intramolecular LD interactions. Our synthetic approach builds on previous work of Paquette *et al.*^{6,8} and substitution of the pyrocatechol as outlined by Ershov *et al.*^{9,10}



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Road to a Full Understanding of the C–H Activation Using Cp*Co(III) Metal Complexes

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Over the last decades, transition-metal-catalyzed C–H activation has emerged as a powerful tool for the construction of carbon–carbon bonds. Until recently, the majority of these transformations were achieved employing precious second- and third-row transition metals. However, the development of novel methodologies based on more cost-effective first-row transition metal complexes has emerged as a very attractive alternative.¹

Among them, cobalt catalysis has shown its potential to construct C–C bonds via C–H activation using cobalt(III) catalysts.² Despite this significant progress, these Co^{III} systems for C–H functionalization are still at their infancy and important, fundamental questions remain unsolved, specially concerning the lack of information on the mechanisms of these transformations and the involved active species.

This presentation will describe our recent efforts on unravelling mechanistic details of Cp*Co(III)-catalyzed C–H functionalization reactions by capturing and characterizing previously elusive transient reactive intermediates.³

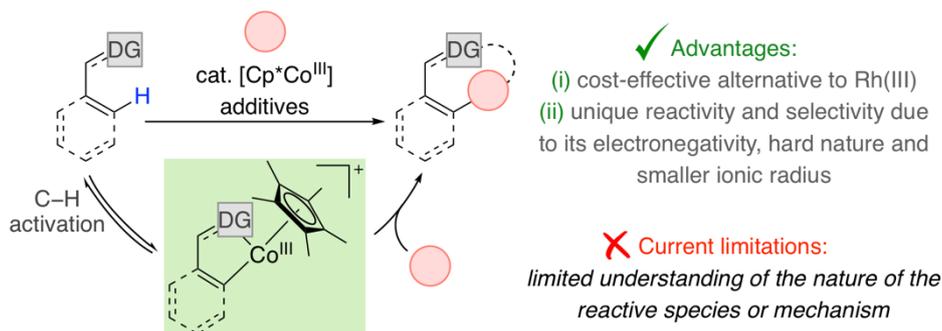


Figure 1. Cp*Co-catalyzed directed C–H functionalization

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iBonD: a Databank of Measured pK_a and BDE Values

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Chemistry is basically the science on bond reorganizations that are governed intrinsically by the energy of relevant bonds and externally by reaction conditions. As well known, the homolysis and heterolysis are two main pathways for bond dissociations and their typical parameters are BDE and pK_a , respectively. In past century, enormous bond energies like BDE and pK_a , have been extensively accumulated,¹ playing key roles in shaping chemistry into a rational science.

To benefit more researchers in various fields, some compilations of experimental values of bond energies for organic compounds in both gas and liquid phases are established in past years. Most are in a printed form,² while others may be accessed directly via the internet.³ However, the limitations of these compilations (e.g. the coverage of the current literature, only available for certain solvents and/or the paucity of a powerful searching engine) have made it a frustrating experience to find the reliable data from the ocean of literature. As a consequence, the great value of bond energy as a quantitative guide in doing rational chemistry has much been depressed.

Hence, an integrated and internet-based compilation of bond-energy databank (iBonD, <http://ibond.chem.tsinghua.edu.cn> or <http://ibond.nankai.edu.cn>) has been established, which provides a convenient, efficient and free access to over 35,000 pK_a values of about 20,000 compounds in various solvents as well as 7,500 BDE values for over 5,000 compounds in gas phase, providing the heretofore most comprehensive bond energy collection via the internet (Figure 1).

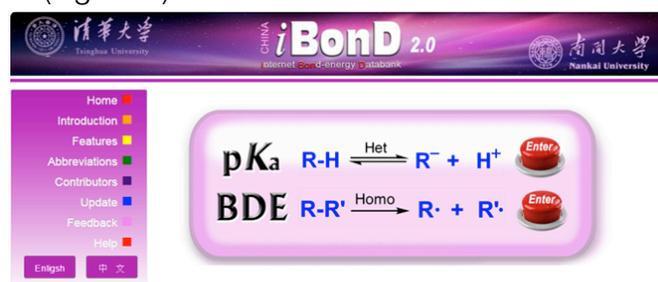


Figure 1. The homepage of internet bond-energy databank (iBonD).

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Computational Study of the Through-Resonance Effect Operating on (Phenylamino)methyl Cations

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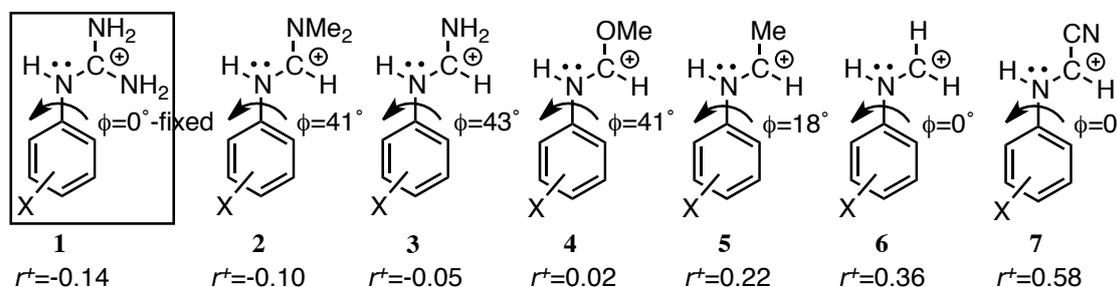
Substituent effects on the stabilities of cations of aromatic compounds are well described by the Yukawa-Tsuno equation (1):

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

The normal substituent constant (s^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 the through-resonance for para -R groups. The resultant r^+ value reveals the degree of the through-resonance effect in a given system. The set of s^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 p-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 s^0 reference system involves some through-resonance effect.

In the course of investigation of the optimum s^0 reference system, we examined the substituent effects on gas-phase stabilities of phenylaminomethyl cations. These cations are derived from 1 by replacement of one NH_2 group with a hydrogen and replacement of the other NH_2 group with various groups keeping the (phenylamino)methyl skeleton. Relative gas-phase stabilities of ring-substituted cations 2–7 were determined computationally using isodesmic reactions (B3LYP/6-311+G(2d,p)). The substituent effects obtained were analyzed by Eq. 1.

The r^+ value increase with increasing electron-withdrawing ability of the substituents connected to the cationic center. Unexpectedly significant through-resonance effects were observed in these cations, although a corresponding resonance structure cannot be drawn. The detailed mechanism of the through-resonance effects in these cations were investigated using NBO analysis.



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Understanding and Utilizing the Role of London Dispersion Interactions in Catalysis

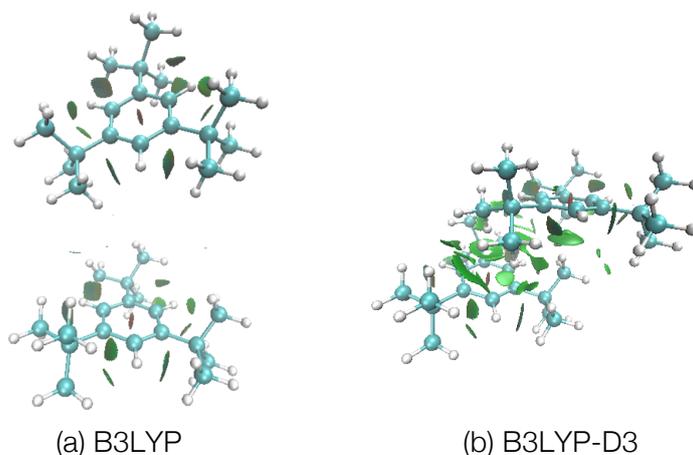
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London dispersion (LD) interactions constitute the attractive part of the van-der-Waals potential and they have been found to provide decisive stabilization in sterically bulky molecules and to enhance catalytic reactivity.¹

We present a systematic study on quantifying LD interactions by correlating LD interactions energies with the intrinsic properties (size and polarizability) of so-called dispersion-energy donors (DEDs).² We employed dispersion-corrected density functional theory that allows to size the significance of LD contributions.³ A group scan of various DEDs illustrates the “DED-strength”. A good linear relationship between dispersion interaction and polarizability per volume (α/V , α : polarizability; V : volume) was established in alkane dimer and benzene derivative dimer. In the hetero alkane dimer, a size match concept was introduced to present the correlation between dispersion energy and α/V . These can be further applied to catalyzed chemical reactions as LD helps understand the contribution of DEDs in the reactivity and selectivity of chemical reactions. The notion of selectivity control by specific rate acceleration through LD stabilization rather than by inhibitory means enables LD interaction to be developed as a control element in the design of catalyzed chemical reactions.



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Protonation of Spiroyrans: Revising Acidochromism and Electrochromism

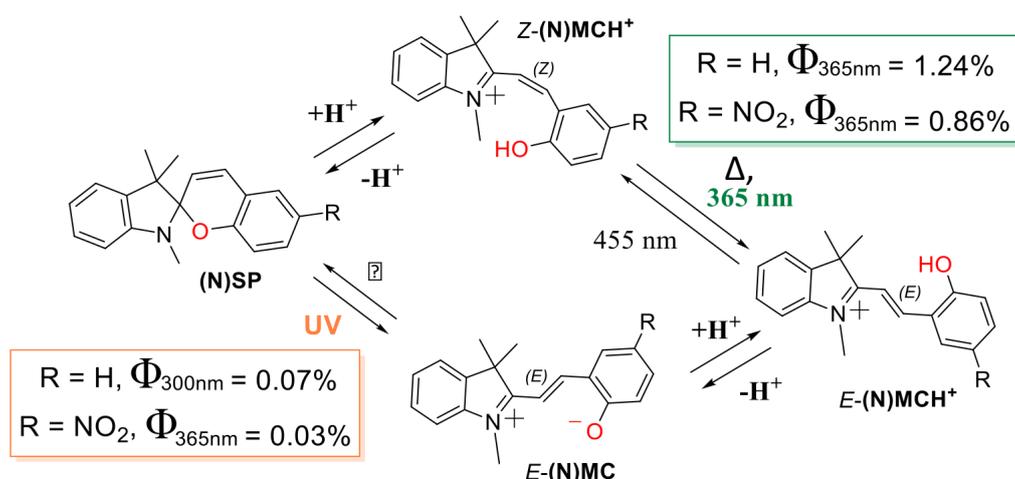
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Spiroyrans are amongst the most widely applied photochromes due to their modularity and flexibility towards modification and the possibility to combine them with other (responsive) units. They have been long-known to undergo C_{spiro}-O bond breaking to their ring-open E-merocyanine form under irradiation with UV-light, providing reversibly accessible distinct properties.¹ Despite their widespread application, the acidochromism still holds surprises and is highly structured and solvent dependent.²⁻⁴ In this contribution, we show through a combined theoretical and experimental study that intermediate protonated Z-merocyanine isomer is formed in apolar solvents and opens opportunities towards pH-gated photochromism. The acidochromic behavior is discussed in the context of the electrochemical and electrochromic properties of the spiroyrans and merocyanine forms and especially the effect of protonation state on redox response.



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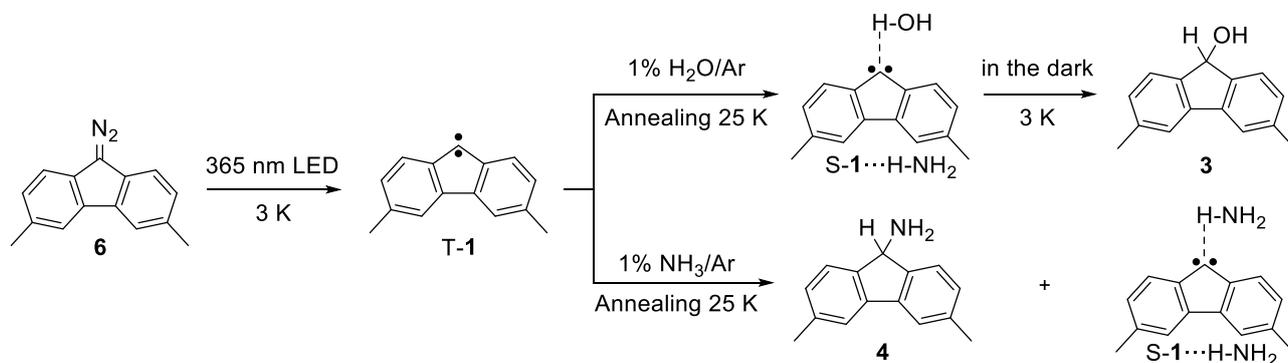
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Interaction of 3,6-Dimethylfluorenylidene with Ammonia and Water at Cryogenic Temperatures

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Recent studies have shown that small molecules like water can influence the spin state of a carbene by hydrogen bonding and thus have an impact on its reactivity.¹ In this work, the interactions of 3,6-dimethylfluorenylidene **1**, a triplet ground state carbene, with water and ammonia were studied by means of the matrix isolation technique. In both cases, the ground state is switched from triplet to singlet via formation of a singlet hydrogen-bonded complex, which is observed upon annealing the matrices to 25 K. While the water complex rearranges to the corresponding insertion product at temperatures as low as 3 K, the ammonia-insertion product is formed during the annealing process along with the singlet hydrogen-bonded complex.



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Solvolytic Reactivity of Organophosphates and Organophosphinates

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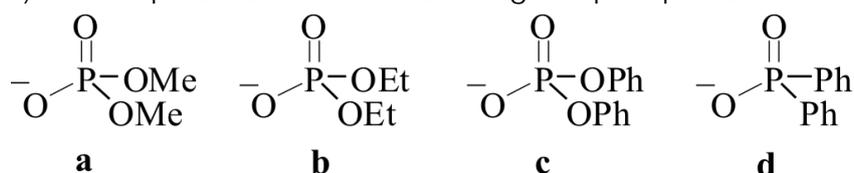
Solvolytic reactivities of some aliphatic and aromatic phosphate (Scheme 1., a-c) and phosphinate (Scheme 1., d) leaving groups (i.e. their nucleofugalities, N_f) in various aqueous binary mixtures have been determined according to Eq (1).¹ For that purpose, logarithms of solvolysis rate constants ($\log k$) for the series of benzhydryl phosphates and phosphinates have been correlated with corresponding electrofugalities (E_f) of the reference benzhydryl electrofuges.

The obtained N_f values enable comparison of nucleofugality of the phosphorus leaving groups with nucleofugality of a large number of other leaving groups, constituted from various functionalities.¹⁻⁵ At the moment the nucleofugality scale covers a reactivity range of 15 orders of magnitude.¹⁻⁵

$$\log k (25\text{ }^\circ\text{C}) = s_f(E_f + N_f) \quad (1)$$

Employing nucleofuge-specific parameters (N_f and s_f) of the leaving groups shown in Scheme 1 and previously established E_f values of corresponding electrofuges,^{1,6} rate constants for solvolysis of various organophosphates and organophosphinates in a given solvent (i.e. their half-lives and kinetic stability) can be predicted.

Organic phosphates demonstrate noticeably higher solvolytic reactivity than organic phosphinates (more than 3.5 orders of magnitude) which, according to NBO analysis, might be rationalized with an additional orbital stabilizing effect (namely the negative hyperconjugation) that is operative in both TS and organic phosphate free anions.



Scheme 1. Some aliphatic and aromatic phosphate (a-c) and phosphinate (d) leaving groups

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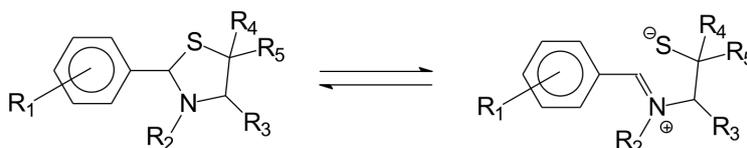
Photochemistry of Thiazolidines in Solution

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A number of relevant chemicals, penicillins among them, can undergo ring opening of their thiazolidine ring in basic aqueous solution, to yield an imine-thiolate anion. Subsequently, the so-formed imine rearranges to the corresponding enamine.¹ An appropriate model to study such process is the ring-opening of simple substituted thiazolidines to yield the corresponding iminium-thiolate zwitterions:



Work carried out on these systems has shown how the ring-opening / ring-closure processes depend on the state of protonation of the different acid positions in the molecule, through a complex pattern of equilibria.² However, depending on the substituents, it can be extremely difficult to ring-open the thiazolidine ring to a reasonable extent that may allow mechanistic investigation.

We show here that the ring opening of thiazolidines and oxazolidines can be easily achieved by photochemical means. The use of 248 or 266 nm laser flash-photolysis allows to produce in good yields the iminium ion ($\lambda=400$ nm) with a variety of compounds (R1 = -OH, -OMe, -MMe₂; R2 = -H, -nBu; R3 = -H, -CO₂H; R4 = R5 = -H, -Me). Results will be presented for the photochemically-induced ring-opening process, as well as for the mechanism of ring-closure under different conditions. Computational chemical calculations support the interpretation of experimental findings.

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Development of a Contrast Agent Based On Fe^{III}-Recordplayer

Morten Peters and Prof. Dr. Rainer Herges^a

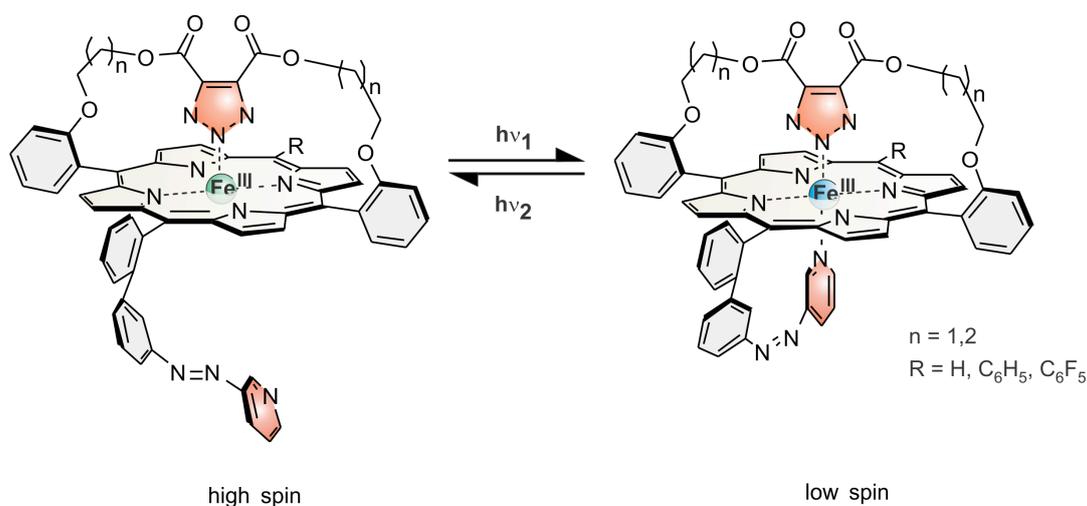
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Magnetic resonance imaging (MRI) is an important technique for medical diagnosis and research. Common contrast agents are gadolinium complexes.

A novel approach is to investigate photoswitchable MRI contrast agents. Ni-porphyrins with covalently tethered azopyridine ligands are applied. The photochromic complexes switch between the diamagnetic low-spin-state (MRI silent) to the paramagnetic high-spin-state (MRI active) by irradiation with light of specific wavelengths. This process is known as light-driven coordination-induced spin-state switch (LD-CISSS).^{1,2}

Within this work the concept should be realized with Fe(III)-porphyrins which require different structures. Five-coordinated complexes have a spin of 5/2 (high spin), whereas six-coordinated complexes tend to have a spin state of 1/2 (low spin).³ The square pyramidal geometry should be realized by a bridged porphyrin.

The higher difference of the magnetic moment between the MRI active and the MRI silent state should improve the efficiency of the contrast switching.



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Quantum Chemical Calculation of SuFEx Reaction Thermodynamics

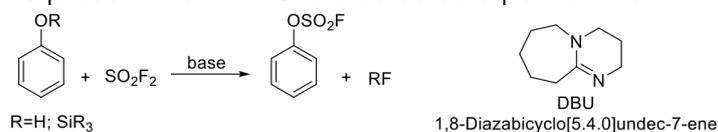
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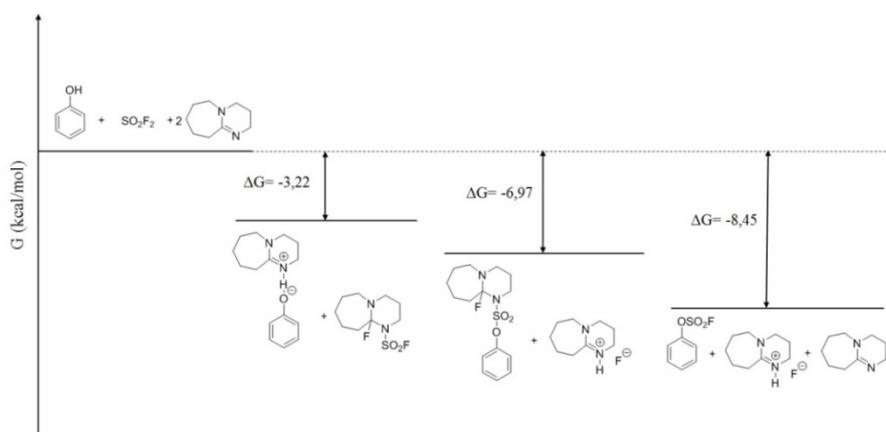
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Sulfur (VI) fluoride exchange (SuFEx) reaction was successfully applied in the synthesis of small molecules, protein labeling, polymer synthesis, and surface derivatization.^{1,2} While the exact mechanism of SuFEx reaction still remains unknown, several observations from these studies are important to note. The aim of this research was investigation of SuFEx reaction mechanism by DFT calculations. Convenient synthesis of aryl fluorosulphates involves application of DBU as a base (Scheme 1). At the present work DBU is studied as a part of intermediate particles.



Scheme 1. Common method for the synthesis of aryl fluorosulfates

It was shown previously that B3LYP functional overestimates S-F bond distance in molecules with hypervalent sulfur such as OSF₄ and H₂C=SF₄, and XAPW91 functional was recommended instead³. Conformational analysis of DBU-SO₂F₂ and (DBU)₂SO₂F₂ intermediates showed that the molecules with the lowest energy are formed upon the addition of SO₂F₂ to DBU via the double C=N bond. Detailed calculation of the energy for subsequent calculations of the thermodynamic quantities was carried out using M11/6-311++G(2d,2p) method after optimization of the molecules in XAPW91/6-311+G(d) approximation with allowance for zero point corrections. Comparing the change in Gibbs energy and enthalpy of various intermediates, the most



thermodynamically stable particles were chosen. Also, a comparison of the calculated thermodynamic values confirmed that the SuFEx reaction with silyl phenol derivatives is thermodynamically more favorable than with phenol. According to our calculations, formation of (DBU)₂SO₂F₂ particle is

thermodynamically advantageous, but it is less stable than DBU-SO₂F₂ + DBU particles. Thus, with the help of quantum chemical calculations, the key stages of the proposed reaction mechanism were determined with high accuracy. A detailed study of the transition states and the influence of solvents is planned.

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Kinetics of Fluorination of 1,3-Dicarbonyls

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Electrophilic fluorination represents one of the most direct and useful methods available for the selective introduction of fluorine into organic compounds.¹ Electrophilic reagents such as NFSI and SelectfluorTM have been widely utilised by the pharmaceutical industry to provide fluorinated molecules with altered binding, pK_a and metabolism profiles. Indeed, 25% of all commercially available small-molecule drugs contain fluorinated groups.² However, the selective fluorination field lacks a firm kinetic underpinning in terms of the reactivities of commonly used reagents.

We have investigated the kinetics of fluorination of substituted 1,3-dicarbonyls by Selectfluor and NFSI (Figure 1a). The effect of the electronic nature of the para-substituent on the rate of fluorination has been studied by Hammett correlation analysis of the reactions, giving a linear relationship and a reaction constant ρ⁺ of -2.0 (with Selectfluor, Figure 1b) and ρ⁺ = -1.9 (with NFSI). It has been determined that the reactivity difference of Selectfluor vs. NFSI with this family of substrates is both electrophile and nucleophile dependent, and that Selectfluor is several thousand times more reactive than NFSI. The reactivity of mono- versus di-substituted 1,3-dicarbonyls towards fluorination was also explored, and we determined that the presence of electron-donating substituents at both para positions gives a greater rate enhancement towards fluorination than the mono-substituted analogues.

Fluorination of the mono-fluoro di-substituted derivatives was carried out on a synthetic scale; to our surprise, we were able to crystallise both keto and enol tautomeric forms, whereby each tautomer was characterised individually. DFT calculations gave further insight into the relative energies of these forms.

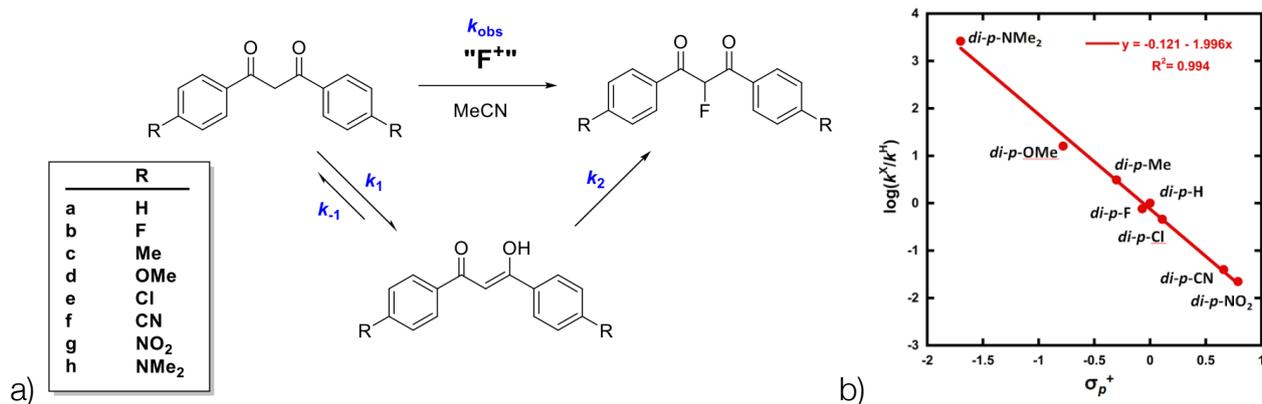


Figure 1: a) Fluorination of disubstituted 1,3-dicarbonyls a-h; b) Hammett correlation for fluorination of a-h by Selectfluor.

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Poster 26

Homolytic Bond Dissociation Enthalpies in Room Temperature Ionic Liquids

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Chemistry is the science on reorganisation of chemical bond via bond-breaking and formation. Bond dissociation energy (BDE), which describes the energy required for bond cleavage, serves as a quantitative basis for analysing the driving force, mechanism and structure-reactivity relationship in organic chemistry.¹

Being composed of entirely ions, ionic liquids (ILs) exhibit a number of remarkable properties, such as negligible vapor pressure, high thermal stability and relatively wide electronic windows, etc., which are distinctive from these of conventional molecular solvents. Largely due to these favorable features, tremendous research attentions have been given to the application development in ILs, whereas in stark contrast, the fundamental aspects of ILs are severely lagged behind, such as explicit solvent structure at micro level, solvation behaviour and solvent effects, etc. These issues are interconnected and are crucial to understand the unique properties of ILs and thus will benefit a rational development of chemistry in ILs. We envisaged that the study of BDEs in ILs may shed a light on these issues.

In recent years, our group have systematically studied heterolytic BDEs (pK_a s) of various series of compounds, involving C-H, O-H, S-H and N-H⁺ acids, in neat ILs, and have found several unique solvation behaviours of ILs which are distinct from those of classical molecular solvents.^{2,3} With these precisely measured pK_a data for acids (HA), in current work we measured the oxidative potentials of anions for these acids [$E_{ox}(A^-)$] by classic cyclic voltammetry (CV) method in two aprotic ILs. Upon designing appropriate thermodynamic cycle, the homolytic BDEs of these acids in ILs are derived (Eqn. 1).

$$\text{BDE(ILs)} = 1.36pK_a(\text{HA}) + 23.1E_{ox}^{\circ}(A^-) + C, C = 66.3 \text{ in ILs} \quad \text{Eqn. 1}$$

The preliminary results show that except for N-H⁺ type of acids, the BDEs of C-H, O-H, S-H acids are smaller than those in gas-phase and DMSO, especially for benzenethiols, which exhibit a much lower (avg. > 10 Kcal mol⁻¹) BDEs in ILs. These experimental results indicate that radicals are more stabilised in ILs than molecular solvents.^{4,5}

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Poster 28

Kinetic Stabilization of Singlet-2,2-Dialkoxy-1,3-Diradical by Introducing Bulky Substituents

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Localized singlet diradicals, which are key intermediates in bond homolyses, are usually very short-lived due to the fast radical coupling reactions. The generation of long-lived localized diradicals allows to investigate the chemistry of homolysis process in detail. Our laboratory had achieved experimental generations of localized singlet 1,3-diradical **S-DR1** (Ar = Ph) by the photodenitrogenation reaction of **AZ1** and succeeded in increasing the lifetime using the steric effect of alkoxy groups at the C2 position.¹⁻³ Therefore, the localized singlet diradical can be kinetically stabilized by the substituents of the alkoxy group.

In this study, bulky substituents are introduced at the meta position of the aryl group in **S-DR2** (Ar = bulky). The steric repulsion is expected to occur between the aryl groups (Ar) and/or between the aryl group (Ar) and the alkoxy group (OR) in the transition state (**TS**) and the ring-closed product (**CP**) of **S-DR2**. The singlet diradicals are expected to be kinetically stabilized (Figure 1). The combined computational and experimental results on the kinetic stabilization of the singlet diradical will be presented in detail.

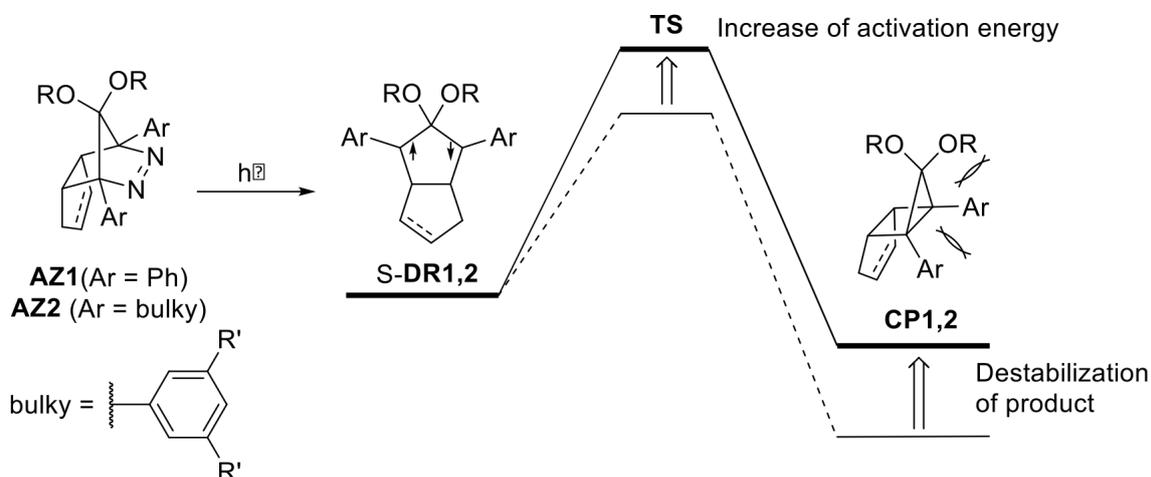


Figure 1. Kinetic stabilization by bulky aryl groups.

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Thermochemistry of Peroxy Radicals: A Combined Photoacoustic Calorimetry, Quantum Chemistry, and Molecular Dynamics Study

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The reaction $R^{\bullet} + O_2 \rightleftharpoons ROO^{\bullet}$, where R^{\bullet} denotes a carbon radical and ROO^{\bullet} the product peroxy radical, is a key step in the interaction mechanism of oxygen with organic matter, hence its enormous importance. Its study is essential, for instance, to optimize the production of energy (and thus limit emissions) from internal combustion engines, or to develop antioxidants to avoid the deterioration of cellular membranes due to lipid peroxidation.

To fully describe the thermodynamics of reaction 1, one needs to know the stability of both the carbon and peroxy radicals. However, while the thermodynamic stability of long-lived organic molecules is well established for a large number of substances, only a few hundreds of carbon radicals are listed in a recent compilation of thermochemical data,¹ and the situation is particularly critical for peroxy radicals: the same compilation includes less than 30! The need for further research on the subject is evident but, to study such demanding species, one needs to use advanced experimental or theoretical techniques (or preferably, both).

Time-resolved photoacoustic calorimetry (TR-PAC) is a recent technique suited to study radical reactions, in which they are started with a laser (photo-) and then followed via a microphone (-acoustic). In this way the radicals can be “temporally isolated”, which allows probing their thermochemistry with chemical accuracy (within ca. 5 kJ/mol). Regarding computational chemistry (CQ) methods, the accuracy of composite approaches together with the explicit treatment of electronic correlation² is comparable to the best conventional methods but, unlike those, it can be used for much “larger” systems (in electron number, such as the peroxy radicals). Finally, molecular dynamics (MD) is essential for the interpretation of the above results at a molecular level, bridging the experimental and electronic structure data.

The interpretation of the TR-PAC results for peroxy radicals is complicated by some poorly understood issues, namely the volume change and the solvation effects of reaction 1. Both these problems can be conveniently addresses by MD. Still, fundamental aspects of this procedure need to be addressed, such as the development of suitable force-fields for the radicals involved. These subjects, which were neglected in previous studies of reaction 1,³ will be discussed and presented as part of our complete and accurate TR-PAC/QC/MD methodology for the study of the thermochemistry of peroxy radicals.

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Proton Dependent Redox Chemistry of Spiropyrans

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The spiropyran photochrome is known for over 60 years, but nevertheless continues to show surprising and unexpected versatility leading to new and exciting applications.¹ Only in the last number of years has the redox chemistry, and in particular the electrochemical mechanisms followed by spiropyrans in solution,² been elucidated.³ Self-assembled monolayers of spiropyrans to surfaces allows for, in addition to their photo-reactivity, further modulation of surface properties through electrochemical write-read functionality.⁴ Recently, we established that in apolar solvents protonation of spiropyrans induces spontaneous ring opening to the protonated Z-merocyanine form.⁵ Considering the local pK_a at electrodes can vary substantially under electrochemical conditions,⁶ our understanding of the electrochemical properties of spiropyrans (Figure 1) must take into consideration the possibility for protonation induced ring opening to form the protonated Z-merocyanine. In this presentation, we apply UV/vis-absorption, IR and Raman spectro-electrochemistry to investigate the nature of species at the electrode and the impact of adventitious protons on their structure.

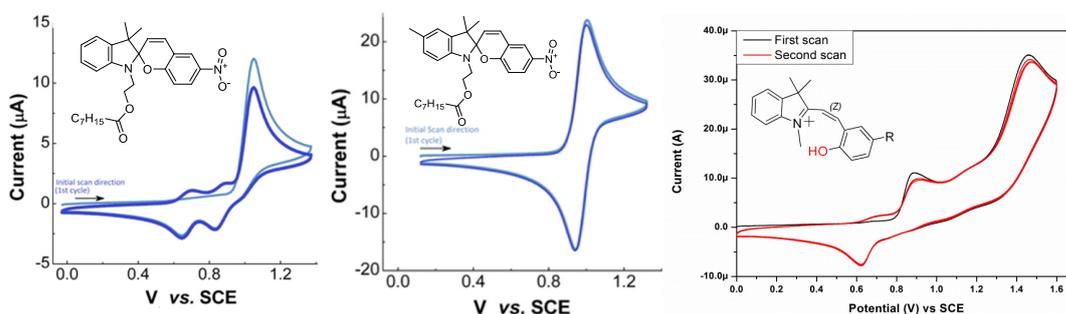


Figure 1. Cyclic voltammetry of (a) non-methylated non-protonated form (b) methylated non-protonated form and (c) non-methylated protonated form

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Development of a Photo-Induced Fast Spin-State Switching Molecule

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Photochromic molecules change their color with conversion of the molecular structure upon irradiation and the photogenerated species go back to their original state thermally or by light irradiation of the appropriate wavelength. Photochromic molecules have been applied to control various properties such as fluorescence, refractive index, electrochemical response, and liquid-crystalline phases or sol-gel transition. T-type photochromic molecules showing the thermal back-reaction at room temperature can enable switching physical properties only by the presence or absence of light irradiation. However, there are few reports on the systems in which the spin-state rapidly changes.¹

Norbornadiene (NBD) is one of photochromic molecules. NBD isomerizes to Quadricyclane (QC) with bond-recombination upon UV or visible light irradiation. The photochemically formed QC has a strain structure and thermally goes back to NBD (Fig. 1). The bond-recombination is one intriguing property for NBD-QC photochromic system. The photochromic behavior of NBD derivatives is also known to be influenced by the donor-acceptor substituents on the double bonds.²

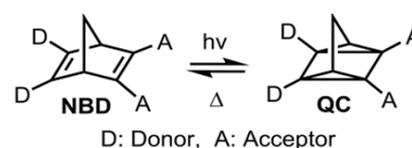
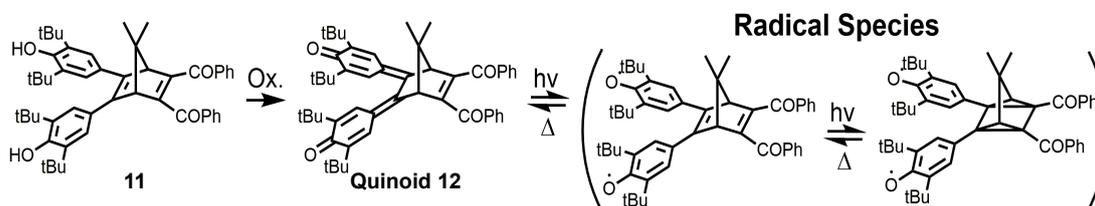


Figure 1. Photochromism of NBD derivative.

In this study, we focused attention on the molecular structure and photo-isomerization with bond-recombination of NBD and attempted to develop a novel NBD derivative by introduction of phenoxy radical moiety having bulky tert-Bu group, being expected to cause the fast spin-state change. By oxidation of the precursor (11), a NBD derivative (Quinoid 12) having quinoid structures was obtained (Scheme 1). The ESR spectrum was measured for the 2-methylTHF solution of Quinoid 12 under low-temperature matrix conditions, and a radical species generated by photo-irradiation was confirmed. Herein, we report the results of investigation of photo-properties of Quinoid 12.



Scheme 1. Plausible mechanism for the photoreaction of Quinoid 12

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Structural Aspects and Reactivity of 5-Methylhydantoin

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5-Methylhydantoin (C₄H₆N₂O₂; 5-MH) was studied in different experimental conditions using a multidisciplinary approach, including infrared (IR) and Raman spectroscopies, differential scanning calorimetry (DSC), polarized-light thermal microscopy (PLTM) and X-ray diffraction (XRD). The experimental studies were complemented by an extensive set of quantum chemical calculations undertaken at the density functional theory (DFT) level.

The electronic structure of the 5-MH molecule was characterized in details using the natural bond orbital (NBO) method, and the unimolecular UV-induced photochemistry of the matrix-isolated compound was investigated and rationalized at light of the electronic characteristics of the molecule.

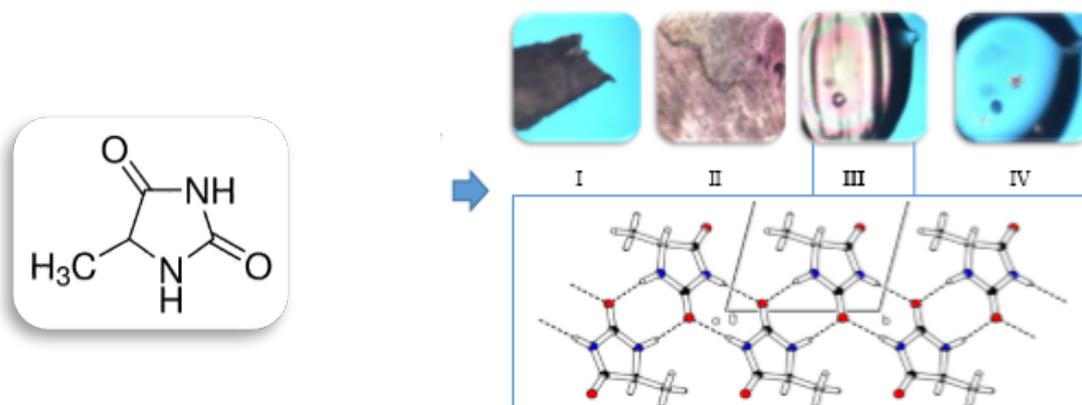


Figure - The molecule of 5-MH (left) and the PLTM images of the four identified polymorphs of the compound (top). The crystal structure of polymorph III (bottom) has been determined by XRD.

The thermal properties of 5-MH were by DSC, PLTM, and IR and Raman spectroscopies, allowing identification of four different polymorphs. The crystal structure of one of this polymorphs (polymorph III) was determined by single crystal X-ray diffraction (XRD), and two additional polymorphs were characterized by powder XRD.

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Chiroptical Properties of Azabora[5]Helicene Architectures

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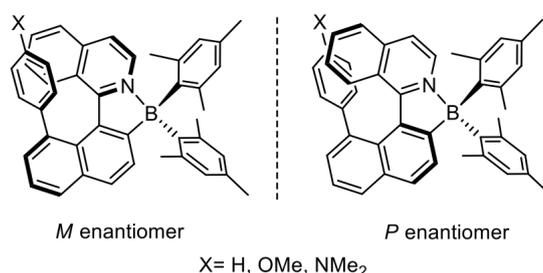
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Helicenes are chiral architectures that have been recently in the limelight of photophysical research for their remarkable chiroptical properties, such as circular dichroism (CD) and circularly polarized luminescence (CPL).¹⁻³ In this context they are considered for applications such as chiral sensing, optoelectronic devices, and chemical switches with CPL output.

This work focuses on the expansion of the photophysical scope of borylated arylisoquinoline (BAI) dyes. As N,C-chelates these dyes are strongly emitting, solvatochromic, and two-photon-adsorbing charge-transfer fluorophores with use in bioimaging.⁴⁻⁶ Herein, we have been able to prepare and optically resolve new chiral BAI helicenes with varying charge-transfer character. These dyes are spectrally tunable and show efficient emission of CPL. In this contribution the synthesis, spectroscopic characterization, and the rationalization of the results based on quantum-chemical calculations will be discussed in some detail.



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Rotation of the π -System Rotor in Crystalline Molecular Gyrotops

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Molecular gyrotops, in which a π -system rotor is encased by three long alkyl chains, have been designed and synthesized (Figure 1).¹⁻³ Because these compounds are crystallized well, their crystal structures can be determined by X-ray diffraction analysis. In the crystalline state, the π -system is confirmed to be sterically protected by the macrocage unit and mean distances between nearest π -systems are 8–12 Å, indicating there are no intermolecular $\pi\pi$ -interaction. Furthermore, molecules are arranged by their rotation axes, alkyl chains are engaged with each other among molecules. According to these crystal structures, the π -system moiety of the molecular gyrotops could rotate even in crystal.

The rotor dynamics of molecular gyrotops in a crystalline state are investigated by solid-state ²H NMR spectroscopy. For this experiments, molecular gyrotops, in which rotor was labeled with deuterium atoms, are also synthesized. Dynamics of the rotor can be revealed by the lineshape analysis of the spectrum. The observed spectral lineshapes of 1-d₄¹, 2-d₄³, and 4-d₂², were remarkably temperature dependent, indicating the rotor rotates rapidly inside a crystal. However, spectra of 3-d₂ showed static Pake doublets indicating no rotation of the rotor.

In this poster presentation, remarkable optical properties (birefringence) change owing to the rotation of the rotor will also be discussed.

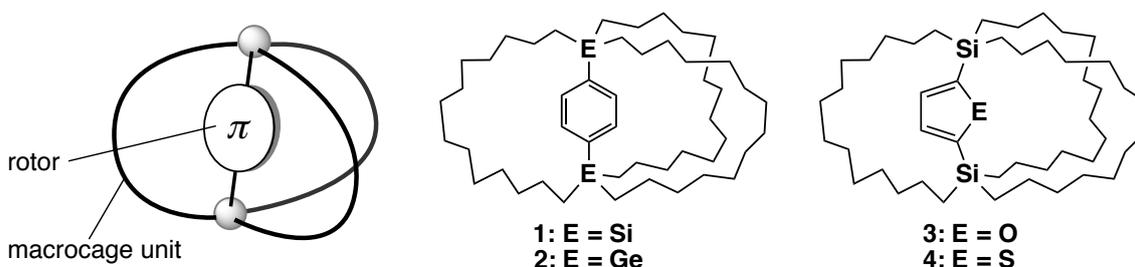


Figure 1. Molecular gyrotops

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The Role of Intramolecular Hydrogen Bonds in Construction of Model Donor-Acceptor Salt Bridged Crystals

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Ever since the guanidine-carboxylate salt bridge with various roles in living systems has been discovered, scientists are trying to use the similar concepts in controlling response of their molecular systems to some external input. Thus, Nocera and coworkers constructed several small donor-acceptor (D-A) systems with salt bridge junction between them.^{1,2} They noticed significant dependence of the electron transfer rates on the direction of the dipole of the salt bridge. It was also shown that amidine-carboxylate salt-bridge can be used to construct photoactive triadic supramolecular assemblies.³ Although, inspired by the natural guanidine-carboxylate salt bridge, both groups were using amidinium salts as a simpler model in which only one hydrogen bonding mode between guanidinium and carboxylate ions is relevant. In continuation of our previous work on guanidinium-carboxylate salt bridge formation⁴, we found significant differences in crystal structures of arylguanidinium dinitrobenzoates caused and controlled by intramolecular hydrogen bonds between guanidinium subunit and aromatic ring attached to it as exemplified by 8-quinolynyl- and 1-naphthylguanidinium dinitrobenzoates (Figure 1).

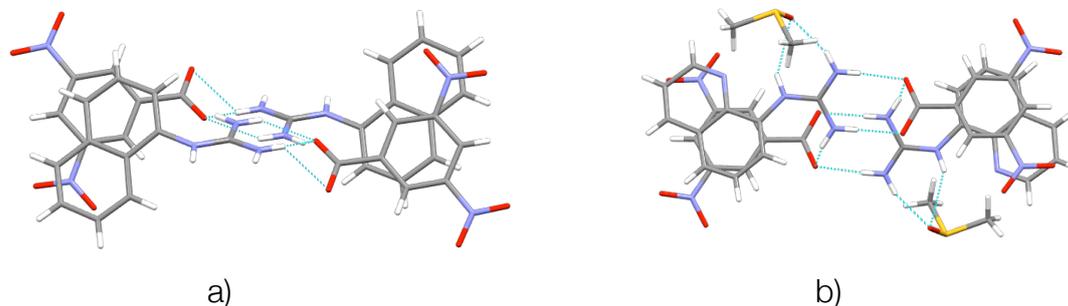


Figure 1. Hydrogen bonding motifs in crystals of (a) 1-naphthylguanidinium dinitrobenzoate and (b) 8-quinolynylguanidinium dinitrobenzoate.

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Decoding the Mechanism of Environmental Radical Polyester Degradation

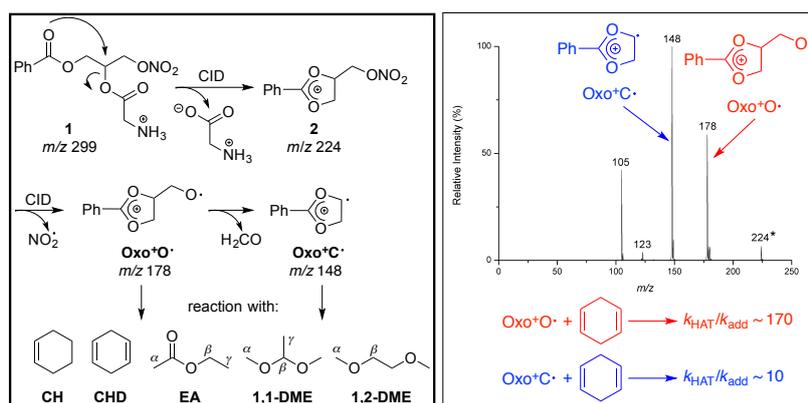
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Synthetic polymers are amongst the most widely used materials due to their extremely diverse properties, which are controlled by their composition (e.g. monomer types), the synthetic and processing techniques as well as the polymer chain length in conjunction with any secondary bond forces operating between polymer molecules. Unfortunately, exposure of polymers to environmental conditions, in particular UV radiation and humidity, leads to dramatic changes of their properties, which result in decreased service life and limited usage. The most important degradation pathways in polymers proceed through radical steps. Key-intermediates are polymer-derived peroxy radicals, ROO·, which are formed through trapping of a carbon-centred polymer radical, R·, through reaction with oxygen, O₂. ROO· acts as carrier in a radical chain process that propagates damage through abstraction of a hydrogen atom from a neighboring polymer strand.

We have recently demonstrated that ROO· reactions with polyester model systems can be explored on the millisecond time scale by mass spectrometry using the distonic radical ion approach.¹ This study revealed clear deficiencies in our understanding of ROO· chemistry and suggests that the current mechanistic model for radical polymer degradation is by far not complete. In particular, the role of C- and O-centred radicals (other than ROO·) in the degradation process requires further investigation.² We have designed a novel precursors of type 1 to generate distonic radical ions Oxo⁺O· and Oxo⁺C·, which were reacted with a series of model systems featuring typical substructures in polyesters. Product and kinetic studies, in combination with computational methods, were employed to elucidate the mechanism of these reactions.³



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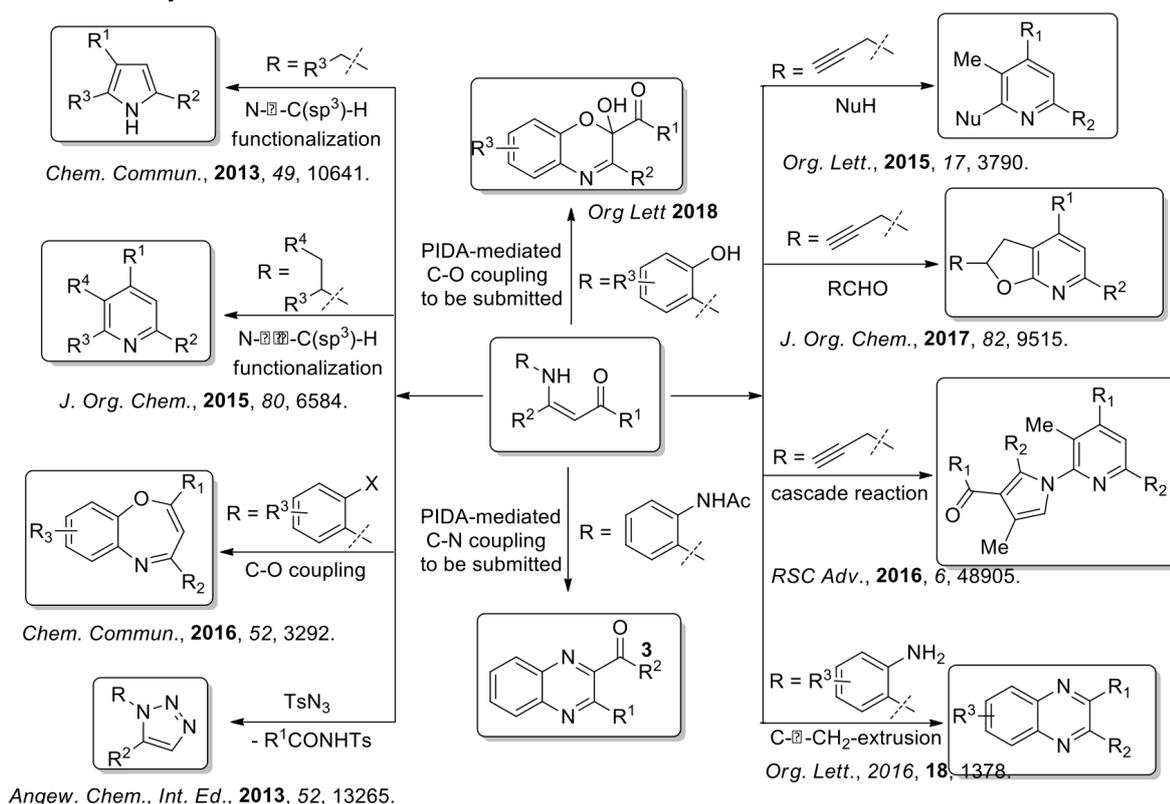
Alkynone-Based Synthesis of Heterocycles

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Alkynones are versatile intermediates in organic synthesis. Enaminoes and enolones, result from the conjugate addition of alkynones with amines and alcohols, have emerged as versatile synthetic intermediates that combine the ambident nucleophilicity of enamines (enols) with the ambident electrophilicity of enones. During the course of our studies on the chemistry and application of alkynone derivatives, we developed series of metal-free approaches for the construction of the skeletons of heterocycles, including functionalized pyrroles, pyridines, 1,2,3-triazoles, chromones, and 4(3H)-quinazolinones. In addition, a metal-free synthesis of diaryl-1,2-diketones by C–C triple bond cleavage of alkynones also has been developed in our laboratory.



Formation of Pillar[5]Arene Based Stable Rotaxane with Azobenzene

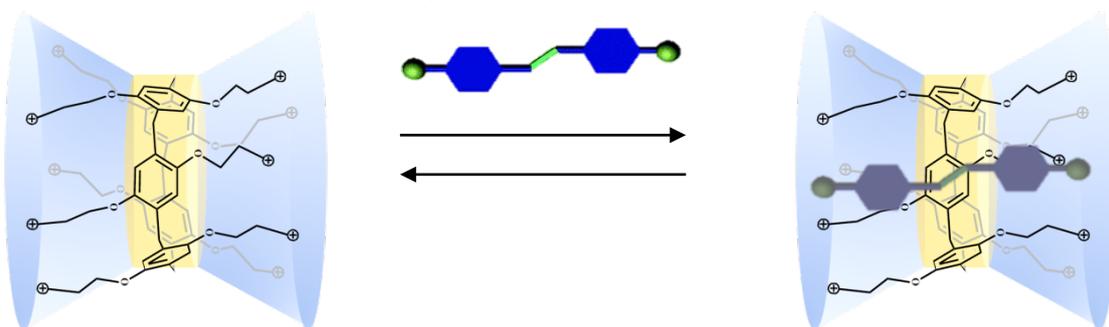
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Pillararenes are a relatively novel kind of synthetic macrocyclic for supramolecular chemistry composed of hydroquinone units linked by methylene bridges at their 2,5-positions^{1,2}. They possess unique characteristics such a facile synthesis and functionality, electron-rich cavities and symmetrical and rigid structure, making them perfect building blocks in the development of molecular and self-assembly for the application in the construction of different systems.

Pseudorotaxanes, a self-assembly threaded structure in which macrocyclic components encircle linear components have been investigated with great interest. However, stable pillar[5]arene-based [1]pseudorotaxanes are still rarely reported because they mostly exist in dilute solutions mixt with linear oligomers, cyclic dimers and so on³.

Herein, we report the slow formation of a stable pillar[5]arene and an azobenzene (Azobenzene-4,4'-dicarboxylic Acid) based rotaxane aqueous medium. The self-complexation was demonstrated by ¹H NMR, change in absorbance and even with a dye displacement assay using methyl orange. Also, we report the influence of pH and salts in the rate of inclusion showing that the inclusion rate increases with medium basicity. The same trend is observed upon addition of high salt concentration.



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Investigation of the Effects of Ionic Liquids as Solvents on a Unimolecular Substitution Process

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Ionic liquids have been shown to affect reaction outcomes differently to molecular solvents, including rate enhancements and increased selectivity.^{1,2} Extensive efforts have been made to explore these effects and the microscopic interactions that cause them, particularly for S_N2 processes.² Comparatively few studies have investigated these effects in unimolecular substitution reactions,^{3,4} often due to slow reaction rates and competing side reactions.

In previous work, the reaction between bromide **1** and 3-chloropyridine **2** that proceeds through both S_N1 and S_N2 pathways was studied.⁵ Focusing on the S_N1 pathway showed that on addition of the ionic liquid 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([bmim][N(SO₂CF₃)₂], **3**) there was an initial increase in the rate constant, followed by a steady decrease as the proportion of salt **3** in the reaction mixture was increased but still an overall increase in the rate relative to the molecular solvent (Figure 1).

These changes were attributed to competing enthalpic and entropic contributions as a result of the ionic liquid stabilising, and ordering about, the transition state. This work investigates the effect of varying the components of the ionic liquid, along with the potential to control these effects through rational choice of the ionic liquid solvent. Additionally, the potential to select which pathway the reaction proceeds through will be investigated using a substrate where reaction may occur preferentially at different sites in the molecule depending on the pathway through which the reaction proceeds.

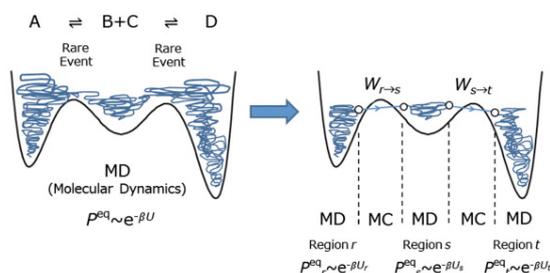
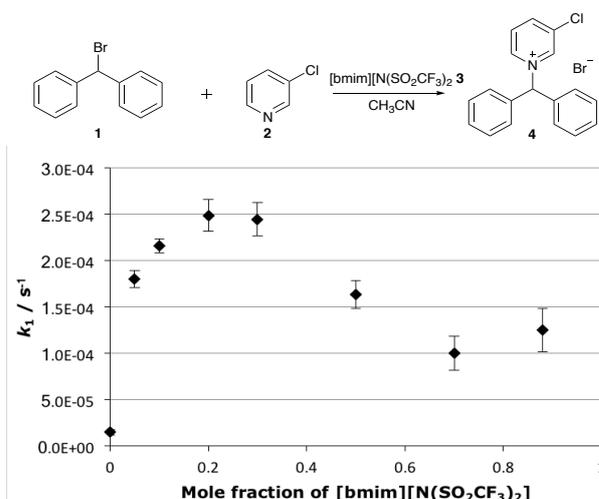


Figure 1. Schematic representation of Red Moon method [1]

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Methods for the Preparation of New 11*H*-Indeno[1,2-*b*]Quinoxalin-11-One Oxime Analogs as Promising JNK Inhibitors

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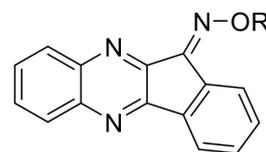
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JNK family enzymes are involved in an embryonal heart development, a regulation of metabolism and normal functioning of a myocardium.¹ Earlier, the authors of the project found that 11*H*-indeno-[1,2-*b*]-quinoxalin-11-one oxime (**IQ-1**) and its sodium salt are effective and specific JNK inhibitors and can be considered as basic compounds for the development of anti-inflammatory drugs.² However, oxime **IQ-1** has extremely low solubility, which was an obstacle to conducting detailed animal studies and possible preclinical trials. This work is directed to the synthesis of **IQ-1** analogues with increased solubility and preserving the considered types of biological activity.

One of convenient synthetic routes to *O*-substituted **IQ-1** derivatives consist in oximation of 11*H*-indeno-[1,2-*b*]-quinoxalin-11-one (**1**) with *O*-*R*-hydroxylamines. In the present work, we used *O*-methyl, *O*-ethyl-, *O*-benzyl, and *O*-allyl hydroxylamine hydrochlorides for the oximation of compound **1**. According to ¹H-NMR spectroscopy, the synthesized products **2a-d** are isomerically pure individual compounds. We have also examined the reactivity of **IQ-1** towards alkylating reagents. The alkylation was studied in dimethylsulfoxide (DMSO); solubility of **IQ-1** in this solvent is about 0.01 M at room temperature. KOH was used as a base. We obtained compounds **3a-3d**, which exist as isomeric mixtures according to ¹H-NMR spectrum. We also used Na₂CO₃ as a base. The synthesized products **3b-d** are isomerically pure individual compounds. Comparison of the NMR spectra of isomer mixtures and individual isomers synthesized in DMSO-KOH and DMSO-Na₂CO₃ systems, respectively, shows that in the latter case the product consists of the isomer that was predominant when the DMSO-KOH medium was used. Observed selectivity of the reactions was in agreement with the results of DFT calculations.

We found that indenoquinoxaline **3c** exhibited binding affinity with K_d in nanomolar range for JNK1, JNK2, and JNK3 isoforms with most potent compound **3c**, which has even lower K_d for JNK1 and JNK3 in comparison with reference compound **IQ-1**.² Moreover, the compound **3c** has much higher specificity toward JNK1 and JNK3 (K_d values are 22 nM and 76 nM, respectively) in comparison with JNK2 (K_d=735 nM).



R: CH₃ (2a), CH₂CH₃ (2b), CH₂Ph (2c), CH₂CH=CH₂ (2d), *i*-Bu (3a), CH₂COOH (3b), CH₂COOCH₂CH₃ (3c), (CH₂)₂OH (3d)

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Catalytic Performance of Pyridyl-Benzimidazole Oxidomolybdenum(VI) Complex in Olefin Epoxidation

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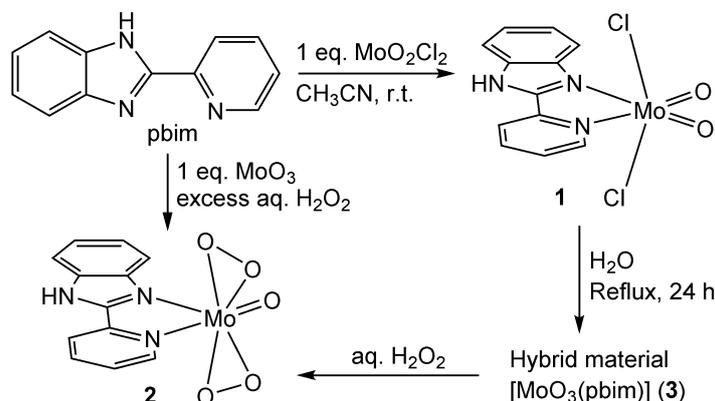
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The search for newer, greener and more efficient catalytic systems attracted the attention of many research laboratories since there is a greater awareness of environmental issues and of separation of catalyst/reaction product during the process. Catalysts consisting of high valent oxidomolybdenum(VI) complexes have been used for several organic reactions, in particular oxidative processes.^{1,2} Complexes that have attracted particular attention include Lewis base adducts $[\text{MoO}_2\text{Cl}_2(\text{L})_n]$ and oxidodiperoxido complexes $[\text{MoO}(\text{O}_2)_2(\text{L})_n]$.

Herein, we report the preparation and the characterization of the complex $[\text{MoO}_2\text{Cl}_2(\text{pbim})]$ (**1**) [$\text{pbim} = 2$ -(2-pyridyl)-benzimidazole].³ This complex was studied as a catalyst in the epoxidation of olefins and we report the characterization of the effective catalysts formed in situ as well as the nature of this catalytic reaction, using two different oxidants (organic TBHP vs H_2O_2).



Scheme 1. Preparative routes to obtain complexes 1-3.

Acknowledgements: This work was carried out with the support of CICECO - Aveiro Institute of Materials - POCI-01-0145-FEDER-007679 (FCT Ref. UID/CTM/50011/2013) and the CENTRO 2020 Regional Operational Programme (Project CENTRO-01-0145-FEDER-028031), co-financed by national funds through the FCT/MEC and the European Union through the European Regional Development Fund under the Portugal 2020 Partnership Agreement. The FCT is thanked for the grants PD/BD/109666/2015, SFRH/BPD/110530/2015 and SFRH/BPD/108541/2015.

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Theoretical Investigation on the Effect of Ligand Bulkiness on the Reactivity of Organometallic Complexes

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In the design of organometallic catalysts, great attention is usually paid to tailoring the metal coordination sphere in order to control reactivity. The electronic properties of the ligands, which can easily be tuned via substitutions, constitute the main focus of synthetic strategies as they are directly correlated to the activity of the system. At the same time, reaction rates are rarely viewed as under control of steric properties of the coordinating molecules, unless the bulkiness of the latter lets one foresee the possible occurrence of interactions that prevent substrate(s) from binding the catalytically active metal center.

Experimental studies on metal protonation in mononuclear transition metal complexes of formula $[W(CO)_5(PR_3)]$ (R= Me, Ph) led to hypothesize the possibility of occurrence of an inversion of reactivity as a function of the medium (vacuum vs polarizable) in which the reaction is conducted.¹ This hypothesis was based on careful consideration of the consequences of the increased relevance of steric factors when the complexes are soaked in a polarizable medium.

Notably, the usage of bulky phosphine ligands for the fine tuning of stereoelectronic features is a popular approach in the case of biomimetic modeling of hydrogenases, the active sites of which include CO ligands bound to iron ion(s). Here, we studied the effects of phosphine ligand bulkiness on metal protonation in the case of biomimetic models of the iron-only [FeFe]-hydrogenase. By means of density functional theory (DFT) calculations, we demonstrate that differences in reactivity toward metal protonation between the biomimetic diiron catalysts $[Fe_2(\mu\text{-adt})(CO)_4(PMe_3)_2]$ and $[Fe_2(\mu\text{-adt})(CO)_4(PPh_3)_2]$ (adt= N-benzylazadithiolate) can be rationalized based on differences in the overall electrostatic properties of the complexes, which acquire key relevance upon changing the nature of the surrounding medium (vacuum vs. acetonitrile soaking).²

These results prompted us to extend the research to different organometallic complexes – e.g. $[(PY5Me_2)MoO]^{2+}$, $[(PY5Me_2)MoS]^{2+}$ (PY5 = 2,6-bis(1,1-bis(2-pyridyl)ethyl)pyridine) – in order to analyze the role of bulkiness on the reactivity of the atoms directly linked to the metal center (i.e. of metal-bound sulphide and oxide groups).^{3,4}

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Investigation of the Caesium Effect in Palladium Catalysed Coupling Reactions

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Caesium bases are regularly used in several industrially relevant reaction systems, such as Suzuki-Miyaura and Sonogashira coupling, and regularly excel as the optimal base in studies involving base screens, however the mechanism by which this superiority, and so called 'caesium effect' arises is not well understood.^{1,2}

In this project kinetic studies and non-commercial caesium species have been used to probe the extent of the 'caesium effect' in palladium catalysed coupling reactions, and optimising which conditions and substrates maximise the increased performance caesium can provide. Evidence is provided against the prevailing theory that solubility is the major reason for rate increase,^[3] and that a change in mechanism is the most likely pathway for increased reaction performance in Buchwald-Hartwig amination and Suzuki coupling reactions. ¹³³Cs and ³¹P NMR monitoring experiments, along with X-Ray Diffraction techniques on Pd species provide evidence towards a possible Pd-Cs bimetallic intermediate species in these reactions.

The utility of caesium phosphate in heteroaromatic boronic acid Suzuki couplings is discussed, with the base providing increased reaction performance when used with boronic acids prone to protodeboronation reactions over reaction timescales.^[4] This finding is particularly relevant to the pharmaceutical industry, where Suzuki cross couplings are the preferred late stage C-C bond forming reaction.

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Oxidation of Aliphatic and Aromatic Amino Acids With H₂O₂ Catalyzed by a Nonheme Imine Based Iron Complex

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Oxidative functionalization of amino acids catalyzed by nonheme iron complexes have received a great attention in recent years.¹ In this context we have investigated the oxidation of a series of N-acetyl amino acid methyl esters with H₂O₂ using the iminopyridine iron (II) complex (**Catalyst 1**)² in order to obtain information on the reactivity and selectivity patterns in these oxidative processes.

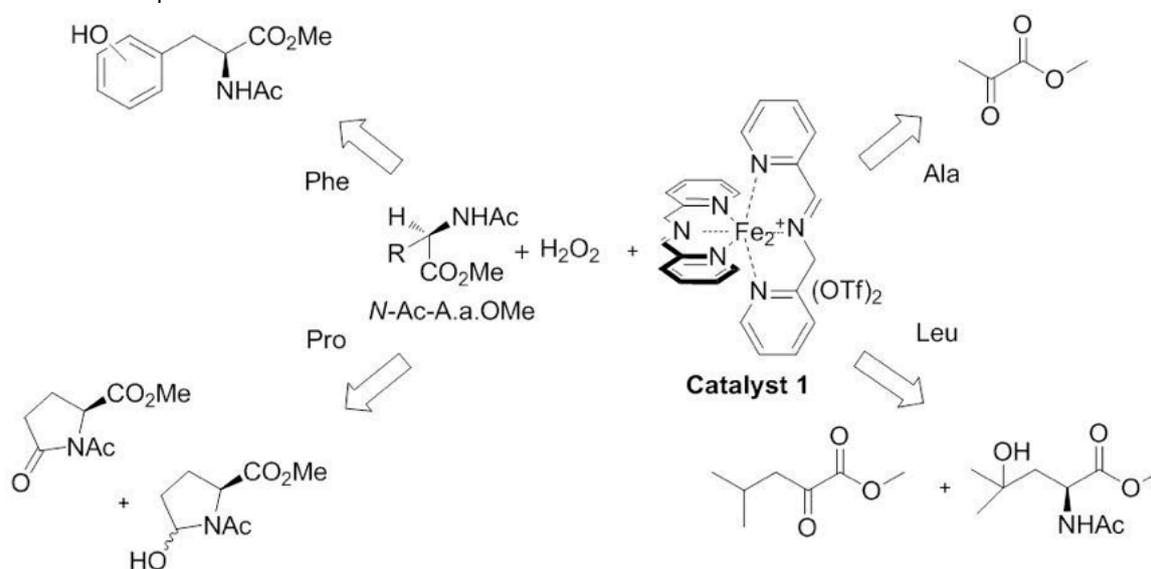


Figure 1

Oxidation of aliphatic amino acids N-AcAlaOMe, N-AcValOMe, N-AcLeuOMe leads to exclusive α -C-H oxidation for the former a.a. and to both side-chain functionalization and α -C-H oxidation for the latter two a.a. with low efficiency. With N-AcProOMe the oxidation is more efficient and regioselective affording exclusively C-5 oxidation products in good yields. A marked preference for the aromatic ring hydroxylation³ over α -C-H and benzylic C-H oxidation was observed in the oxidation of the aromatic a.a. N-AcPheOMe, leading to the formation of tyrosine and its phenolic isomers with high yields.

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A Mechanistic Examination of the Influence of Alkene Substitution on Rates of Biomimetic Platinum-Promoted Polyene Polycyclizations

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Polyene polycyclizations have been utilized in nature throughout history, an example being the formation of the terpenoid family of natural products. In recent decades chemists have sought to explore these reactions using a variety of reagents, including protic acids, Lewis acids or reagents which induce radicals. In this work, the Pt(II)-promoted polycyclizations of select polyenes (Figure 1.) were examined through quantum chemical computations and compared to the synthetic experimental results.¹ The polyenes examined were chosen to examine the influence of the selective positioning of a disubstituted alkene within the polyene, on the polycyclization mechanism and the products produced. Through these calculations insight was gained into the mechanism of polyene cyclization; the effect substitution has on the concerted nature of product formation and why previous synthetic examination of these polyenes found no side products.

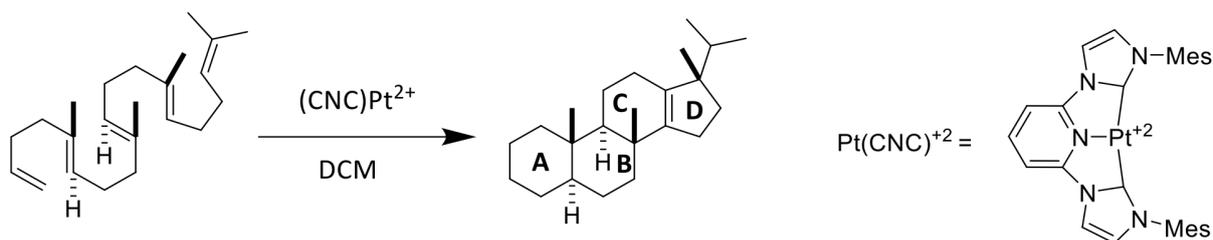


Figure 1.

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Thermodynamic Reaction Control in Radical Enzymes and the Role of Orientated Electric Fields

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Radical S-adenosylmethionine (SAM) dependent enzymes¹ are a relatively recently discovered enzyme family with great prospects for biotechnological applications, not least because of their essential role in a number of biosynthetic pathways towards products with anti-viral, anti-cancer and antibiotic effects. The enzymes' key catalytic commonality is to deal with highly reactive radical intermediates during catalysis. They are perfectly designed to control these highly reactive intermediates in order to facilitate and drive the desired reaction and prevent unwanted side reactions.

We recently demonstrated how radical reaction control can be computationally assessed efficiently by investigating thermodynamic reaction profiles of the desired reactions, and the influence of enzyme binding on those.² We did so by assessing radical stabilization energies (RSEs)³ of key intermediates for central steps in radical SAM enzyme catalysis. For the example of the bacterial 7-carboxy-7-deazaguanine (CDG) synthase (QueE),⁴ we showed how the enzyme controls the radical reaction during catalysis by tightly constraining the conformational space of the reaction.

A second key influencing parameter for many examples in enzyme catalysis is the internal electrostatic field in the enzyme active site, often referred to as electrostatic preorganization.⁵ Recently Shaik et al.⁶ and others further demonstrated how externally orientated electric fields can influence biocatalytic reaction rates by orders of magnitude. Hydrogen abstraction reactions and effects on the reactivity of metal clusters in enzymes, both important in radical SAM enzyme catalysis, are prone to be highly influenced by changes in the surrounding electrostatic field.

Along similar lines to the example of QueE, we will discuss the thermodynamic reaction control in a model radical SAM enzyme. We will then discuss very recent investigations on the role of orientated electric fields at different stages of the catalysis. A second example will target the enzyme biotin synthase and the question how electric fields might influence the reactivity of the iron-sulfur clusters inevitably involved in catalysis. Finally, we will conclude with an outlook on how orientated electric fields might be engineered inside these types of enzymes in order to either facilitate or change catalysis.

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UV-Induced Photolysis of a Dispiro-1,2,4-Trioxolane with Antiparasitic Activity

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Artemisinin and derivatives (**1**, Figure 1a) are widely used antimalarials, with artemisinin-based combinations (known as ACT's) providing effective therapeutic tools against *P. falciparum* malaria.^{1,2} Previous works established the peroxide bond in artemisinin as the pharmacophore^{2,3} suggesting that the anti-parasite action is subsequent to peroxide bond reductive cleavage, catalyzed by heme released during parasite hemoglobin digestion.^{2,3} This irreversible reaction may generate primary or secondary carbon-centered free radicals, or carbocations, that react with parasite biomolecular targets.^{2,3} However, recent reports indicate that the efficacy of artemisinins is threatened by resistance,⁴ urging the development of new endoperoxides with improved antiparasitic properties. Trioxolanes and tetraoxanes steamed as promising leads, with some attaining critical trials.⁵ However, few studies are available regarding their detailed monomeric structure and photochemistry.

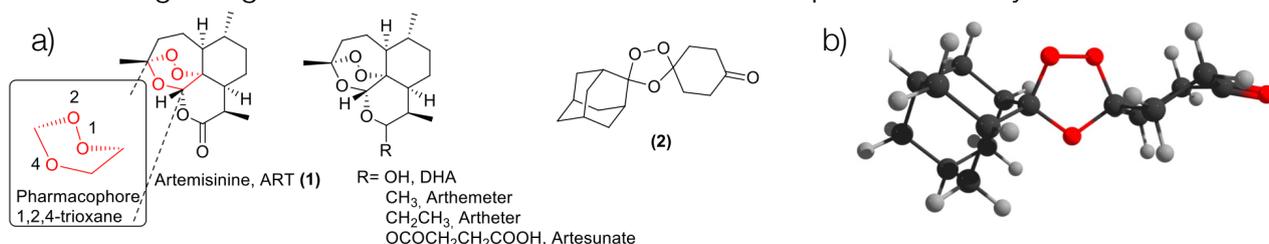


Figure 1. Structures of endoperoxides with antiparasitic activity. a) Artemisinin-derived drugs; b) Calculated structure of dispiro-1,2,4-trioxolane 2.

Herein, we report on the photochemistry of a matrix-isolated dispiro-1,2,4-trioxolane (**2**, Figure 1b). Broadband UV irradiation of the compound isolated in a cryogenic argon matrix led to cleavage of the O–O bond, followed by a radical-mediated rearrangement with formation of a Criegee-type intermediate^{2,6} in line with the postulated mechanism of photodegradation in solution².

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Evans Enolates: Lithium Hexamethyldisilazide-Mediated Enolization of Acylated Oxazolidinones

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Lithium hexamethyldisilazide (LiHMDS) is one of the most important bases in organic chemistry due to its prominence as a selective Brønsted base and its high thermal stability.¹ Although the results of numerous crystallographic, spectroscopic, and computational studies have been published, chemists have assiduously avoided mechanistic studies due to the complexity stemming from a shifting dimer–monomer equilibrium of LiHMDS in THF–hydrocarbon mixtures. As part of our research program of oxazolidinone-based enolates, — the so-called Evans enolates that have appeared in more than 1600 patents and countless academic and industrial syntheses²— we were drawn to the sequential enolization–aldol addition used by Pfizer that proved challenging during the kilogram scale-up of the hepatitis C drug filibuvir.³

LiHMDS-mediated enolization of (+)-4-benzyl-3-propionyl-2-oxazolidinone in THF–hydrocarbon mixtures⁴ showed unusual sensitivity to the choice of hydrocarbon cosolvent (hexane versus toluene) and to isotopic labeling. Four mechanisms corresponding to monosolvated monomers, trisolvated dimers, octasolvated monomers, and octasolvated dimers were identified by examining and quantitating complex reaction coordinates using FT-IR & NMR spectroscopy, mathematical software, and a unique combination of traditional kinetics with novel numerical integration and computational methods. Even under conditions in which the LiHMDS monomer was the dominant observable form, dimer-based metalation was shown to be significant. The mechanism-dependent isotope and cosolvent effects are discussed in the context of ground-state stabilization and transition-state tunneling. Finally, the LiHMDS mechanistic model developed to describe this complex scenario proves to be general and will enable the exploration of the indisputably important chemistry of LiHMDS and enolates — and many other substrates — to detailed mechanistic analysis.

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On the Mechanism of Direct Amidation Catalyzed by the B₃NO₂ Heterocycle

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Amide-bond linkage is a major structural component of biomacromolecules (protein) and synthetic polymers (polyamides). It is also found in many small molecule pharmaceuticals. Since typical procedure for amide bond formation involves use of stoichiometric amounts of activating reagents, development of catalysts to directly couple carboxylic acids and amines has been in high demand.

We recently reported that a multiboron catalyst featuring a B₃NO₂ heterocycle (1,3-dioxa-5-aza-2,4,6-triborinane: DATB) promoted direct amidation of carboxylic acids and amines.¹ The DATB catalysis has proven well suited for the coupling of sterically congested substrates as well as chiral ones including α-amino acids.² Of note, DATBs outperforms the known catalysts such as an arylboronic acid and a group IV metal complex (Scheme 1a). The unique structure and high catalytic activity of DATBs have led us to garner mechanistic insights by a combined experimental and computational approach (Figure 1b).

In this presentation, the detailed mechanism of the DATB-catalyzed direct amidation will be discussed. Particular emphases will be put on understanding the different catalytic activity of DATB 1 and 2, and the nature of the carboxylic acid activation step by the catalyst.

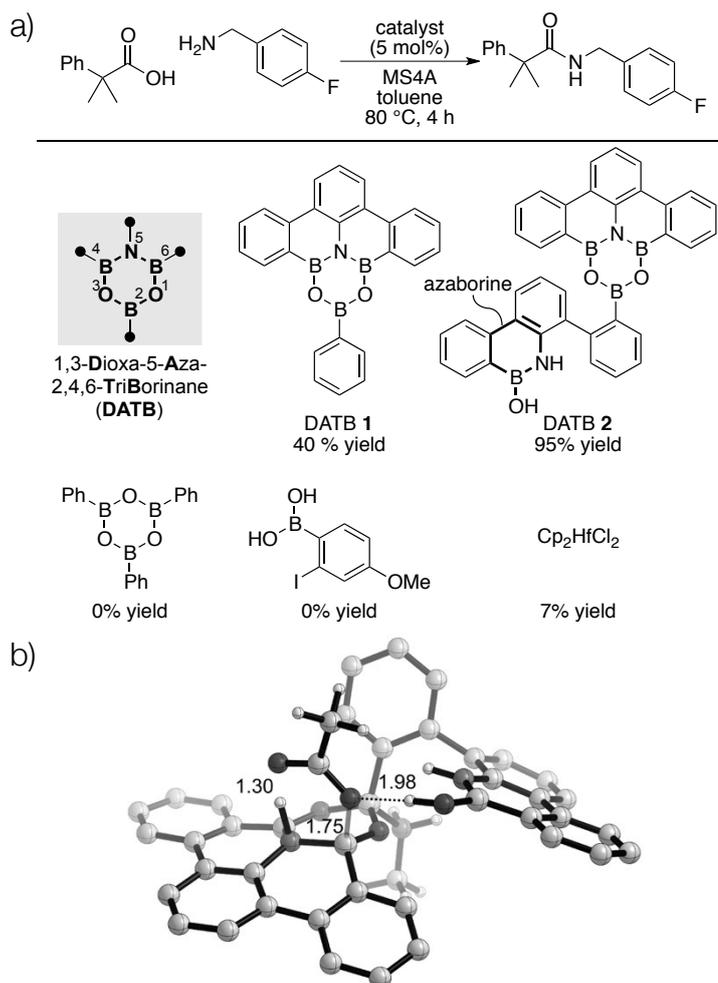


Figure 1. a) Catalytic direct amidation with DATBs and known catalysts. b) Calculated transition state for the acid activation by DATB 2.

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Oxidation of Desmetryn by Peroxynitrous Acid

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The majority of soil on The Earth is used on farming, therefore, agriculture is the main agent for soil degradation due to the use of fertilizers and pesticides. There is a special sensitivity to pollution caused by certain persistent organic, toxic and bioaccumulative substances. Among them, triazines, including desmetryn (N2-isopropyl-N4-methyl-6-methylthio-1,3,5-triazine-2,4-diamine), are persistent herbicides that penetrate plants through the roots causing chlorosis, drying, wilting and death of plants¹.

On the other hand, peroxynitrite anion (ONOO⁻) is an interesting inorganic species that is involved in several oxidation processes in the environment. It is formed by the photoisomerization of nitrate with UV radiation in the atmosphere of the Earth. In this way, peroxynitrite, could be dragged to soils due to its solubility in the droplets of rain and come into contact with the remaining herbicide during the growing season².

The present work has focused on the kinetics study of the reaction between desmetryn and peroxynitrite in aqueous media in order to understand the mechanism of this process. Data show that the reaction rate for the oxidation process follows a first order with respect to the concentration of ONOO⁻ and a first order with respect to the concentration of pesticide (Figure 1 and 2).

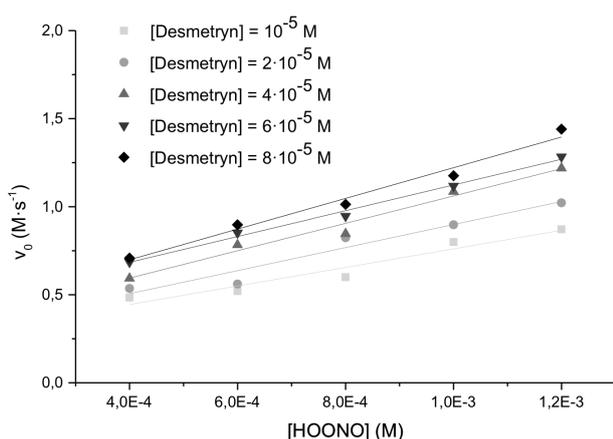


Figure 1. Dependence of the reaction rate with respect to [HOONO] pH = 2, T = 25°C

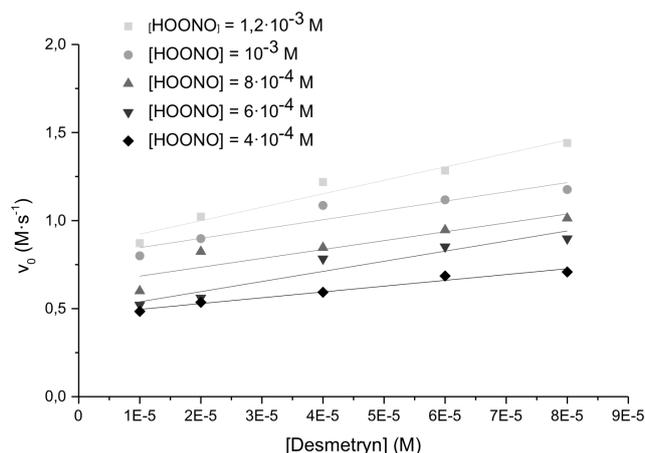


Figure 2. Dependence of the reaction rate with respect to [Desmetryn] pH = 2, T = 25°C

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Self-Assembly and Dimerization of Aromatic Dinitroso Derivatives on Gold Surface

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Aromatic C-nitroso compounds appear in three different forms, as monomers, and Z- and E-azodioxides. Nitroso monomers and their azodioxy dimers are in equilibrium in solution, in which monomers are dominant at ambient conditions while lowering of temperature promotes dimerization. In solid state, aromatic C-nitroso compounds are usually present as E-azodioxides.

Adsorption of compounds with exposed aromatic C-nitroso groups on metal surfaces provides opportunities for design of self-assembled bilayers (SABs). Bilayers could be formed by interactions of nitroso groups at the monolayer interface and those free in solution through azodioxide bonds. Our recent studies suggested that sulfur-containing nitrosobenzene derivatives form both self-assembled monolayers (SAMs) and bilayers (SABs) on gold surface.^{1,2} Scanning tunneling microscopy (STM) revealed that within monolayers and bilayers molecules are arranged into ordered hexagonal structures.

Here, we investigated self-assembly and possible dimerization of aromatic dinitroso derivatives on an Au(111) surface. Aromatic dinitroso compounds are interesting because they can generate oligomers and polymers by the intermolecular formation of azodioxide bonds. We prepared two new aromatic dinitroso derivatives with nitroso groups in mutual meta-position and with alkyl chains of various lengths ending with thiocyanate group for adsorption on an Au(111). Adlayers of dinitroso derivatives on gold surface were studied by polarization modulation infrared reflection-absorption spectroscopy (PM-IRRAS), atomic force microscopy (AFM), STM, ellipsometry and water contact angle measurements. The results obtained revealed the appearance of monolayers and bilayers of aromatic dinitroso compounds on an Au(111), the latter being formed by intermolecular interactions of nitroso groups through E-azodioxide bonds. Adlayers of aromatic dinitroso derivatives on gold surface seem to be less ordered in comparison to those of mononitroso derivatives, probably because of the steric hindrance induced by nitroso groups in mutual meta-position.

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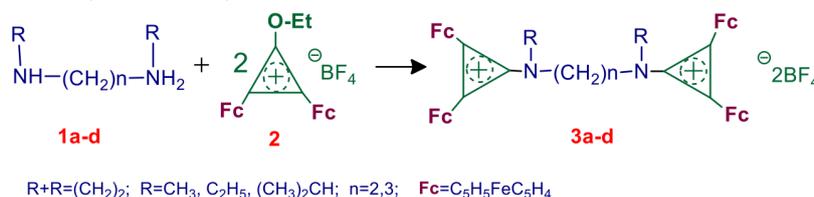
Bis-Cations with Two (2,3-Diferrocenylcyclopropenium) Fragments Stabilized with Diamino-Alkanes: Synthesis and Reactivity

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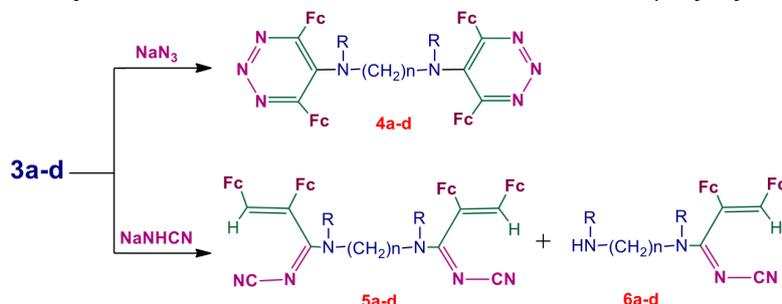
The reaction of 2,3-diferrocenyl-1-ethoxycyclopropenium tetrafluoroborate **2** with piperazine **1a**, N,N'-dimethylpropanediamine **1b**, N,N'-diethyl-1,3-propanediamine **1c** and N,N'-diisopropylethylenediamine **1d** (in a ratio of ~2,5:1) in a CH₂Cl₂ medium results in the formation of a salt with two cations: 1-amino-2,3-diferrocenylcyclopropenium. The cations are connected by the methylene groups **3a-d** (Scheme 1).



Scheme 1. Bis-cation formation reaction

The reaction of salts **3a-d** with sodium azide reflux in benzene results in the derivatives of bis-4,6-diferrocenyl-1,2,3-triazines **4a-d** (~56-71%). Bis-cations **3a-d** react with sodium cyanamide during refluxing in acetonitrile to form the products containing one or two fragments of 1-cyano-3,4-diferrocenyl-1-aza-1,3-butadiene **5a-d** and **6a-d**, respectively (Scheme 2). The structures of the compounds obtained were determined by IR, ¹H and ¹³C-NMR spectroscopy, mass spectrometry, elemental analysis and single-crystal X-ray diffraction analysis for compound **6a**.

The interactions of the salts **3a-d** with NaN₃ and NaNHCN formed due to the opening of the three-membered ring as a result of the nucleophilic attacks of the cyclopropenium cations of the **3a-d** with anions N₃⁻ or NHCN⁻ on the carbon C(2) and C(1) respectively of the three-membered cycles,^{1,2} giving rise to one type of compounds **4a-d** and **5a-d**. The products **6a-d** in the reaction of **3a-d** with NaNHCN were obtained via the fragmentation of the salts **3a-d** respectively. This feature should be of general nature, pertaining to all compounds of a similar structure; thus, they can be used in organic synthesis of the macromolecules as six-atom polyaryl-building blocks.



Scheme 2. Reactivity of bis-cations with NaN₃ and NaNHCN

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Towards an Organocatalytic Route for the d¹-Deuterated of Aldehydes

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Triazolium and bis(amino)cyclopropenium salts, precursors to N-heterocyclic carbenes (NHCs) and bis(amino)cyclopropenylienes (BACs), have been recognised as versatile organo-catalysts for synthetic modifications. Recently, a kinetic evaluation of the benzoin condensation in the presence of NHCs and BACs suggested potential pathways towards d¹-deuterated aldehydes¹⁻⁴.

Overall, sixteen N-aryl substituted 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 from the reaction of triazolium catalyst with aldehyde, clearly highlighting differential effects of fused-ring size of catalysts. Moreover, the extent of H/D-exchange of aldehyde at d¹ position was evaluated, with up to 70% of d¹-deuterium incorporation obtained.

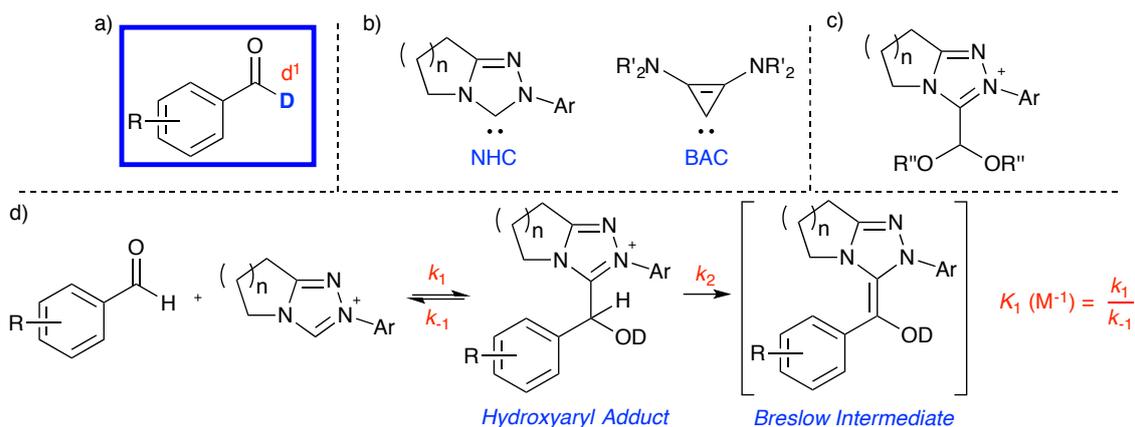


Figure 1. a) d¹-deuterated aldehyde, b) N-heterocyclic carbene (NHC) and bis(amino)cyclopropenyliene (BAC), c) novel NHC adducts, d) equilibrium and rate constants determined from the benzoin condensation.

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Chemistry of Model Catalytic Systems at Very Low Pressure: Studies by RAIRS

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The real heterogeneous catalysis processes are often very complex and chemically hard to understand, with a large number of different components that contribute to the system catalytic activity. To have detailed information on the chemistry of such systems the studies involving selected components in controlled environment are very important and can lead to a better understanding of how catalysts work and how they can be improved.¹

Ruthenium can easily adopt various formal oxidation states in chemical bonds, forming many remarkable compounds often with unique properties, thus being an important catalyst in homogeneous and heterogeneous catalysis. It is used in a variety of organic reactions, such as hydrogenation, oxidation or synthesis (it is the most active catalyst in ammonia synthesis). Nevertheless, single crystal surfaces with low structural complexity are the more attractive to be used as model catalysts for a better understanding of the catalyzed reaction at molecular-level. Therefore, the (0001) close-packed surface of a Ru single crystal (clean and oxygen modified) is used in this work to get further insight on the chemical behavior of some organic molecules under ultrahigh vacuum conditions. Reflection absorption infrared spectroscopy (RAIRS), used on these studies, is a versatile vibrational technique, which has the advantage of only being able to observe modes with a vibration component perpendicular to the surface, allowing to predict the conformation and/or geometry adopted by the molecules adsorbed at metal surfaces.

The model systems selected in this presentation include molecules containing oxygen or nitrogen, such as acetic acid, formic acid, methanol and pyrimidine. The spectroscopic studies provided a wide range of information, including the identification of adsorbed molecular species and their geometry and the nature of chemisorbed intermediates and products formed upon thermal activation.²⁻⁵

For all the molecule/Ru(0001) systems, the more general conclusions are: (1) molecular adsorption is only observed at very low temperatures (90-100 K), forming a multilayer if the exposure is high; (2) the chemical bond between the molecule and Ru involves the heteroatom; (3) the heteroatom has a crucial role on the further species formed on the metal surface; (4) decomposition by thermal activation is observed at lower temperatures than on other single crystal metal surfaces.

The pyrimidine case, in particular, may have important implications for optimizing the design of Ru-containing drugs that involve pyrimidine rings or derivatives as the active principle (e.g., antiviral, antileukemic, or photodynamic agents).

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Kinetics and Mechanism of Cu(I)-Catalyzed [3+2]Cycloaddition Between Phenyl Sydrones and Phenylacetylenes

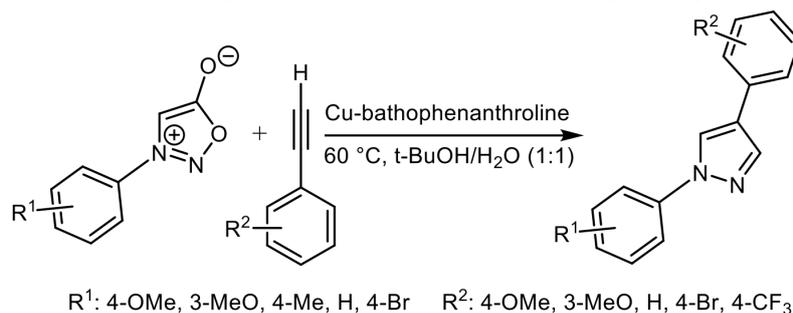
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Since Huisgen discovery of [3+2]-cycloaddition between 3-substituted sydrones and both terminal as well as internal alkynes¹ many descendants tried to utilize this synthetic approach for synthesis of polysubstituted 1,2-diazoles (pyrazoles, indazoles). However until 2013 when Taran's group introduced regioselective Cu(I)-phenanthroline catalysis² this method was sometimes of limited value due to harsh reaction conditions and sometimes due to worse regioselectivity in those cases when non-symmetrical alkyne was employed as an reactant. Although some mechanistic studies of thermal³ as well as Cu-catalyzed⁴ cycloaddition were performed, their conclusions were somewhat contradictory⁵. Especially substitution effects are therefore worth of further investigations.

In our group we have studied the influence of substitution on kinetics and mechanism of [3+2] cycloaddition between subst.phenyl sydrones and subst.phenyl acetylenes (Scheme 1).



Scheme 1

It was surprisingly found that the reaction kinetics obeys zero-order kinetics in homogeneous solution. The rate constants derived from those kinetics roughly fulfill Hammett correlation for substituted phenylacetylenes with unusually high sensitivity ($\rho \approx -3$). For substituted phenyl sydrones such correlation shows linear character ($\rho \approx +2$) too (except 4-Br derivative). Very high sensitivity of both series of reaction rate constant is very unusual and not consistent with concerted mechanism suggested for thermal cycloaddition.

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Catalytic Conversion of Glycerol to Value-Added Products

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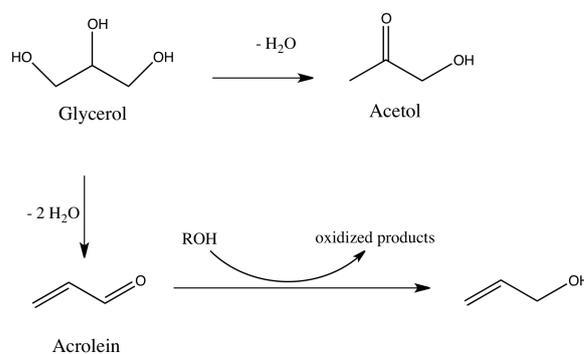
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Glycerol, a polyalcohol readily obtained from biomass, is a chemical product with wide applications in pharmaceutical, cosmetic and food industries. This compound is found in association with fatty acids forming triglycerides and it is consequently produced as a by-product in the soap and biodiesel industries. In the last years, the continuous demand for more sustainable alternatives to fossil fuels, that includes biodiesel, gave rise to a surplus of glycerol production that tends to reduce its market price. The conversion of glycerol into value-added commodity chemicals and fuels is thus of paramount importance to improve the biodiesel economic viability.¹⁻³

The gas-phase catalytic dehydration to acrolein is one of the most studied ways for the valorisation of glycerol. This reaction has been shown to be highly dependent on the textural and acid properties of the catalyst.⁴⁻⁷ The formation of acrolein is favoured in presence of medium to strong Brönsted acid sites, however, in these conditions the formation of coke is also an issue, giving rise to a deactivation of the catalyst.

A less explored way for the valorisation of glycerol is its conversion to allyl alcohol, an important chemical intermediate due to the presence of a C=C and O-H functionalities. Although the mechanism for the one-pot formation of allyl alcohol from glycerol remains a matter of debate, the available data obtained with bifunctional catalysts suggest that it involves a hydrogen transfer reaction from a compound containing a hydroxyl group to acrolein resulting from the dehydration.



In this work we explore different ways of glycerol valorisation through the control of acid and bifunctional zeolite-type catalysts properties aiming to selectively obtain acrolein and/or allyl alcohol.

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Kinetic Investigation of Methyl Bromide Reaction With Ethanolamine

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Methyl bromide was produced as a volatile organic by-product in a process that we were developing. It is an ozone depleting agent and therefore needs to be abated so that its release to the atmosphere is controlled to below the appropriate threshold (2 mg/m³air). Ethanolamine has been reported as a reagent for methyl bromide removal¹. Kinetics information on its reaction with methyl bromide was needed to underpin the design of a scrubbing protocol. We used reaction calorimetry coupled with gas volumetry as in-situ techniques to measure the reaction rate. We were able to determine the different rate constants of the reaction scheme of Figure 1 by fitting calorimetry data². We also applied ¹H NMR to measure ethanolamine conversion and selectivities at end of reaction as orthogonal experimental techniques.

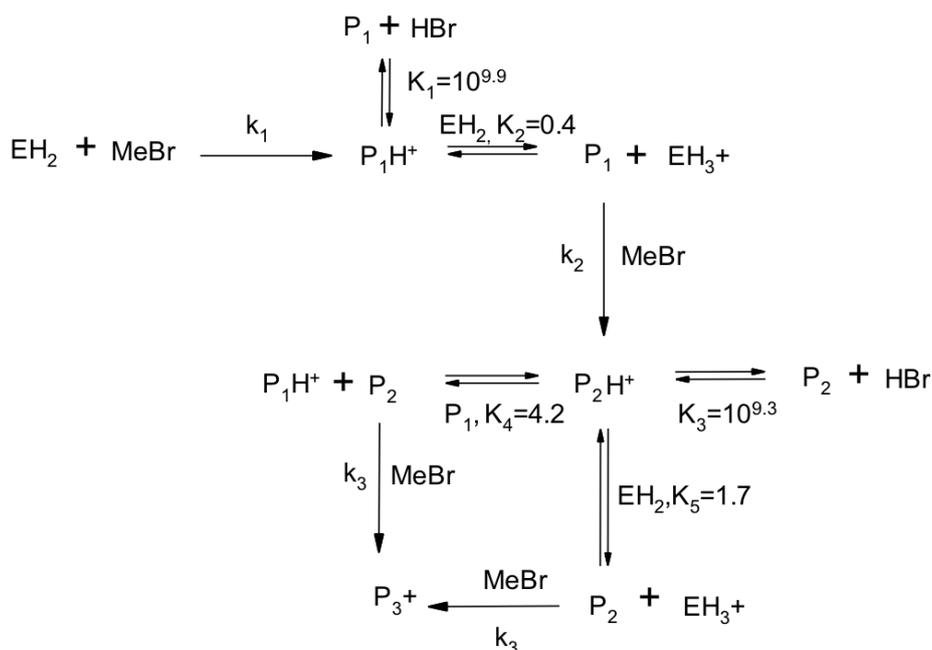


Figure 1: Reaction paths for the reaction between ethanolamine and methyl bromide. Equilibrium constants were calculated from pK_a values in water at 25°C. EH₂ represents ethanolamine - P₁, P₂ and P₃⁺: mono, di and tri-methylated products respectively. Bromide counter-anions are omitted for clarity.

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The Phosphane-Catalyzed Oligomerization of Isocyanates – Mechanistic Study and Identification of a Transient Intermediate

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The oligomers of aliphatic isocyanates are used as building blocks for highly durable PU (polyurethane) coatings and to tune and improve polymer properties.^{1,2} Therefore, the corresponding Lewis base-catalyzed oligomerization reaction is an important industrial process. Earlier mechanistic studies by Richter and Horvath found evidence for a presumably zwitterionic dimeric intermediate in the phosphane-catalyzed oligomerization in low temperature NMR studies.² Subsequent computational studies by Gibb and Goodman found additional reaction pathways and identified an oxygen-bridged cyclic intermediate for the phosphane-catalyzed oligomerization.³ Using a combination of low temperature NMR studies with ¹⁵N-labeled isocyanates and DFT chemical shift calculations, we have now structurally identified the previously reported intermediate as a nitrogen-bridged cyclic species. The relevance of this species is further supported by extended reaction path calculations.

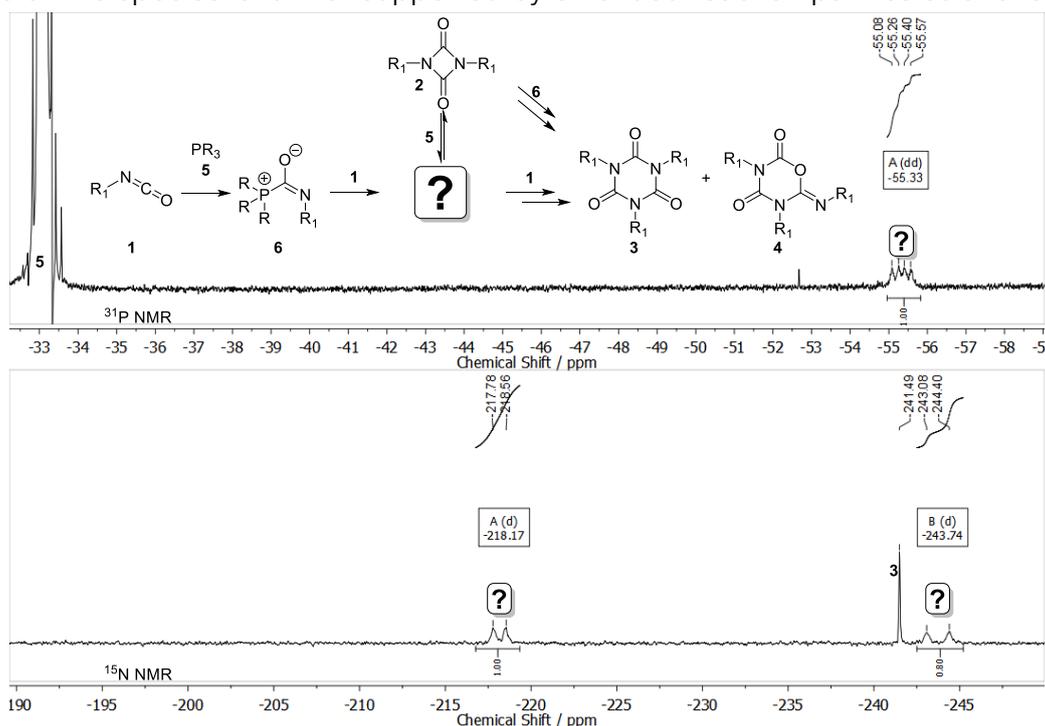


Figure: ³¹P and ¹⁵N NMR spectra of the transient reaction intermediate and its role in the oligomerization reaction.

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Interactions of the Components of Ionic Liquids With Species Along the Reaction Coordinate of Substitution Processes

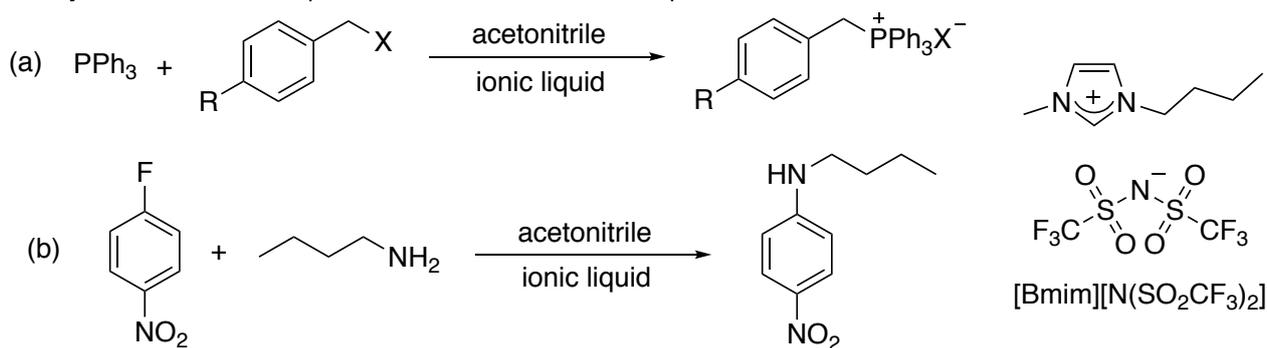
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Ionic liquids, salts with melting points below 100 °C,¹ affect reaction outcome in hitherto unpredictable ways compared to conventional organic solvents.² This work endeavours to extend the predictive framework for ionic liquid solvent effects, particularly exploiting how interactions in solution change on changing the nature of the reagents. Along with considering what determines the dominant interactions, there is the potential to control this feature (along with reaction outcome) through rational selection of the ionic liquid; i.e. solvent control of reaction outcome.

Two exemplar reactions have been considered: the S_N2 and S_NAr processes shown in Scheme 1. In the S_N2 reaction, nucleophile-ionic liquid interactions have been shown to provide entropically driven rate enhancements.³ In the S_NAr reaction, when an oxygen nucleophile was used the key interactions responsible for the rate enhancement were found to vary with the ionic liquid used and the amount present in the reaction mixture.⁴



Scheme 1. (a) S_N2 and (b) S_NAr processes that have been examined in ionic liquids (such as [Bmim][N(SO₂CF₃)₂]) to determine the effect of reagent structure on reaction outcome (X = Cl, Br, I, OAc, R = MeO, Me, H, Br, CF₃, NO₂).

In each case, the effect of the amount of ionic liquid in the reaction mixture on reaction rate was determined, and temperature-dependent kinetic studies provided insight into the interactions between the ionic liquid and species along the reaction coordinate. The knowledge gained will expand our understanding of how ionic liquids affect substitution processes and thus underpin the practical application of ionic liquids in chemical synthesis.

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Synthetic and Kinetic Evaluation of Triazolyl Mimics of Thiamine Pyrophosphate (TPP) for Biocatalysis

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Enzyme-bound thiamine pyrophosphate¹ (TPP, **1**) has been used to catalyse several transformations requiring stereoselective C-C bond coupling, both on a preparative and commercial scale.² Results obtained with enzyme-promoted reactions usually give excellent enantioselectivities but relatively low yields.² Although a broad range of TPP mimics have been developed and used directly as organocatalysts in the absence of enzyme,^{3,4} there have been limited studies in conjunction with TPP-utilizing enzymes.

Of the TPP mimics applied as organocatalysts to date triazolyl systems are frequently the most efficient.⁴ We aim to develop triazolyl TPP mimics closely resembling the original TPP cofactor such that binding, recognition and catalysis is possible with TPP-utilizing enzymes. As the catalytic cycle involves initial deprotonation of the C2-H to yield N-heterocyclic carbene **1'**, initial estimation of carbon acidities was deemed essential to understand the mechanistic roles of the various substituents. Herein, we present the synthetic and kinetic studies of N-alkyl triazolyl mimics **2** (Figure 1) including the use of a ¹H NMR spectroscopic method^{5,6} to estimate C2-H pK_a. Results may be compared with data for a broad range of N-aryl triazolium salts **3**.

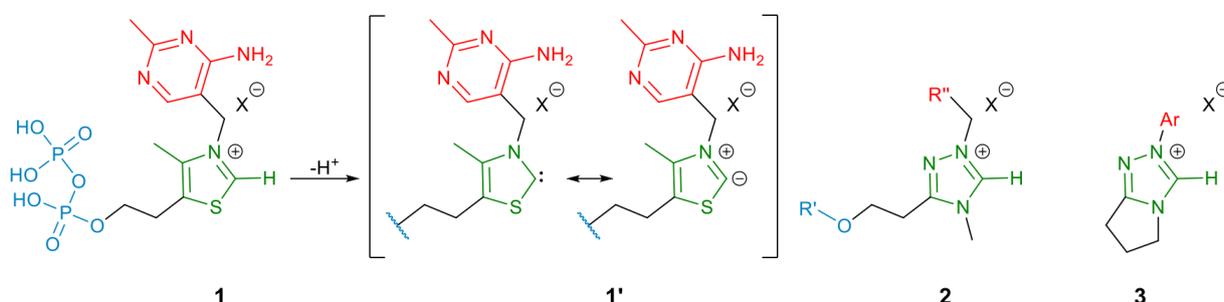


Figure 1. (1) Thiamine pyrophosphate (TPP) and conjugate base N-heterocyclic thiazolyl carbene **1'**; (2) N-alkyl triazolyl mimics **2**; (3) N-aryl triazolium salts.

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Oleuropein: A Valuable Chiral Building Block

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Olive tree (*O. europaea*) is a natural source of oleuropein (Figure 1), a secoiridoid present only in plants from Oleaceae family. Although it can be found in fruits and small branches, oleuropein is present in higher amounts in olive leaves, which are considered a cheap and easily available source of oleuropein, since are industrial by-products with no practical applications. Oleuropein has potent biological and pharmaceutical properties: anticancer, cardioprotective, neuroprotective, gastroprotective, anti-diabetes and anti-obesity, in large part attributed to its antioxidant and anti-inflammatory effects.¹

Extraction and analytical methods have been developed and widely reported for qualitative and quantitative studies of olive polyphenols, including oleuropein. Published transformations of oleuropein are generally related to the removal of hydroxytyrosol and glucoside moieties. Since few research has been done at this level², we will describe the synthesis of new scaffolds from oleuropein at the level of monoterpene unit, through semi-synthetic transformations.

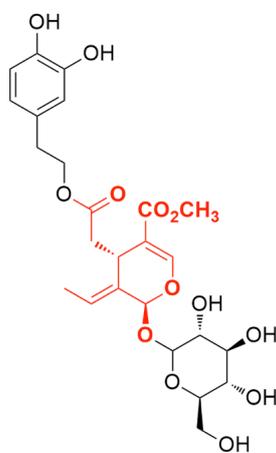


Figure 1: Molecular structure of oleuropein. Monoterpene unit highlighted (red).

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The Enantiocontrol in Primary Amine Catalysis

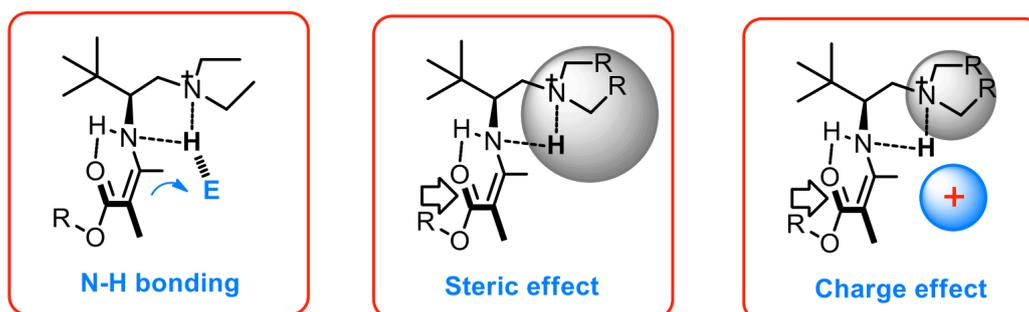
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The construction of chiral carbonyl compounds has long been the central task in asymmetric catalysis and the development of new catalysts is crucial to achieve this goal. During the past decade, we have developed a series of chiral primary-tertiary diamine catalysts and enable a number of enantioselective transformation of ketones and aldehydes.¹ The protonated tertiary amine moiety was found to play a critical role in the enantiocontrol step. In most cases, it can guide the approach of the electrophile via Hydrogen-bonding effect.² Recently, we found that the protonated tertiary amine group can also affect the facial selection via steric effect in the asymmetric allylic alkylation reactions,^{3,4,5} In addition, a charge repulsion controlled facial selection mode was also observed in the Fluorination reaction.⁵ These findings provide a guiding principle in tuning stereoselectivity and enabled the Prediction of stereoinduction for new reactions.



Different Enantiocontrol Mode in chiral primary amine catalysis

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Concurrent S_N1 and S_N2 Mechanisms in Solvolysis Reactions

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There has been a long lasting controversy, whether S_N1 and S_N2 reactions are distinct mechanisms or extreme cases of a continuous mechanistic change.¹ In order to elucidate this question, we studied the Menshutkin reaction (figure 1) of 1-halo-1-arylethanes with amines² in methanol/acetonitrile mixtures at 20 °C.

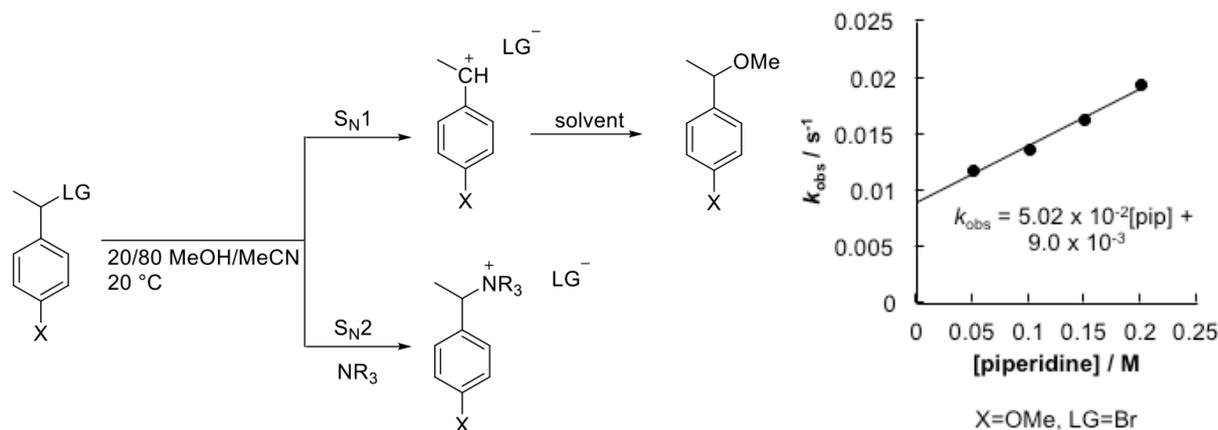


Figure 1.

We attempted to quantify the contributions of the S_N1 and S_N2 reaction channels by analyzing the kinetics of the reactions of the 1-halo-1-arylethanes in the presence of variable concentrations of primary, secondary and tertiary amines. Conductometry was used to monitor the reaction progress in all cases. The observed first-order rate constants k_{obs} follow the relation $k_{\text{obs}} = k_1 + k_2[\text{amine}]$, in which k_{obs} represents the sum of the nucleophile-independent term k_1 (S_N1 path) and the nucleophile-dependent term $k_2[\text{amine}]$ (S_N2 path). The effect on the concurrent S_N1 and S_N2 reactions was studied by variation of the nucleophile, the substituents on the aryl moiety, the solvent, the leaving group (Cl, Br, OTs) and the temperature. We found conclusive evidence that S_N1 and S_N2 are two distinct mechanisms. The relative leaving group abilities of tosylates and bromides depend on the mechanism of the substitution reaction.^{3,4} Protic solvents have a rate accelerating effect on S_N1 reactions and a rate decelerating effect on S_N2 reactions when compared to dipolar aprotic solvents.

$k_{\text{OTs}}/k_{\text{Br}}$ S _N 1: approx. 10 ³ S _N 2: approx. 0.5
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Dual function of Amino Acids Ionic Liquids (AAILs) on the Degradation of Organophosphate Pesticide, Paraoxón®

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To date, the room temperature ionic liquids (RTILs) most used as reaction media are those petroleum-derived, composed by an organic cation such as dialkylimidazolium and alkyipyridinium, and inorganic anions such as hexylfluoroborate [PF₆], tetrafluoroborate [BF₄] and dicyanamide [DCA]; among others.¹ Nevertheless, in the last years several reports have put under debate its greenness through toxicological studies which indicate that toxicity is basically attributed to the anion present in the IL.²

In this context, biomolecules, such as amino acids (AAs) have an enormous potential to improve the green credentials of ILs, because they are biodegradables and non-toxic. Furthermore, they could be easily used as cations or anions due to their variety of functional groups in their structure.³

Herein, we prepare amino acids ionic liquids (AAILs) using butyl methylimidazolium (Bmim) as cation and L-cysteine (L-Cys), L- alanine (L-Ala), L-proline (L-Pro), L-histidine (L-His), L-phenylalanine (L-Phe) and L-Serine (L-Ser) as anions to use as media reaction in the degradation of Paraoxon®. Previously, we have demonstrated a favorable effect in the degradation of some organophosphate pesticides when petroleum-derived ionic liquids were used as reaction medium. In this work, we will show that the degradation of Paraoxon using AAILs as the reaction media, proceeds more efficiently and the degradation occurs without the need of an extra nucleophile agent. The kinetic results ($t_{1/2}$) will be discussed in function of solvent parameters such as Kamlet and Taft.

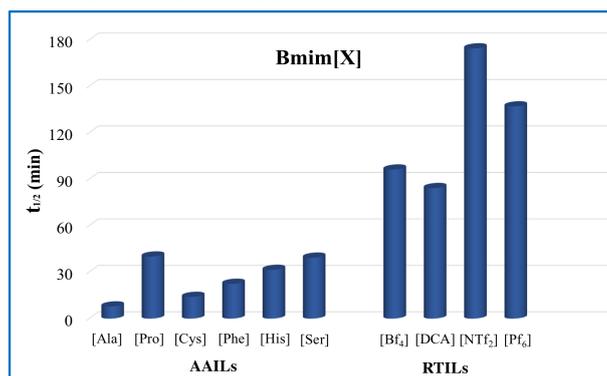


Figure: half-life ($t_{1/2}$, min) for the degradation of Paraoxon with Piperidine (0.2 M) in RTILs and $t_{1/2}$ values obtained for the degradation of Paraoxon in AAILs without an extra nucleophile group.

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Synthesis and Structure of a Novel O-Linked Diazirine-Quinolone Conjugate

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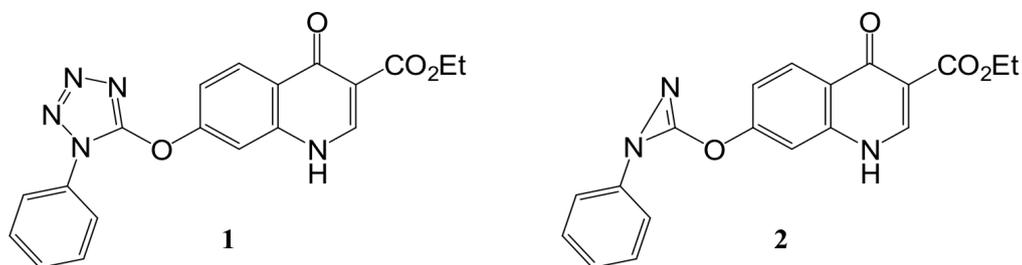
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Malaria remains a global health concern and the development of effective antimalarials is a priority.¹ Selected quinolone 3-esters were proposed as potent inhibitors targeting the Qo site of the Plasmodium falciparum bc1 protein complex. Inhibition of bc1 complex leads to a drop of mitochondrial function, collapse of the trans-membrane electrochemical potential and parasite death.^{2,3} It has been found that the nature of substituents in position 7 of quinoline 3-esters impacts in pharmacological properties,³ so we proceeded with the preparation of a library of 7-functionalized analogues and investigation of their detailed molecular structure, chemical stability and antimalarial activity.⁴⁻⁶ The synthesis and structure of quinoline 3-esters revealed challenging, due to reaction conditions and the possibility of 4-oxoquinoline /4-hydroxyquinoline tautomerism.⁵

Attempts to synthesize the tetrazole-quinolone conjugate (1) following the Gould-Jacobs methodology led to diazirine-quinoline conjugate (2). Formation of 2 arises from thermally induced extrusion of N₂ from 1, favored by the high temperatures required for intramolecular cyclisation to the quinolone core. The structure of 2 was investigated, using FTIR spectroscopy and theoretical calculations.



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Poster 67

NMR Evidence for the Aromatic, Thiamine-like Breslow-Intermediate

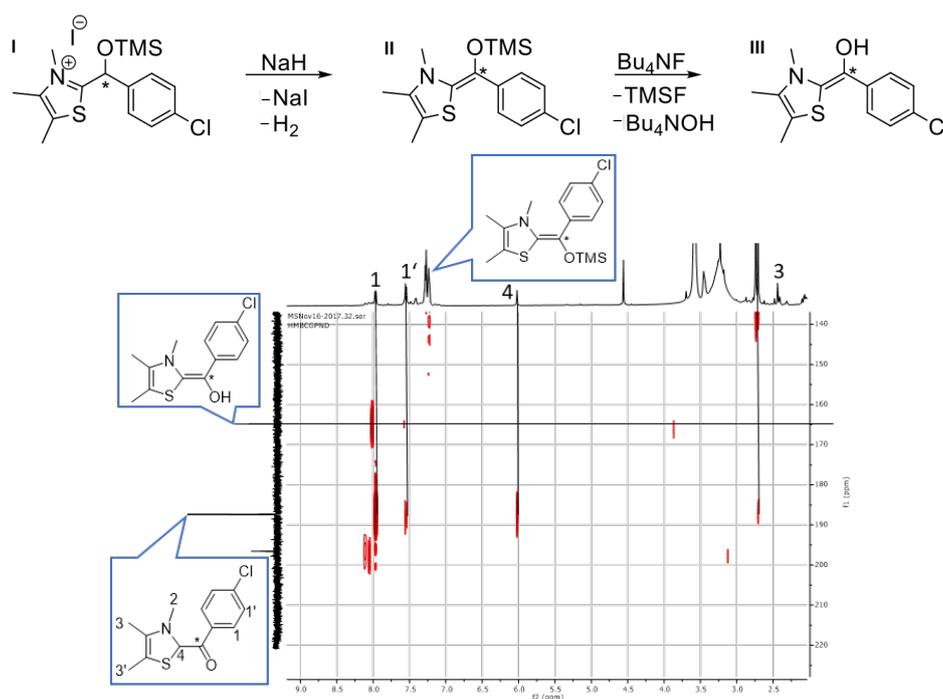
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Since Breslow postulated his mechanism for the “Umpolung”-reaction of thiamine pyrophosphate in 1958, the characterization of the henceforth named “Breslow-intermediate” failed due to its extremely low stability.¹ 2,2-Diamino enols show reactivity similar to thiamine-based Breslow-intermediates and were only recently identified and investigated with NMR-spectroscopy, XRD-techniques, and theoretical methods by Berkessel et al.²

We present NMR spectral investigations towards the long elusive conjugated/aromatic thiazolium-type Breslow-intermediate. Our plan was to first deprotonate isotopically labelled I to II under inert atmosphere at r.t. followed by addition of TBAF at $-60\text{ }^{\circ}\text{C}$ to give III. The precursor salt I is used for the experiments as these systems were employed for the in situ generation of carbene-catalyzed reactions.³ The HMBC-spectrum shows the enaminol and the ketone.



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Push-Pull Dicyanoimidazoles in Photoredox Catalysis

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Photoredox catalysis currently represent a renascent synthetic tool allowing conversion of the solar energy to energy of a chemical bond.¹ Based on our recently developed X-shaped dicyanopyrazine organic photoredox catalyst,²⁻⁵ we focused herein on utilization of five-membered imidazole for construction of Y-shaped push-pull molecules with tailored photoredox properties. Hence, two new push-pull molecules with imidazole-4,5-dicarbonitrile acceptor (dicyanoimidazole, DCI, Figure 1), thiophene and 2-methoxythiophene donors with potential use in photoredox catalysis were designed and prepared.⁶ The synthesis started from commercially available imidazole-4,5-dicarbonitrile and its gradual bromination, methylation and final Suzuki-Miyaura cross-coupling reactions. The fundamental properties of target molecules were studied by available analytical methods including X-ray analysis and DSC. The extent of the intramolecular charge-transfer were further investigated by UV-VIS absorption spectra and DFT calculations. Both push-pull molecules were tested as photoredox catalysts in cross-dehydrogenative coupling reaction between tetrahydroisoquinoline and nitromethane and the results were compared with previously obtained results. Fundamental structure-property-catalytic activity relationships were elucidated.

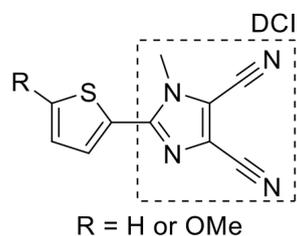


Figure 1. Molecular structure of investigated DCI photoredox catalysts.

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Modelling the Repair of Damaged Proteins by Antioxidants

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Free radicals are very reactive species that can damage proteins and other biomolecules. One of the first products of these reactions are carbon-centred protein radicals, which may subsequently become other species. Certain molecules, known as antioxidants, can scavenge free radicals by several mechanisms, including hydrogen atom transfer (HAT) and single electron transfer. This way antioxidants could repair damaged proteins.

A particularly interesting group of antioxidants are those with thiol groups in their structure. Dihydrolipoic acid (DHLA) and glutathione (GSH) are examples of these antioxidants in which the S-H bond is weak enough to efficiently repair protein carbon-centred radicals by the HAT mechanism. GSH is a natural tripeptide (L-glutamate, L-cysteine and L-leucine) which takes part in many biochemical reactions that regulate the levels of free radicals. Phenolic compounds, such as α -tocopherol (vitamin E) or its water soluble analogue Trolox, are also known for their antioxidant activity. Trolox is commonly used as a reference molecule against which the antioxidant capacity of other species and mixtures is assessed.

In this work, we have used the M06-2X functional with the 6-31++G(d,p) basis set and the SMD solvation model to study the thermodynamics and the kinetics of the HAT repair reactions between the antioxidants GSH and Trolox and four N-formyl leucinamide radicals (centred at the α , β , γ and δ carbons). Calculations have been performed in water and in pentyl ethanotate, to mimic the effect of the microenvironment (hydrophobic or hydrophilic) of the damaged amino acid within the protein. The protein model N-formyl-leucinamide was recently used to study the antioxidant capacity of DHLA following a similar repair mechanism.^{1,2} The results obtained in this work allow the antioxidant activity comparison between Trolox, GSH and DHLA.

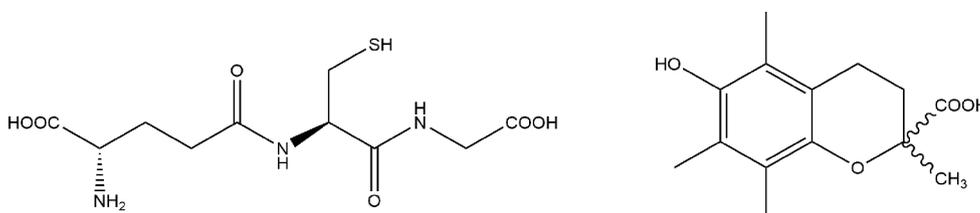


Figure 1. Antioxidants used in this study: GSH (left) and Trolox (right)

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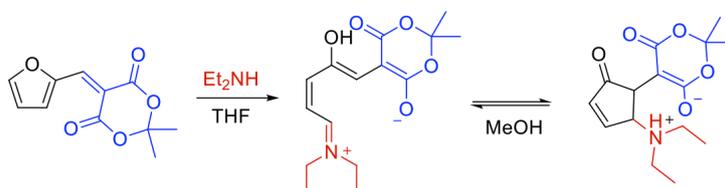
Mechanistic Studies on the Formation of Novel Cyclopentenones from Activated Furans

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Recently the formation of cyclopentenones and their precursor Stenhouse Salts have been subject of intense research.¹ Amino cyclopentenones can be prepared from furfural^{2a} or furyl alcohol^{2b} via formation of Stenhouse-like salts followed by Nazarov type electrocyclization. In 2014 Alaniz and coworkers described the formation of Donor-acceptor Stenhouse Salts (DASA) from furfural derivatives containing a Meldrum's or Barbituric acid.³ DASAs showed remarkable photophysical characteristics such as intense color and possibility of reversible photoisomerization to the corresponding colorless cyclopentenones. Several applications of DASAs have been later developed such as colorimetric detection of amines and nerve agents or adsorption in photoresponsive polymers.¹ Feringa and coworkers have contributed for the elucidation of the photoisomerization process of DASA^{4a,b} and have recently developed an orthogonal photoswitching system consisting of a DASA and an azobenzene^{4c}. Driven by this work we have developed a new generation of Meldrum's acid activated furans and have studied the mechanism for the formation of new cyclopentenones by in situ ¹H-NMR kinetic studies, mass spectroscopy and DFT calculations. The synthetic utility of the novel cyclopentenones have been demonstrated by several model reactions.⁵

DASA formation and corresponding electrocyclization:



Acknowledgements: We thank the Fundação para a Ciência e Tecnologia (SFRH/BPD/100433/2014, PTDC/QEQ-QOR/3644/2014, COMPETE Programme (SAICTPAC/0019/2015) and European Research Area Net-work; ERANet LAC (ref. ELAC2014/BEE-0341) for financial support.

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5. Manuscript under revision

Photocatalytic Synthesis of Benzaldehyde Derivatives

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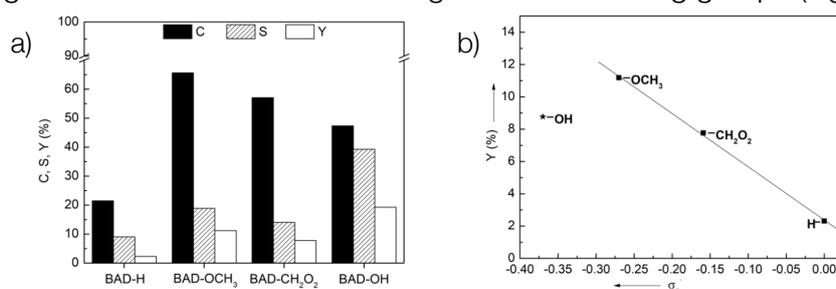
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Aromatic aldehydes are a class of chemicals widely applied as flavoring and fragrance agents in pharmaceutical and food industries. Their industrial production normally involves harsh conditions of pressure and temperature, the use of hazard solvents and catalysis to reach feasible yields. By operating under mild conditions of temperature and pressure and using water as solvent, photocatalytic synthesis appears as a promising alternative to the conventional synthetic routes.^{1,2}

In the present work, composite materials of zinc oxide (ZnO) and carbon nanofibers (CNF) were synthesized and used as photocatalysts for the synthesis of benzaldehyde (BAD-H) and its derivatives, namely 4-methoxybenzaldehyde (BAD-OCH₃), 3,4-methylenedioxybenzaldehyde (BAD-CH₂O₂) and 4-hydroxy-3-methoxybenzaldehyde (BAD-OH), from the respective alcohols in aqueous medium under UV-LED irradiation ($\lambda_{exc}=370\text{nm}$). The effect of substituent groups of benzyl alcohols was studied, using bare ZnO and the composite material CNF/ZnO. In general, the introduction of CNF induces a positive effect in the efficiency of the photocatalytic process, the carbon phase acting as electron scavenger of ZnO conduction band electrons. It was also observed that the nature of the substituent groups influences the selectivity of the photocatalytic reaction, being higher for the molecules containing electron-donating groups (Figure 1).



Acknowledgments: This work is a result of project "AIProcMat@N2020 - Advanced Industrial Processes and Materials for a Sustainable Northern Region of Portugal 2020" (NORTE-01-0145- FEDER-000006), supported by NORTE 2020, under the Portugal 2020 Partnership Agreement, through the European Regional Development Fund (ERDF) and of Project POCI-01-0145-FEDER-006984 - Associate Laboratory LSRE-LCM funded by ERDF through COMPETE2020 - Programa Operacional Competitividade e Internacionalização (POCI) - and by national funds through FCT - Fundação para a Ciência e a Tecnologia. C.G.S. acknowledge the FCT Investigator Programme (IF/00514/2014) with financing from the European Social Fund (ESF) and the Human Potential Operational Programme. R.A.F. acknowledges the PhD fellowship funded by Project NORTE-08-5369-FSE-000028, supported by Norte Portugal Regional Operational Programme (NORTE 2020), under the PORTUGAL 2020 Partnership Agreement, through the ESF.

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Rational Selection of the Components of an Ionic Liquid Solvent to Control The Reaction Outcome of Some Organic Processes

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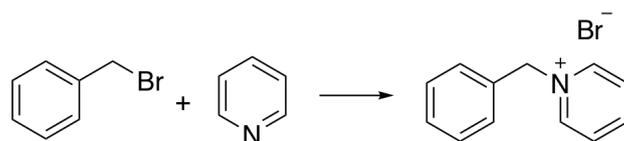
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When used as solvents, ionic liquids have the ability to affect the outcome of a range of organic processes.¹ These effects include altered reaction rates, different selectivity of products, and biasing of reaction pathways.^{1,2} Through systematic analysis of the kinetics of reactions with different mechanisms in a variety of ionic liquid solvents, the effects of ionic liquid solvents are being better understood.³

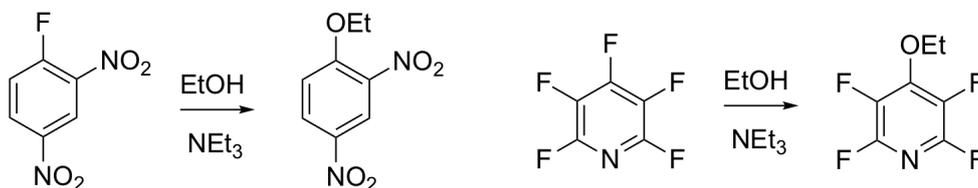
There are several key questions that remain to be answered.

- Can the solvent effects observed for ionic liquids be exploited?
- Which ionic liquid is the 'best' solvent for a given reaction type?
- Is kinetic analysis the only way to determine the solvent effects?

These questions will be addressed with reference to three different reactions; a bimolecular nucleophilic substitution (S_N2) reaction⁴ (Scheme 1) and two nucleophilic aromatic substitution (S_NAr) reactions^{5,6} (Scheme 2).



Scheme 2. The nucleophilic aromatic substitution reactions between 1-fluoro-2,4-dinitrobenzene and ethanol and 2,3,4,5,6-pentafluoropyridine and ethanol.



Scheme 1. The bimolecular nucleophilic substitution reaction between benzyl bromide and pyridine.

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A Radical Twist In The Mechanism Of Lithium-Halogen Exchange

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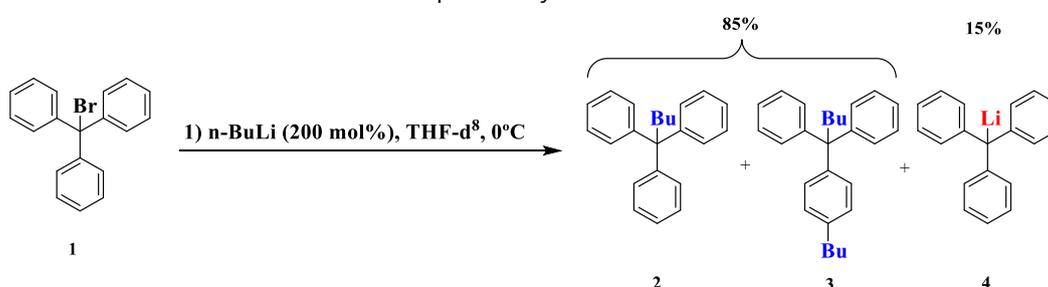
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Organolithium compounds are widely used in organic synthesis¹ as they are good nucleophiles and strong bases and, no less importantly, simple organolithiums are commercially available and inexpensive. As organolithium reagents play a central role in organic chemistry, their reactivity, structure, and stability have been the subject of numerous studies.²

Our group has developed a system based on UV/Vis spectroscopy, which allows kinetic measurements at -80 °C under argon. Using this technique, we have focused our interest on the reactivity of n-butyllithium (n-BuLi), the most used organolithium reagent in organic synthesis, and more specifically, on the deprotonation of compounds with and without donor atoms, as benzylethers, TPM (triphenylmethane) or DPM (diphenylmethane).³

Now we want to report the results obtained by studying the lithium-halogen exchange on halogenated triphenylmethanes. Kinetic studies and reaction products analysis with different organolithium reagents, together with EPR experiments, strongly suggest the formation of a trityl radical intermediate in the reaction pathway.



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Synthesis of Amino Acid Ionic Liquids (Aails) and their Effect in the Reactivity of Thiol-Michael Addition Reaction

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The Michael addition reaction is one of more versatile tool for the formation of C-C (carbon-Michael), C-S (thiol-Michael) bonds and others, which leads to the synthesis of compounds with diverse applications.¹ This reaction is usually performed in conventional organic solvents (COS), which are not compatible with the environment. In this context, ionic liquids (**ILs**) have emerged as a “green” alternative reaction media to COS in many reactions. More recently, amino acid **ILs** (**AAILs**) have acquired a high importance. In addition, some of them are called as “task-specific **ILs**” (**TSILs**) with a capacity to be considered not only as reaction medium but also as catalyst.² Considering the latter, in this work were synthesized 6 amino acid ionic liquids (**AAILs**) containing 1-butyl-3-methylimidazolium as cation and amino acid anions Bmim[AA], were synthesized according to reported previously by Ohno et al.³ and assessed as **TSILs** in thiol-Michael addition reaction. Where AA: L-proline, L-alanine, L-serine, L-histidine, L-phenylalanine and L-cysteine.

Regarding to this, we also present a kinetic study of the reaction between cysteine and the Michael acceptor trans- β -nitrostyrene (S1, Fig. A) in H₂O using different **AAILs** as catalyst.

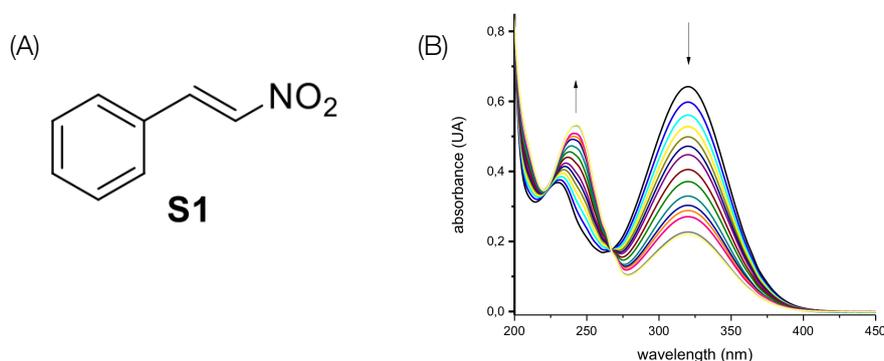


Figure. (A) Structure of the Michael acceptor. (B) Time-dependent absorbance spectra of S1 (50 μ M) upon addition of cysteine (500 μ M) in H₂O with [Bmim][His] as catalyst at 25 °C.

The Michael addition reactions between cysteine and S1 were performed spectrophotometrically by following the disappearance of S1 (λ_{max} 320 nm, at 25 °C, as shown in Fig. B). Under amine excess, pseudo-first-order rate coefficients (k_{obsd}) were found. Results show that the highest effect was observed by [Bmim][His] as catalyst of the studied reactions.

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Synthesis and Characterization of Pillar[5]Arene Functionalized with Hydroxy-L-proline. Searching an Enantioselective Organocatalyst

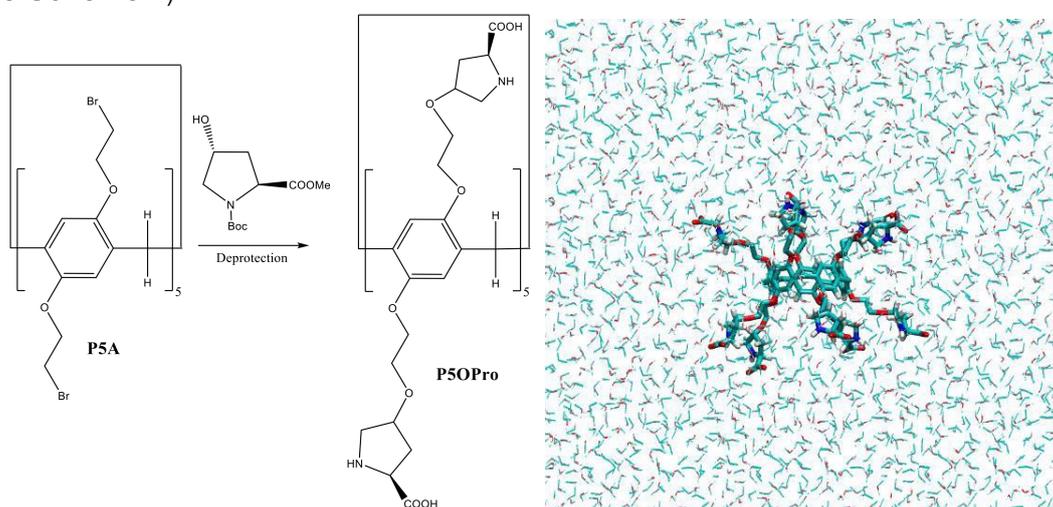
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Supramolecular chemistry focuses on the development of host-guest systems, in which a host molecule can recognize and bind a certain guest molecule. Recent developments show that the application of supramolecular strategies in homogeneous catalysis can be extremely powerful.¹ Pillar[5]arene (P5A) is a macrocyclic compound that can be functionalized with different chemical groups. In this work, we synthesize an Amino Acid-functionalized Pillararene (P5OPro) from the reaction of Boc-trans-4-Hydroxy-L-proline methyl ester and P5A (see Scheme 1).



Scheme 1. (Left) Reaction to obtain P5OPro. (Right) MD simulation of P5OPro in water.

The P5OPro is evaluated as organocatalyst by the reaction between cyclohexanone and benzaldehyde.² The host-guest complexes are characterized by NMR studies and Molecular Dynamics (MD) simulations. The asymmetric products of the aldol reactions are characterized by Chiral HPLC analysis and optical rotation studies.³

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Experimental and Theoretical Evidence of Intramolecular Bifunctional Catalysis in Amide Cleavage

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Although amide hydrolysis are usually slow and inefficient reactions, which is translated into the high stability of peptide bonds, amides that are positioned between two carboxyl groups - where one of which is ionized - are far more susceptible to hydrolysis.^{1,2} In the present work we have investigated the pH dependent hydrolysis of 2-(2-carboxybenzamido)benzoic acid (**2CPA**). Figure 1 (left) shows the bell-shaped pH-rate profile for conversion of **2CPA** to anthranilic acid (**AA**) and phthalic anhydride (**PA**), monitored by UV-spectrophotometry at 25 °C. Benzamide, for example, has no observable hydrolysis at pH 5.0³ whereas **2CPA** observed $t_{1/2}$ is about 100 minutes at pH 5.0, and only 7 min at pH 3.5. DFT calculations indicate that the reaction involves nucleophilic/general acid catalysis via direct displacement of amine by carboxylate without discrete intermediates, and minimum perturbation of the carbonyl bond in transition state (Figure 1, right). The high reactivity is a result of both appropriate orientation and interatomic distances shorter than water diameter. The difference between the experimental and theoretical free energy of activation is only 1.5 kcal.mol⁻¹, supporting our hypothesis.

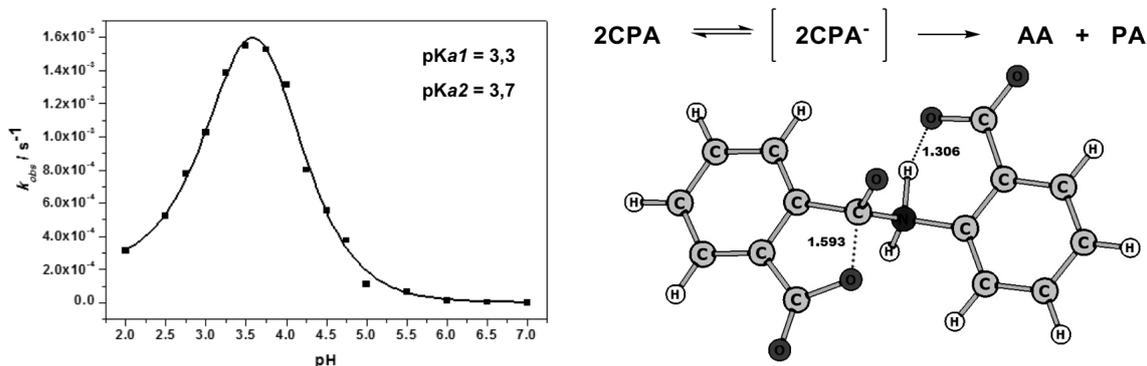


Figure 1. pH rate profile for decomposition of 2CPA at 25°C (left) and SMD/M06/31+G(d,p) transition state (right).

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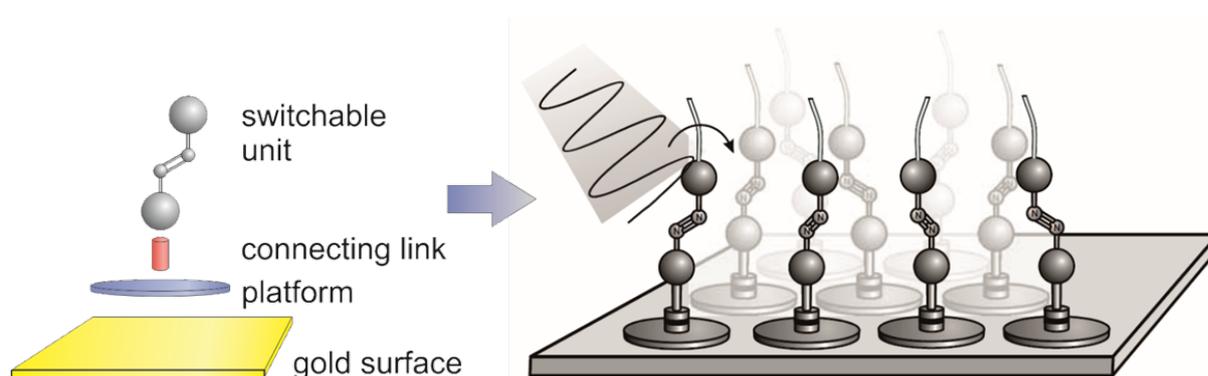
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Relaxation Time Measurements of Azo Functionalized TATA Platforms

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The azo TATA (triazatriangulenium) platform concept can be used for the functionalization of surfaces and is supposed to reach an oriented transport of particles or molecules. For a sterically unhindered light-induced switching process between trans and cis isomers the azobenzenes need a certain distance to each other. For this requirement the azobenzenes are functionalized over a spacer on triazatrianguleniumions, which serves as platforms. Certainly the azobenzenes have different thermal relaxation times in solution and on gold surfaces from the cis back to the trans configuration. While the relaxation times in solution are in the range of hours, on gold surfaces the back relaxation happens in the seconds scale. With different spacer units it is possible to enhance the thermal relaxation times of the azo unit especially on gold surfaces.¹



Scheme 1. Shown is a modular system of the azo TATA platform concept. The size of the platform determines the distance between the functional molecules on gold surfaces and the linker connect the switchable unit with the platform. The azo unit can be switched with different wavelength between the cis and trans isomer.²

Reference

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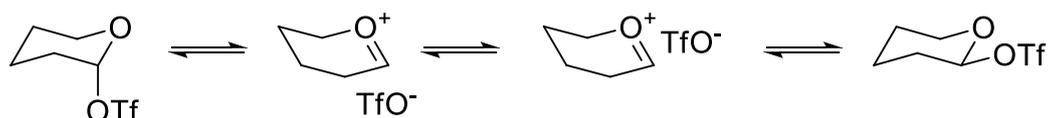
Computational Study of the Mechanism of Glycosylation of L-Idose Derivatives

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Glycosylation is one of the most fundamentally important transformations in the field of carbohydrate chemistry, but many aspects of glycosylation reaction mechanisms remain poorly understood. Recent experimental results on glycosylations with L-ido-configured donors bearing participating protecting groups have revealed unexpected stereochemical outcomes that offer a novel means to probe the reaction mechanism.¹

This project seeks to investigate the glycosylation reaction mechanism involving L-ldose derivatives. Building upon recently published computational and NMR studies,² which have suggested an important influence of counterions on the stability of the putative oxocarbenium ion intermediates, we have performed density functional theory calculations to explore the structures and stabilities of possible reactive intermediates and the transition states for their interconversions.



This work represents our efforts to develop, for the first time, a unified approach to the theoretical modelling of a glycosylation reaction, which considers all aspects of the mechanism including the role of the leaving group, activating agent, counterion, solvent, and conformational equilibria. Correlations with experimentally observed stereoselectivities offer a valuable test of the validity of possible glycosylation pathways.

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A Mechanistic Insight into CNT-Catalyzed Oxidative Dehydrogenation of Ethylbenzene to Styrene. A DFT Computational Study

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The direct hydrogenation of ethylbenzene to styrene can be considered one of the most important industrial process in petroleum industry. The main problems encountered in ethylbenzene direct dehydrogenation (and, in general, in alkanes dehydrogenation) are the high endothermicity of the reaction, the excess of steam, which is very energy consuming, and a slight irreversible deactivation of the catalyst.¹ Another interesting possibility is the oxidative dehydrogenation (ODH) of ethylbenzene. Nanostructured carbon-material were demonstrated to be valid alternatives to metal oxides and phosphates catalysts for ODH reaction.^{2,3} The role of surface chemistry on the catalytic properties of carbon nanomaterials and, in particular, of carbon nanotubes, has long been recognized and there is now a general consensus that the oxygen functionalities generated during the synthetic process (carbonyl-, carboxyl-, quinone- and phenolic-type groups often localized on the edge and highly stable epoxide-like structures) are the active catalytic sites. Su and co-workers,^{4,5} using a novel in situ titration process found evidence that the active sites are identical on various nanocarbon catalysts (including graphene oxides, CNTs and OLCs) and that ketonic carbonyl groups are active sites for alkane ODH reactions. Since a complete analysis of the reaction pathway of the oxidative dehydrogenation of ethylbenzene catalysed by CNTs is still lacking, we carried out a computational investigation using two different model-systems to emulate the catalytic oxygen-containing groups on CNT (oxidized CNT): two adjacent epoxy groups and a quinone functionality on the edge of the tube. Other possible functionalities due to the chemisorption of an oxygen molecule on CNT were discarded since they correspond to less stable structures. Our computations indicate that either epoxide groups or a quinone groups can effectively catalyze the ODH reaction of ethylbenzene. The activation energies required in the two cases are very similar value and in both cases the reaction proceeds via a two steps corresponding to the transfer of the two hydrogen atoms from the substrate to the oxygen atoms on the tube.

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Mechanism of the Annulation of 4-Ethynylanisole with Mixed Phosphonium-Iodonium Ylide

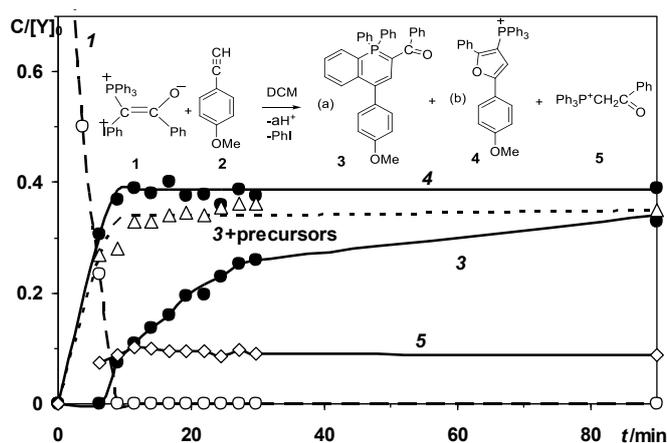
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The main challenges in the investigation of the interaction of mixed phosphonium-iodonium ylides (1) with acetylenes (2) occurring only in microheterogeneous solutions in DCM are concerned with mechanisms of the heterocyclic products (3) and (4) formation (Scheme). The reaction kinetics for the mixture of ylide 1 and 4-ethynylanisole (2) was investigated by ¹H and ³¹P NMR, UV-vis and EPR spectroscopy. Heterocyclic products 3 and 4 for this system are formed with comparable yields (a ≈ b) that makes this mixture convenient for investigation. The ³¹P NMR data of the reaction kinetics shows that 3 and 4 form by different reaction paths. The observed negative CIDNP effect for 4 implies that 4 is formed in the primary radical pair generated via ET from 2 to 1 and this is the only path for its formation. As for 3, its formation occurs with participation of three precursors (Figure), with a small amount being



formed from a radical pair (negative CIDNP effect).

At least one of these precursors is the long-living radical monitored by EPR, with the structure of the radical involving the fragments of 1 without PhI and 2.¹ Large positive CIDNP effect is observed for 5 until 1 is not consumed, although the final yield of salt 5 is lower than 10%. The feasible mechanisms of the products formation will be presented and discussed.

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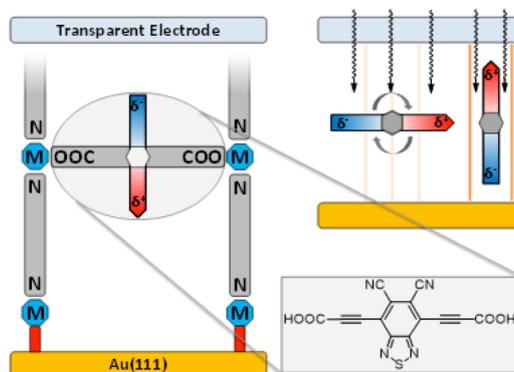
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Dipolar Molecular Rotors in Surface-Anchored Metal Organic Frameworks

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The functionalization of surfaces with molecular machines is highly interesting due to the vast field of applications. Transferring the function of individual molecules to a macroscopic scale by bringing a multitude of them to act collectively is essential for materializing new technologies. For this purpose, dipolar rotors can be put into a supra molecular structure to switch the light transmission of a material by changing their orientation. A high three-dimensional order can be achieved by using rotors as linkers in surface-anchored metal organic frameworks (SURMOFs).¹⁻³ Crafted SURMOF thin films allow the alignment of the dipolar rotors in an external electric field.⁴ Making use of this behaviour, the transmission of light can be modulated with the application of the field and be investigated towards its uses in optical technologies. In this project, different organic linker molecules with permanent dipole moments are synthesized and used in SURMOF fabrication. Dielectric loss spectroscopy of the SURMOF thin films gives information about the dipole-dipole interaction within the layers and the alignment of rotors along the applied electric field.⁵ Devices are being constructed with a transparent top electrode for electric field application. Information gathered from the behaviour of first generation linker molecules will refine the molecule designs for the next generation so that the optical and electronic properties of the material can be tuned as desired.



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The Role of Perchlorate Anion on Dimerization of a Macroacyclic Binuclear Cu(II) Complex: Comparison with a Mononuclear Ni(II) Macrocylic Complex

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New macroacyclic Cu(II) and macrocylic Ni(II) complexes, $[\text{Cu}_2\text{L}^1(\text{ClO}_4)_2]_2$ (1) and $[\text{NiClL}^2]\text{ClO}_4$ (2), respectively, have been synthesized (L = Schiff base). Single crystal X-ray structure analysis of 1 showed that the complex is tetranuclear, with two binuclear Cu(II) units connected through coordination of deprotonated OH groups of one of the propanol amine arms of each unit to the other one. In the structure of each binuclear fragment, none of the donor atoms of the potentially heptadentate (N_2O_5) ligand remained uncoordinated, and one oxygen atom is bridged between the two Cu(II) ions. In addition, the crystal structure analysis shows that two perchlorate ions are coordinated to the Cu(II) metal centers. DFT studies show that the coordinated perchlorate anions have the key role in the dimerization of the binuclear Cu(II) species that give rise to complex 1. X-ray structure analysis of 2 shows that it is a macrocylic complex where all nitrogen and oxygen atoms of the potentially pentadentate (N_2O_3) ligand are coordinated to the Ni(II) central ion. In addition to the macrocylic Schiff base ligand, a chloride ion is also coordinated to the Ni(II) ion.

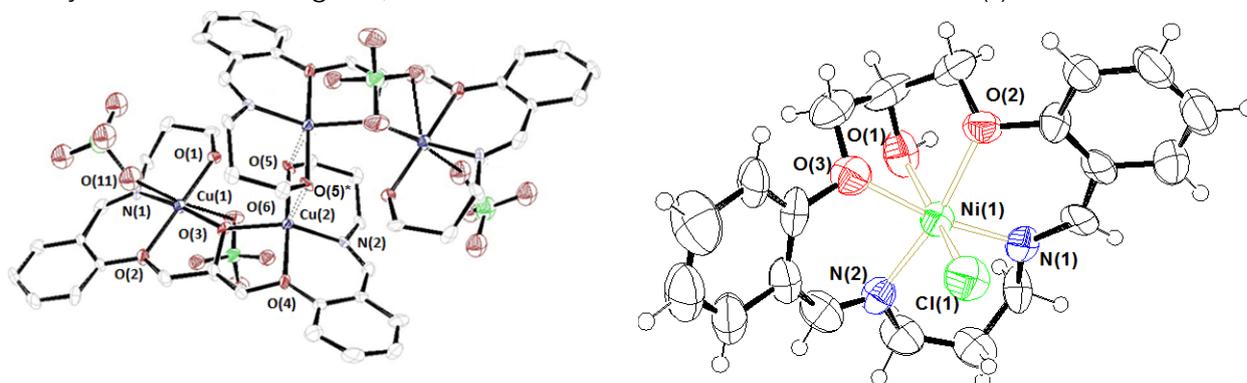


Fig. X-ray crystal structures (ORTEP diagrams) of complexes 1 (left; hydrogen atoms were not shown for better visualization of the structure) and 2 (right).

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Theoretical Design and Spectral Investigations of Tautomeric Rotary Switches

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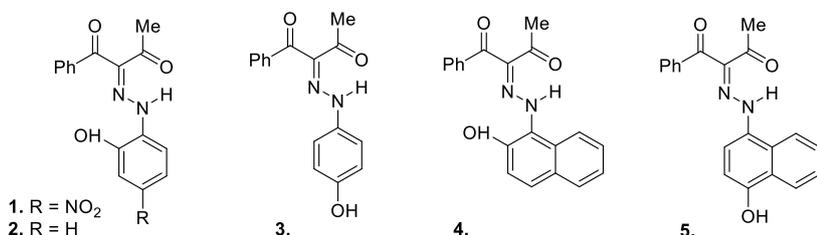
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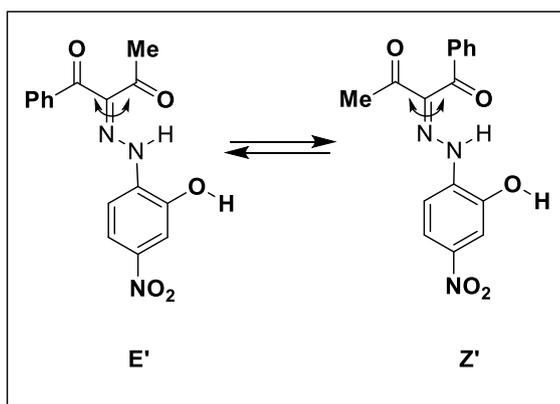
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The rotary switches are one of the possible promising platforms for development of molecular switching systems. Exhibiting well defined structural parts (rotor-axis-stator) they can be potentially used as molecular motors and proton cranes. The rotation action is based on intramolecular and catalyzed, proton transfer.

The rotary switches exhibit three major weaknesses, which have to be solved in order to achieve real applicability: a) inability to provide conditions for pure isomeric forms in solution; b) slow rotation of the rotor; and c) uncontrollable rotation of the stator.



Compound 1 belongs to a series of arylhydrazones of β -diketones, where an additional tautomeric functionality is added in the stator. We have studied, theoretically and experimentally (UV-VIS, NMR and X-ray), the effect of the additional OH group on ortho position in the stator, because such structural modification could provide condition to limit its free rotation. It has been found that the studied compound exists as two isomers of a single tautomer in different solvents¹. In proton acceptor solvents spontaneous deprotonation has observed at low concentrations.



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Use of Photolabile Ru(II) Complexes for Supramolecular Release

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The stimulation of supramolecular assemblies by irradiation with light is an attractive tool to achieve the spatiotemporally and remotely controlled release of functional guests.¹ This has been shown for different types of hosts,^{2,3} including cucurbit[n]urils (CBn).⁴ Several ways of using UV-light-triggered photochemical reactions that change the equilibrium conditions of a supramolecular cucurbituril complex were recently devised by our group.⁵⁻⁷ Herein we discuss the use of photolabile Ru(II) complexes to achieve the same objective by irradiation with visible light, which should bear various advantages in the context of potential bio-relevant applications.

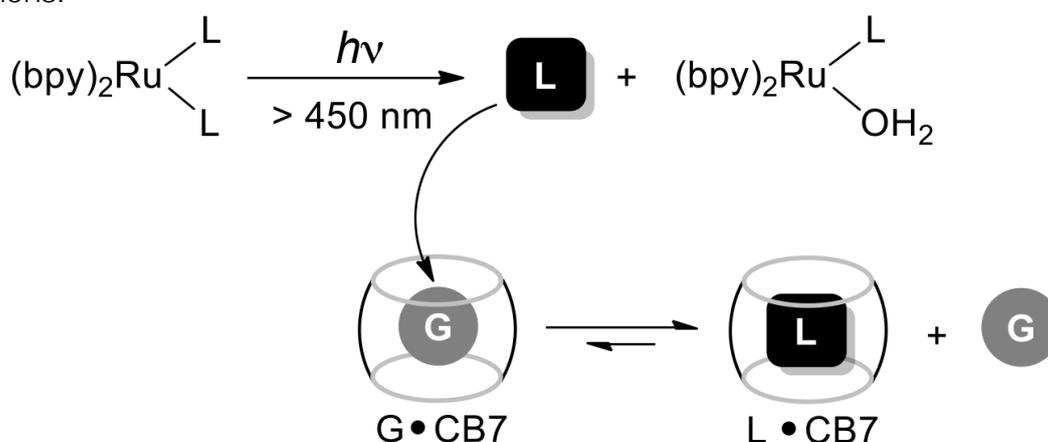


Figure 1. Principle of light-induced guest release by using Ru(II) complexes as triggers.

Acknowledgement. The work was supported by the Spanish MINECO (CTQ2017-89832-P) and the ERDF.

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A Brief Survey on Diffusion Wave Spectroscopy in Soft Matter Systems

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The development of new colloidal systems is of high demand in a plethora of fields, such as dairy and food industry, medicine, cosmetic, pharmaceutical sciences, textile, agriculture and construction engineering. However, the composition of these systems is often complex and therefore, to fine-tune their final properties and develop improved formulations, it is necessary to understand in detail their different physicochemical properties. For that, a breath of experimental methods has been traditionally employed such as rheology, microscopy, light scattering and ultrasonics¹. However, most of these experimental methods are invasive, resulting in a certain degree of disruption to the sample¹. To fulfill the need of a non-invasive method, a relatively novel optical technique started being employed, Diffusing-wave Spectroscopy (DWS). This technique is based on the assumption that at sufficiently turbid media the transport of light can be treated as a diffusion process, enabling to extract information about the micro-rheology of the samples². Recently, LS Instruments, a company from Switzerland specialized in the development of light scattering technologies, developed the Rheolab, the first commercialized equipment for real-time measurements of DWS³. Over the past few years our research team have dedicated work on the design and characterization of cellulose-based colloidal systems, which resulted in several publications with high scientific impact in this field^{4,5}. In this work we will expose the potentials of the DWS technique by revealing its contribution on the characterization of cellulose-based systems. Importantly, DWS was also complemented with the mechanical rheology and a good concordance was obtained between the macro- and microrheology analysis.

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Synthesis and Anion Recognition by Dinitrophenylurea-Dihomooxalix[4]arene Receptor

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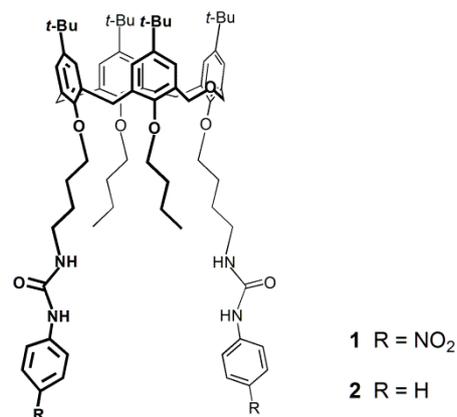
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Over the last decade anion receptors based on calixarenes, as well as on other macrocyclic compounds, have been more investigated due to the recognized importance of anions in biological and environmental areas.¹ Organic hosts with hydrogen bond donor groups have the ability to recognize anions with different geometries. Urea and thiourea moieties are able to provide such strong and directional hydrogen bonds, and have been introduced into the calixarene scaffolds.

Following our previous studies on cation binding properties of dihomooxalix[4]arenes (calix[4]arene analogues in which one CH₂ bridge is replaced by one CH₂OCH₂ group),² we have recently extended our research into the study of anion complexation.^{3,4}

In the present work, we report the synthesis and the NMR conformational analysis of a new dihomooxalix[4]arene bearing phenylurea moieties substituted with an electro-withdrawing group (R = NO₂) at the lower rim via a butyl spacer. 1D and 2D NMR experiments carried out in CDCl₃ at r.t. indicated the cone conformation for receptor 1. Its binding properties towards some relevant anions with different geometries were assessed by proton NMR and UV-Vis absorption titrations. The results are compared to those obtained with the closely related phenylurea 2 receptor.



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Synthesis and Spectroscopic Characterization of 4-(Diethylamino)Salicylaldehyde Bearing at Coumarin Derivative. Effect of Cucurbit[7]Uril Encapsulation on its Spectral Properties

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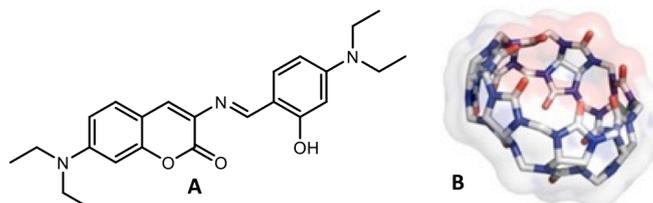
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Coumarins are interesting compounds by their biological and spectroscopic properties. In this line, we have recently demonstrated that the incorporation of a host as β -cyclodextrin (β -CD) or cucurbit[7]uril (CB7), can induce changes in the UV-Vis or fluorescence spectra of the coumarin containing dyes, as well as in their tautomeric forms. For example, ethyl acetoacetate bearing 7-hydroxy coumarin by encapsulation of β -CD forms an inclusion complex with the enol tautomer of the dicarbonyl group attached at coumarin in position 3. On the other hand, we demonstrated that the CB7 is able to stabilize the keto tautomeric form of 7-N,N-diethylamino coumarin derivatives bearing ethyl acetoacetate and methyl β -ketodithioester, contrary to the observed for β -CD.

Following this line, we are interested in assess the effect that could have the encapsulation by the host, cucurbit[7]uril (CB7) on the spectroscopic properties and possible changes in the structure of the (E)-7-(diethylamino)-3-((4-(diethylamino)-2-hydroxybenzylidene)amino)-2H-chromen-2-one (DSCou) see Scheme. Results show that: (i) DSCou derivative was synthesized in moderate yield (45%) and fully characterized by ¹H NMR, ¹³C NMR, IR, HRMS, UV-Vis and fluorescence, (ii) this coumarin derivative in aqueous media exhibited a characteristic absorption band at 439 nm, which in the presence of an excess of CB7 shift at 528 nm. This bathochromic shift evidence the encapsulation of DSCou by CB7 and (iii) flash photolysis, mass spectrometry and modeling molecular studies allow to establish the stoichiometry 2:1 for the host-guest complex (DSCou@CB7).



Scheme. Structure of dye used in this study: (A) (E)-7-(diethylamino)-3-((4-(diethylamino)-2-hydroxybenzylidene)amino)-2H-chromen-2-one (DSCou) and (B) the host CB7.

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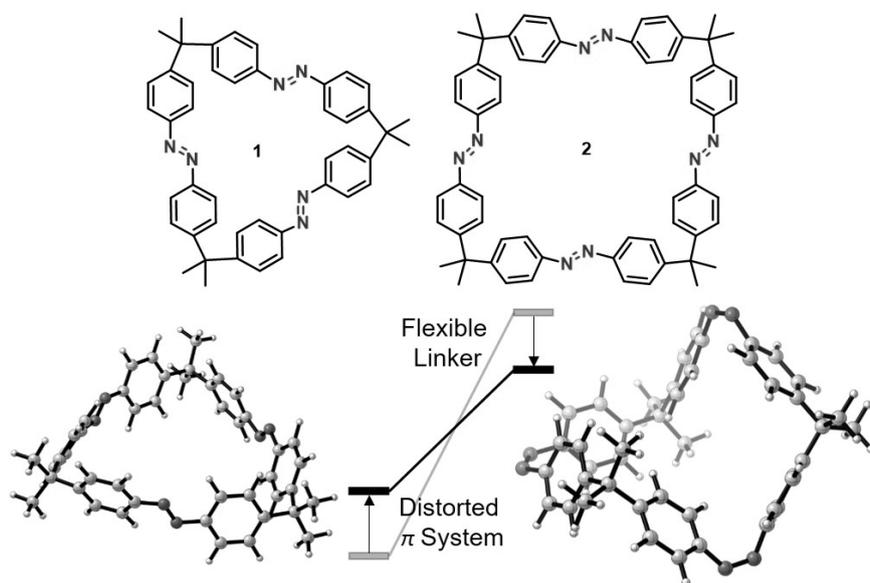
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Tuning the Switching Properties of Macrocyclic Azobenzenes by Ring Strain

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Azobenzenes have gained increasing interest due to their applicability as molecular switches in diverse scientific fields. Macrocyclic azobenzenes exhibit unique isomerization behavior due to the influence of ring strain.¹ We² and others³ have shown that the thermal stability of E and

Z azobenzenes can be reversed when the azobenzene scaffold is arranged in a strained macrocycle. Nevertheless, drastic changes in ring strain during isomerization prevent most azobenzophanes from full isomerization.⁴ To overcome this, we synthesized and investigated macrocyclic azobenzenes 1 and 2 with flexible linkers. Within our study, isomerization experiments showed almost complete and reversible isomerization of tris- and tetraazobenzophane 1 and 2. Moreover, DFT computations and X-ray crystallography revealed that the all-E isomers feature higher ring strain than the corresponding all-Z forms. This knowledge opens new avenues in the design of novel switches for applications especially in supramolecular chemistry, in materials or life sciences.

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Nitric Oxide Release From a Cucurbituril Encapsulated NO-Donor.

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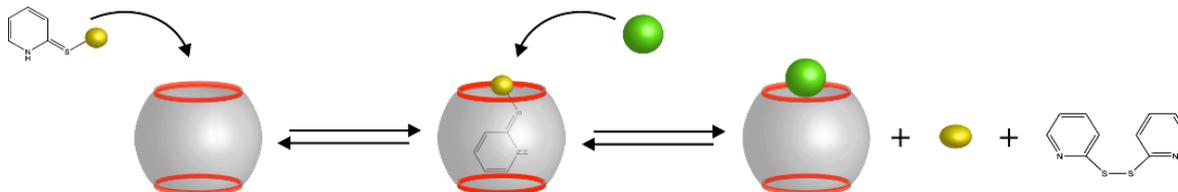
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The importance of nitric oxide¹ (NO) is well known and studied for being an important part in processes of vasodilation and platelet adhesion and aggregation, immune response to infection, wound repair and cancer pathology and biology.

At present, there are deficiencies in the release of nitric oxide under certain medical conditions; therefore, it has been developing potential donating agents² of NO: such as organic nitrates, nitrites, metal complexes with NO, nitrosamines, S-nitrosothiols, among others. These NO donors have shown great antiplatelet, antimicrobial, antitumor and vasodilatory activity. The encapsulation, stabilization and release of NO from these agents has been previously reported.

In this work, we introduce the idea of a NO donor (2-mercaptopyridine) stabilized by a macrocycle (cucurbit[7]uril) thus controlling its decomposition into a disulfide. The complexation into the cucurbit[7]uril cavity results in an increase of the nitrosation equilibrium constant as a consequence of a drastic reduction of the denitrosation rate constant.



Release of nitrosomercaptopyridine because of an external guest addition (tetraethylammonium chloride, TEACl) increases its decomposition rate. It should be noted that nitrosomercaptopyridine decomposition to disulfide results in NO release that can be modulated by external guest addition and quantified by a selective NO electrode.

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Comparison of the Chemical Composition and Biological Activities of Essential Oils Obtained by Classical Steam Distillation (SD), Instant Controlled Pressure Drop (DIC) and Ultrasound Assisted Extraction (UAE) from Myrtle Leaves Growing Spontaneously In Algeria

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In this present study, the essential oils and volatile extract obtained from leaves of *Myrtus communis* L., growing spontaneously in Algeria were extracted by conventional steam distillation (SD) and two innovative processes: Instant Controlled Pressure Drop (DIC) and ultrasound assisted extraction (UAE). The impact of extraction on yields, extraction time, chemical composition, antioxidant and antimicrobial activities were investigated.

The in vitro antioxidant activity of essential oils was determined by 2,2-diphenyl-1-picrylhydrazyl (DPPH) method while the antimicrobial activity against several foodborne pathogens of each extract was examined in vitro assays by the minimal inhibitory concentrations (MIC) using a microdilution broth method. For the three different extracts, the chemical composition was determined by GC-FID and GC / MS.

The yield of essential oil (EO) and time extraction obtained using SD, UAE and DIC methods were 0.43g EO/100 g dm for 240 min, 0.43g EO/100 g dm for 30 min and 0.56 g EO/100 g dm for 2 min respectively. The most predominated compounds identified in DIC extract are α -pinene (23.33 %), eucalyptol (21.76%), eugenol (4.06%), methyleugenol (5.38 %), caryophyllene oxide (4.21%) and limonene(2.20%). The main identified components in SD are α -pinene (36.94%), followed by eucalyptol (19.08%), eugenol (3.73%), methyl eugenol (3.71%), α -terpineol (3.14%), and limonene (2.37%). For ultrasound assisted extraction (UAE), the chemical composition was dominated by α -pinene and eucalyptol with 36.05 and 19.10% respectively. These compounds were escorted by eugenol (4.13%), methyl eugenol (4.02%), limonene (3.55%), geranyl acetate (3.18%), β -linalool (2.92%), and α -terpineol (2.33%).

All EOs reveal a moderate antioxidant activity but exhibit a good antimicrobial activity against the various tested pathological strains.

Analysis of the microstructure has also been undertaken on solid residue of myrtle leaves by Scanning Electronic Microscopy (SEM). They showed significant modifications of the cellular structure of DIC and AUE in comparison with conventional SD residual solid.

The obtained results have shown the remarkable differences in the composition of the three OEs which are richer in oxygenated compounds in the case of DIC.

Keywords: *Myrtus communis* L., Essential Oils, Extraction, Steam Distillation, Ultrasound Assisted Extraction , Instant Controlled Pressure Drop (DIC), Antioxidant and Antimicrobial Activities.

Self-Assembly of Aromatic Donor-Acceptor Systems by Guanidine-Carboxylate Binding

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Self-assembly of aromatic donor-acceptor (D-A) pairs was achieved via guanidine-carboxylate hydrogen bonding (Figure 1). Supramolecular assemblies which were obtained via guanidine-carboxylate salt bridges were used for a study of fundamental physico-chemical properties of supramolecular systems built by non-covalent interactions. They are artificial systems which serve as models for study of photo-induced electron transfer processes through guanidine-carboxylate bonds in more complex natural photosynthetic systems.¹ As model electron donor systems, 1-pyrenylguanidine and structurally more complex 5-(4-phenyl guanidyl)-10,15,20- triphenylporphyrin, were synthesized. In addition to multistep synthetic procedure in which amines are converted to guanidines in low yields, more efficient N,N'-di-Boc-1H-pyrazole-1- carboxamide guanylation reagent was employed giving almost quantitative yield. Synthesis of aromatic guanidinium chromophores was optimized by using environmentally more friendly high-speed vibration milling technique.² Guanylation of amines and N-Boc deprotection were efficiently carried out in ball mill in solvent-free conditions.³ Photophysical properties of guanidinium chromophores and self-assembly to aromatic D-A systems with 1,3-dinitrobenzoic acid as an acceptor component were studied spectroscopically. Molecular modelling (DFT B3LYP/6-31G* method) was used in design of D-A systems and study of their molecular and electronic structure.

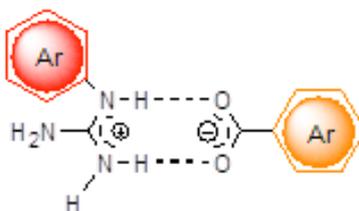


Figure 1.

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Encryption of Chemical Information in a Supramolecular Assembly

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Recently the use of molecular and supramolecular systems for the purpose of the encryption, secure communication, and authentication of data has received increasing interest. Several strategies that include multichromophoric sensor platforms or supramolecular assemblies have been developed to encrypt data.¹⁻³ The coupling of supramolecular equilibria in intricate multi-component systems is a viable path to arrive at stimuli-responsive scenarios, where the response dependence on the inputs is non-linear and therefore back-engineering is made difficult.

In this contribution we draw on the rich and highly versatile chemistry of cucurbituril complexes in combination with guests that show differentiated optical fingerprints (fluorescence and/or UV/vis absorption). The supramolecular equilibria of mixtures of various cucurbituril homologues (CB7 and CB8) and guests that compete with each other in dependence on the equilibrium conditions are used to arrive at non-linear optical responses and the setup of a versatile system for data encryption and as security ink.

Acknowledgement. The work was supported by the Junta de Andalucía (P12-FQM-2140).

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Electrochromic Properties of Metallo-Supramolecular Polyelectrolytes (Mepes)

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The structure and properties of metallo-supramolecular polyelectrolytes (MEPEs) self-assembled from rigid ditopic terpyridine and pyrimidine ligands and metal ions like Fe(II) and Co(II) are presented. Viscosity and static light scattering measurements reveal that the molar masses of these MEPEs are in the range of 10^8 g/mol under the current experimental conditions. Thin films of high optical quality are fabricated by dip coating on transparent conducting indium tin oxide (ITO) glass substrate. Optical, electrochemical and electrochromic properties of the obtained MEPEs are presented. Green to red and blue to colorless electrochromism is observed. The results show that the electrochromic properties are affected by the ligand structure and the metal ions. Generally, Fe-MEPEs show a reversible redox behavior of the FeII/FeIII couple and display an excellent redox cycle stability under switching conditions.

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How Does Cholesterol Affect the Fluidity of Model Lipid Bilayers at the Molecular Level?

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Cholesterol (Chol) constitutes from 30 to 50% of the lipid mass in plasma cell membranes and modulates physical-chemical properties of lipid bilayers, such as increasing the thickness of the hydrophobic region; change the lipids phase transition temperatures; ordering of acyl chain region and decreasing the area/volume ratio, as well as polarity, fluidity and permeability.¹⁻³ Model lipid bilayers containing 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), egg-sphingomyelin (egg-SM) and Chol are usually used to partially mimic the lipid component of plasma cell membranes, since these are the most abundant phospholipids in biological membranes.² The stable lyotropic phases resulting from the interaction between lipids, at defined temperature and molar proportions of Chol are represented in thermotropic phase diagrams, which can be found in literature.⁴ However, these phase diagrams are not completely established.⁵ The aim of this study is to clarify how addition of Chol affects the fluidity of lipid bilayers at molecular level, since it is of utmost importance to evaluate physicochemical properties that modulate the structure, dynamics and organization of biological membranes.

To provide a proper experimental conditions that fulfilled the sensitivity and accuracy of fluorescence spectroscopy, we used model lipid multibilayers consisting of pure 1,2-dimyristoyl-sn-glycero-3-phosphorylcholine (DMPC) to settle the mandatory experimental conditions and to determine the effect of the addition of cholesterol, we used model binary mixtures consisting of POPC/Chol and egg-SM/Chol. The fluidity of lipids was studied by steady-state fluorescence anisotropy, using 1,6-diphenyl-1,3,5-hexatriene (DPH) as fluorescent probe. The spectra were normalized for the absorption at the excitation wavelength and corrected for the fluorescence intensity and quantum yield at the emission wavelength. In order to evaluate the DPH anisotropy dependency upon temperature and the addition of certain molar proportions of Chol, the results were analyzed by quantitative approaches as linearization of exponential dependence on temperature and first derivative of sigmoidal variation curve, applied to unsaturated and saturated phospholipids, respectively. Our results suggest that the fluorescence technique, the fluorescent probe and the quantitative approaches for the analysis are utmost suitable to the aim of this work, since it is possible to determine the exact transition temperature of DMPC. Furthermore, this approach allows us to identify specific phases of mixed lipid bilayers which agree with literature.

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New Double Functionalizable *Trans*-Cyclooctenes for Enhanced Spatial and Temporal Resolution Study of Biological Systems

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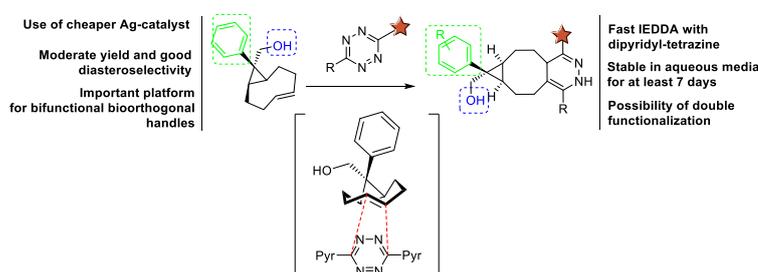
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Bioorthogonal chemical reactions are a thriving area of chemical research in recent years as an unprecedented selective technique for probing and spatial and temporal controlling biomolecule functions in vitro and in living systems^{1,2}

Strained molecules play lead roles in one of major class of bioorthogonal cycloadditions: Diels–Alder ligations. *Trans*-cyclooctene (TCO) reacts efficiently with electron-deficient tetrazines, being highly accelerated in aqueous solution ($2000 \text{ M}^{-1} \text{ s}^{-1}$ in 9:1 MeOH/water) due to the hydrophobic effect.³ By later fusing a *cis*-cyclopropane ring onto the cyclooctene moiety, the bicyclic system was sterically forced into a “half-chair” conformation increasing its reactivity 19-fold⁴ and establishing TCO -derivates as the gold bioorthogonal tool for in vivo radiolabelling and click-to-release therapy.⁵ Despite the incredible kinetics, problems still remain as the scaffold is highly sensitive to modification, prone to degradation via isomerization and cyclopropane ring opening and so far only tolerates the appendage of one payload.

We envisioned a cheap silver-catalysed method to allow double functionalization of TCO scaffold and studied its impact to minimize loss of reactivity and stability, and therefore bringing potential for more spatial and temporal resolution, as well as more double introduction of therapeutic and/or fluorogenic payloads.



Scheme 1: IEDDA between TCO and tetrazine

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Reactivity of Carbonates and Thiocarbonates Derivatives Toward Hydrolysis Reaction in the Presence of Calixarene

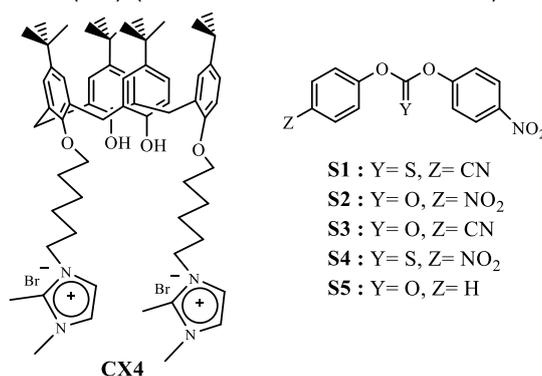
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Most hydrolysis reactions, which have long been subject to investigation, are conducted to form carboxylic acids from acid derivatives such as esters, amides, acid halides, anhydrides and some of their sulfur derivatives¹. On the other hand, calix[n]arenes (where "n" is the number of benzylic units) have been playing a prominent role in supramolecular catalysis².

This work reports the synthesis of **CX4**, which was done according to a modified procedure published earlier,³ and a kinetic study that allow to assess the effect of the macrocycle calix[4]arene 1,2-dimethylimidazole bromide (**CX4**) on the hydrolysis reactions of 4-cyanophenyl 4-nitrophenyl thionocarbonate (**S1**), bis(4-nitrophenyl) carbonate (**S2**), 4-cyanophenyl (4-nitrophenyl) carbonate (**S3**), bis(4-nitrophenyl) thionocarbonate (**S4**) and 4-nitrophenyl phenyl carbonate (**S5**) (see structures in Scheme).



Scheme. Structures of the studied substrates (S1-S5) and the macrocycle (CX4).

In general terms, results show that: (i) the binding constants for each of the complexes formed between substrates (**S1-S4**) and **CX4**, determined by kinetic measurements, presented values on the order of 10^4 M^{-1} , (ii) the stability of each one of these complexes was also assessed by molecular modeling studies, (iii) the k_{obs} values for the hydrolysis reaction of S5 were not affected by the presence of the **CX4**, however, an increase of these values was observed for the other substrates (**S1-S4**) and (iv) in the case of substrate **S2**, the k_{obs} values for the hydrolysis reaction were fitted to a 2:1 model (**CX4:S2**).

Acknowledgement: FONDECYT of Chile (Projects 1160271 and 1170753) and CONICYT PFCHA/Doctorado Nacional 21170793 for financial support.

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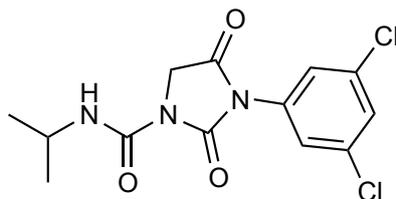
Stability of Iprodione in AOT-Based Reverse Micelles Under Alkaline Conditions

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A study of the effect of AOT/isooctane/water microemulsions upon the stability of 3-(3,5-dichlorophenyl)-N-isopropyl-2,4-dioximidazolidine-1-carboxamide –iprodione– has been investigated in basic media.



Iprodione

The presence of these microheterogeneous media implies a large inhibition upon the basic hydrolysis of iprodione on increasing surfactant concentration and, also, on increasing water contain in the microemulsion.

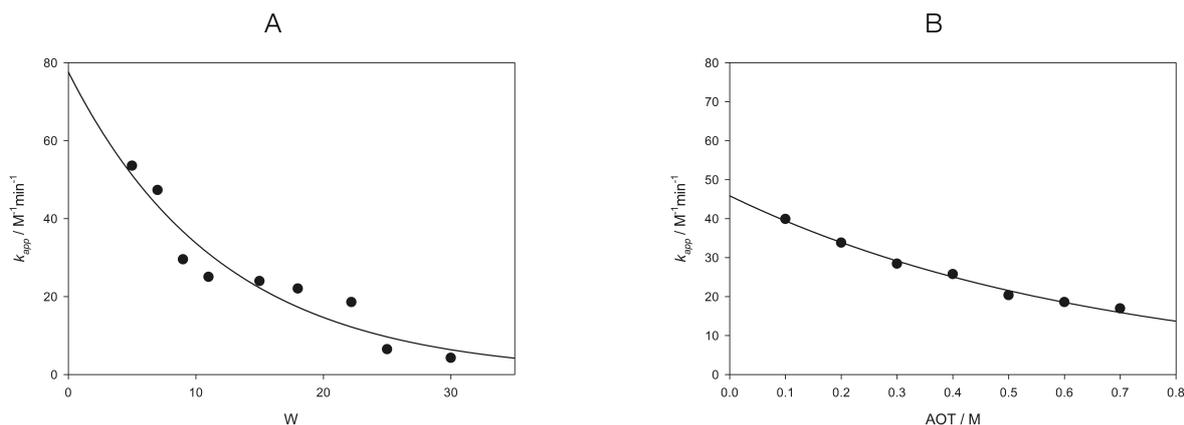


Figure 1. A) Influence of W on the apparent bimolecular rate constant of IP basic hydrolysis in the presence of AOT/*i*C₈/H₂O microemulsions. [AOT]=0.5 M. B) Influence of [AOT] on the apparent bimolecular rate constant of IP basic hydrolysis in the presence of AOT/*i*C₈/H₂O. W=22.2 M.

These results have been compared with the corresponding ones in other colloidal aggregates and with three carbamate pesticides (carbofuran, 3-hydroxy-carbofuran and 3-keto-carbofuran).

Measuring Dielectric Constants of Lipid Bilayers: Excluding Experimental Artifacts From Pyrene Fluorescence in Liposome

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Chemical and biochemical reactions that take place within amphiphilic aggregates such as micelles and most importantly lipid bilayers occur in media that are inherently heterogeneous. For instance, a fluid lipid bilayer is a highly stratified structure with a distinct trans-bilayer molecular profile, e.g. the so-called fluidity and polarity gradients, which in turn may influence or determine the roles of biological membranes as selective barriers, as functional arrays or as therapeutic targets.¹ However, the analysis of electron transfer reaction in cellular bioenergetics and redox processes occurring in membranes is based in a theoretical formalism that assumes the solvent as a continuum whose dielectric constant is well defined.² Also, the domain formation in lipid bilayers also presumes dielectric constant values analogous to those of apolar methylenic solvents.³

There have been diverse attempts, both theoretical (calculations and molecular dynamics) and experimental (mostly EPR and fluorescence), to estimate the dielectric constant of lipid bilayers.⁴ We present here the measurement of equivalent dielectric constants, and their thermal behavior, of fluid lipid bilayers composed of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) and its binary mixtures with cholesterol using the pyrene Ham Effect (I_1/I_3).⁴ The physical-chemical properties of pyrene (Py) settle its location in the ordered section of the methylenic palisade stating the values of dielectric constants as being averaged transversally in space (the longest axis of Py, 9.2 Å) and laterally in time (due to lateral diffusion of Py during its lifetime in aerated samples, ~150 ns).⁵ To do so, the fluorescence spectra must be adequately corrected for the turbidity and Raman band from the aqueous liposome suspensions that fatally affects the measurements of Py fluorescence. Analogous procedure is adopted (only for Raman band) to settle a reference plot for Py fluorescence in isotropic alcohols of known dielectric constants at 20 °C. Henceforth, POPC bilayers exhibits higher dielectric constant at 20 °C than the mixtures at high cholesterol proportions, pointing to features observed in the available thermal phase diagrams.⁶ It is worth to emphasize that POPC bilayers display equivalent dielectric constant values analogous to 1-propanol which is much higher than those of apolar methylenic solvents such as hexadecane.

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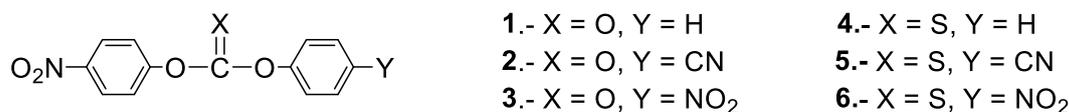
Hydrolysis Reactions of Carbonates and Thiocarbonates Derivatives. Supramolecular Catalysis by Cucurbit[7]Uril.

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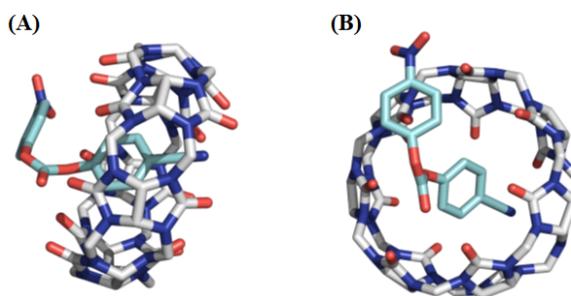
Diverse kind of macrocycles have been playing a prominent role in supramolecular catalysis.¹⁻³ In the present work, we studied experimentally and theoretically the hydrolysis reaction of a series of carbonates and thiocarbonates derivatives 1-6 (Scheme 1) in the presence of the macrocycle cucurbit[7] uril (CB7).



Scheme 1. Structures of the studied substrates (1-6).

Kinetic results show that the thiocarbonyl substrates forms inclusion complexes with CB7 whose binding constant values are higher than their carbonyl homologues and that significant rate enhancements for the hydrolysis of thionocarbonates were observed in comparison with the corresponding carbonates, in the presence of CB7.

The preliminary results by molecular simulation show that the formation of all the complexes are favorable ($\Delta G < 0$) and are preferably generated with the thiocarbonyl derivatives. When evaluating the position of this functional group is observed to be located within the macrocycle, which would favor host-guest interactions. Scheme 2 shows, as an example, the host-guest complex CB7@2.



Scheme 2. Host-guest complex CB7@2. (A) side look of the complex. (B) look from the top of the complex.

It is worth mentioning that the difference in the binding energy values are not significantly different which indicates that in a vacuum all the complexes are favorable.

Acknowledgements: FONDECYT of Chile (Projects 1160271, 1170753) for financial support. J.A. thanks Conicyt for a fellowship.

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Dynamic Control of Ion-Pair Binding by Photo-Tunable Azobenzene-Derived Hosts

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The majority of molecular receptors developed so far perform well only under laboratory conditions, when the strong electrostatic interactions within the ion-pair are greatly reduced by using a suitable soft and noncompeting counterion. In real-life situations, however, the counterion of the target salt is usually hard and strongly solvated, hence strongly compete with the receptor.¹

One way to counter this problem is to develop ditopic receptors which can simultaneously bind cation and anion. However, most of the reported salt receptor are still not effective since they bind ion-pair as spatially separated ions which implies that prior to salt binding event the so-called "Coulombic energy penalty" must be paid to enforce charge separation. One strategy to circumvent this problem is to design the putative receptor that could bind salt as an associated, preferably contact ion pair. To date, there are only few examples in which this approach was successfully implemented.²

We envisioned that reversible switching between these two different binding modes should allow for construction of new type of receptor, in which one geometrical isomer can tightly bind close ion-pair while the second isomer cannot bind it so efficiently due to spatial separations of the ions (Fig. 1)

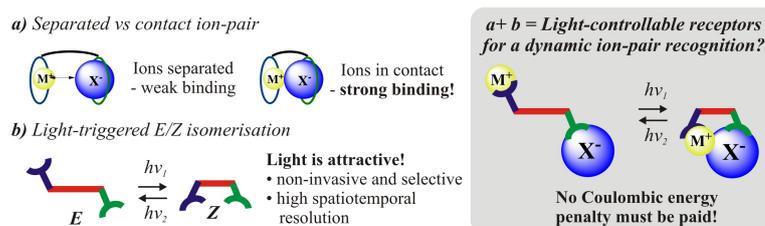


Figure 1

We selected azobenzene chromophore as photoswitch owing to its synthetic availability, robustness, and ability to undergo fast and reversible light-induced E/Z isomerization, which is accompanied by a large-amplitude structural changes between extended (E) and folded (Z) isomers. Structure analysis of photoswitchable ion receptors developed by us and others suggest that attachment of ion binding groups in meta positions relative to the N=N bond should facilitate binding of contact ion-pair by the metastable Z- over the E-isomer since no Coulombic energy penalty must be paid during binding.³ Here, we will present the design, synthesis, and binding properties of a series of new hybrid molecular ion-pair receptors based on azobenzene scaffold equipped with cation (benzo-crown ethers) and anion (amide or urea groups) binding groups.

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Synthesis and Structures of Nanometer-Sized Geodesic Phenylene Bowl

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Geodesic design that makes curved structures by an arrangement of polygons has been widely employed for a creation of curved polyaromatic hydrocarbons. The geodesic design is now applied to arrays of benzene units, and a bowl-shaped aromatic hydrocarbon, geodesic phenylene bowl 1, has been designed and constructed by arranging polygonal structures of [n]cyclo-meta-phenylene ([n]CMP).¹ The bowl 1 was synthesized from [5]CMP via 3-step transformations, and the nanometer-sized bowl structure was revealed by X-ray crystallographic analysis. The bowl in the crystal assembled in a bowl-in-bowl manner (Figure 1), and the formation of the assembly was also observed in solution. The bowl accommodated a C₆₀ molecule in the concave space to form a ball-in-bowl assembly.² Thermodynamic analysis revealed that the assemblies were entropically formed in a favorable manner.

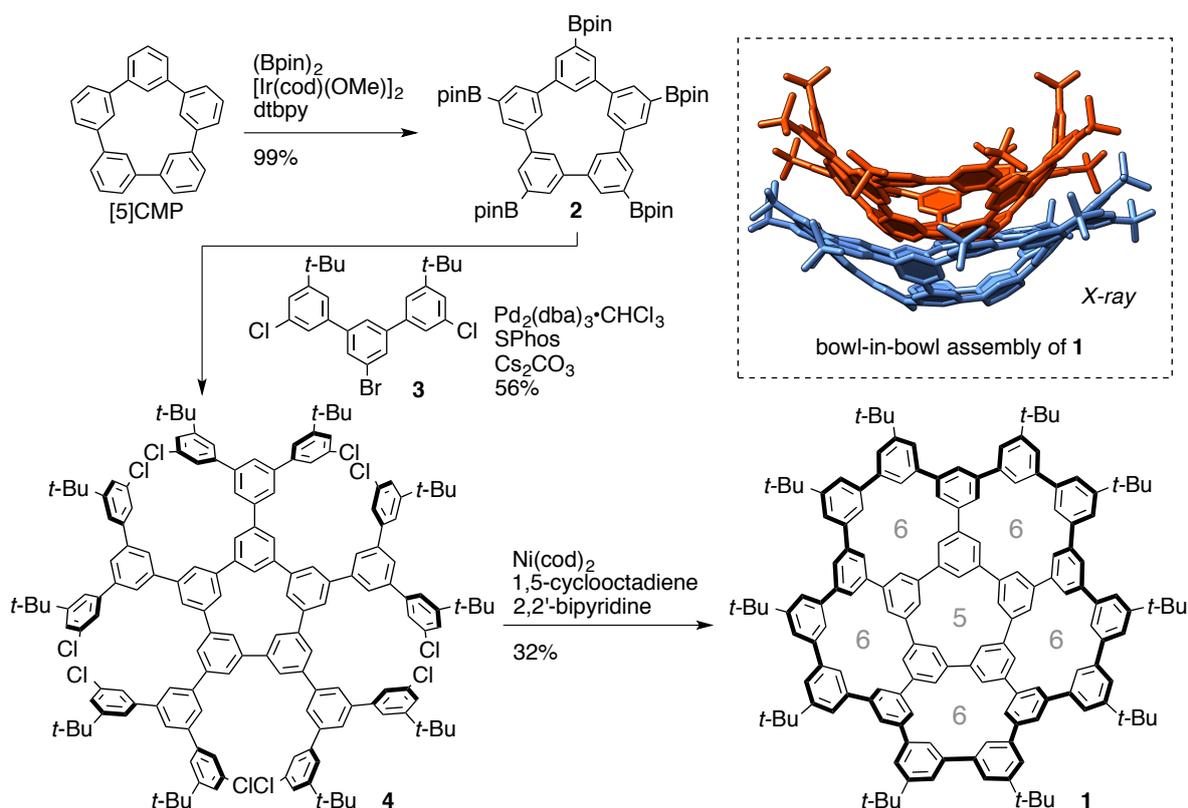


Figure 1. Synthesis of geodesic phenylene bowl 1 and its bowl-in-bowl assembly.

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A Kinetic Study with Neutral and Cationic Dioxolanes Catalyzed by CB7

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The cucurbituril macrocycle has recently been applied to several reactions that use its cavity as a reactive site. The affinity and size of these macrocycles are directly related to the number of glycoluril units in the macrocycle.¹ The hydrolysis reactions can be evaluated with cucurbituril progressive concentrations.² For example, the hydrolysis of 4-methoxybenzoyl chloride is accelerated by about 5 times in the presence of 6.0 mM of cucurbituril CB7.³ In this work the hydrolysis of dioxolanes using CB7 and the dependence of the reaction as a function of catalyst concentration and addition of ammonium quaternary salts, is studied. The dioxolanes evaluated are 2-(4-methoxyphenyl)-1,3-dioxolane (MFD), neutral dioxolane, and cationic dioxolanes 3-(4-(1,3-dioxolan-2-yl)phenoxy)-N,N,N-trimethylpropan-1-aminium bromide (TMAFD) and 3-(4-(1,3-dioxolan-2-yl)phenoxy)-N,N,N-triethylpropan-1-aminium bromide (TEAFD). The acid hydrolysis of MFD, TMAFD and TEAFD were performed in aqueous solution and the formation of products was monitored by UV/Vis spectroscopy at 286 nm. The kinetic measurements were performed in solutions containing 0 to 5.0 mM of CB7 at pH = 5.0 (acetic acid/sodium acetate buffer 0.01 M) at 25 °C, and the kinetic data was fitted using the equation that considers two well-differentiated environments: water and host cavity.³ For MFD (Figure 1A), the ratio of the first order rate constant inside the cavity of CB7 (k_{CB7}) and in water (k_w) is 462 and the association constant is small ($K_{CB7} = 120 \text{ M}^{-1}$). Importantly, hydrolysis of MFD is inhibited by addition of $\text{N}(\text{CH}_3)_4\text{Br}$ and $\text{N}(\text{C}_2\text{H}_5)_4\text{Br}$ (Figure 1B) indicating that the interaction of CB7 with $\text{N}(\text{R})_4^+$ cations is greater than interaction with substrate to be hydrolyzed, making it impossible for dioxolane to enter the cucurbituril cavity. Finally, cationic dioxolanes exhibit high association constants with CB7 (6516 and 10153 M^{-1} for TMAFD and TEAFD, respectively) which is attributed to the position in which the charged groups associate with the cucurbituril cavity, in agreement with the literature.⁴

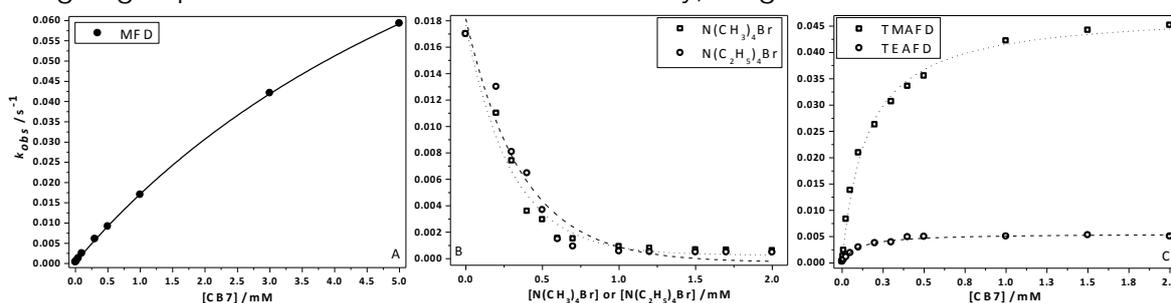


Figure 1. (A) Observed rate constants for hydrolysis of MFD with addition of CB7. (B) Addition of ammonium salts inhibit the hydrolysis of MFD, $[\text{CB7}] = 1.0 \text{ mM}$. (C) Hydrolysis of TMAFD and TEAFD in the presence of CB7.

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Study of Phase Solubility of Bioactive Naphthoquinones

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The naphthoquinones (NQs) are small molecules with well defined functional activity, occurring in several living organisms¹. Since 1960, naphthoquinones have been used as natural sources of potentially bioactive substances.^{2,3} Motivated by promising results in several preclinical and clinical studies of β -lapachone (β Lap) in formulations with cyclodextrins (CD), preformulation studies were initiated with β Lap itself, epoxy- α -lapachone (Epx α L), o-allyl-lausone (OAL) and nor- β -lapachone (N β L) with known trypanocidal activity and cytotoxicity against mammalian cells.⁴⁻⁶

The present study aimed at the synthesis of different bioactive naphthoquinones and their study of phase solubility in different cyclodextrins (α -CD, β -CD and 2HP β -CD) and aqueous solutions of different pH.

The study of phase solubility for β -Lap in different cyclodextrins (α -, β -, γ - and 2HP β -CD) using phosphate buffered saline (pH 7.4) was studied,⁷ however no news of this type of study for the other NQs. Intrinsic solubility was evaluated of naphthoquinones in the different aqueous solvents - buffer solutions (pH 1.2, pH 5.0 pH 7.4) and ultrapure water (pH 5.5), were used to prepare the solubility of phases in different cyclodextrins at room temperature.⁸ The apparent stability constants (Ks) and the encapsulation efficiency (EE) were calculated from the inclination values of the phase solubility diagrams and the respective solubility values of the NQ at room temperature in the absence of cyclodextrin (SO).

The enhancement of solubility in solution is highly dependent on the type of CD molecule and the pH of the medium where inclusion occurs, soon, pH plays an important role in determining the complexing strength between NQ and cyclodextrin. The pH values were independently included. The best EE results were obtained in 2HP β -CD, for β Lap (0.1436) and N β L (0.0621) in buffer pH 7.4, for OAL (0.0520) in buffer, pH 1.2, while for the Epx α L in pH buffer, these corroborate with the values of intrinsic solubility. However, the values of the solubility constant do not follow the same correlation, suffering numerical influence by SO, and thus following another standard. By plotting the Ks values with the pH values, a linear correlation can not be observed. All the slope values of the phase solubility diagrams were smaller than one, indicating that the inclusion complexes are formed in the molar ratio of 1:1 between the host (NQ) and host (CD).

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Cucurbit[7]uril Encapsulation Effect on Tautomerism Equilibrium in Aza-Coumarin and Quinoxalinone Scaffolds. Experimental and Molecular Modeling Studies

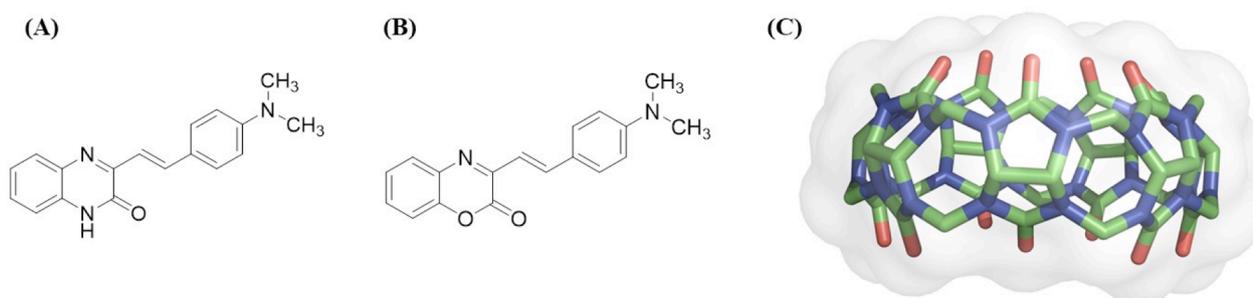
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It is recognized that a number of tautomerism equilibria of different dyes can be modified by the solvent polarity or by the presence of different macrocycles.^{1,2} In this vein, we are interested in assessing the effect of the encapsulation by the host, cucurbit[7]uril (CB7), on the different tautomeric forms present in (E)-3-(4-(dimethylamino)styryl) quinoxalin-2(1H)-one (C1) dye, and for comparative purposes of the (E)-3-(4-(dimethylamino)styryl)-2H-benzo[b][1,4]oxazin-2-one (C2) dye, see structures in Scheme. To this end, traditional spectroscopy techniques (UV-Vis, fluorescence and NMR), mass spectrometry and molecular dynamic simulations were used. Results show that: (i) C1 and C2 form inclusion complexes with the macrocycle CB7, with enormously large bathochromic shifts (> 100 nm), (ii) when the dye C1 is assessed, firstly a 1:1 complex is formed and then, in an excess of CB7, a 2:1 host:guest complex is formed, (iii) the latter complex shifts the lactam-lactim equilibrium of C1 toward the lactim tautomer by preferential binding of this tautomeric form with CB7. Finally, the molecular modeling studies indicate that the most stable complex is C1@CB7 in its lactim form. Therefore, our results evidence the importance of the encapsulation by CB7 as another form of controlling the tautomerism equilibrium of quinoxalinones derivatives.



Scheme. Structure of dyes used in this study: (A) (E)-3-(4-(dimethylamino)styryl) quinoxalin-2(1H)-one (compound C1) and (B) (E)-3-(4-(dimethylamino)styryl)-2H-benzo[b][1,4]oxazin-2-one (compound C2) and (C) the host CB7.

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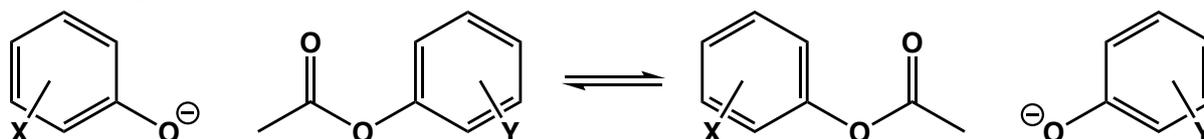
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Predicting Reactivity in Binary Solvent Mixtures Using a Supramolecular Solvation Model

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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-solute interactions as discrete, electrostatic interactions that are proportional to the α and the β hydrogen bonding parameters which can readily be measured, rather than using bulk solvent properties or computationally expensive quantum mechanical modeling. Treating solvents in this way allows both pure and 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 towards using acetyl transfer as a probe to see how the β parameter of anionic nucleophiles and leaving groups affect the rate of reaction:



The β values for a series of phenolates were measured via titration with a common hydrogen bond donor trifluoroethanol. Rate constants of phenolate exchange have been correlated with this parameter and the corresponding α values of the solvents in binary solvent systems. Shifts in the equilibrium are considered whilst varying the macro properties of the solvent i.e. protic and aprotic solvents. We consider whether the electronic and structural changes involved in this simple acetyl transfer reaction can be combined into a simple predictive model extending Guthrie's "no barrier" description of reactions pathways.²

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Binding of Terpenes by Cucurbituril Macrocycles

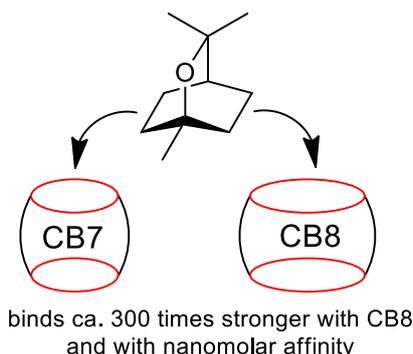
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Cucurbit[*n*]urils (CB*n*) are a family of macrocyclic hosts^{1,2} that is characterized by high guest affinities (up to 10^{17} M⁻¹) and selective binding in aqueous solution. Terpenes as guests are of special interest because they are important components of essential oils that are used in perfumery. The supramolecular interactions and the phototriggered release of these natural products from their CB7 complexes in aqueous medium were previously described by us.³ In order to gain additional information about the complexation of terpenes by synthetic macrocycles in water, we also studied the binding of selected guests (eucalyptol, fenchyl alcohol and geranylamine) by the larger homologue CB8. This was done by means of competitive displacement titrations (fluorescence and UV/vis absorption), isothermal titration calorimetry (ITC), and NMR spectroscopy.⁴ It was found that the investigated terpenes show a high selectivity towards CB8, which is explained with a better size fit.



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Macroscopic pK_a Prediction of Polyprotic Acids from DFT Calculations: The Case of Acetohydroxamic Acid

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Acetohydroxamic acid (AHA), commonly known as lithostat, is a drug used with antibiotics and/or surgery to treat certain types of bladder infections. It is also used as a chelating ligand for organometallic compounds. AHA exists in an equilibrium involving four main isomers (the amide and imide forms in their Z and E conformations, see Figure 1) each of which possesses two acid sites. Hence, each neutral form can dissociate in aqueous solution and exists in equilibrium with its corresponding anionic forms. These multiple dissociation equilibria contribute to the relatively low overall pK_a (the quantitative measure of the strength of an acid in solution) of this compound.

The accurate computational calculation of pK_a values in solution is a challenging task. The goal of this theoretical study is to account for the existence of all the acid-base equilibria in AHA and come up with a methodology to accurately calculate its pK_a in water, which could be extended to other hydroxamic acids. The initial approach followed makes use of continuum solvation methods in which the solvent is modelled as a continuum. The cluster approach, making use of explicit solvent molecules together with the continuum has also been applied with one and two explicit solvent molecules.

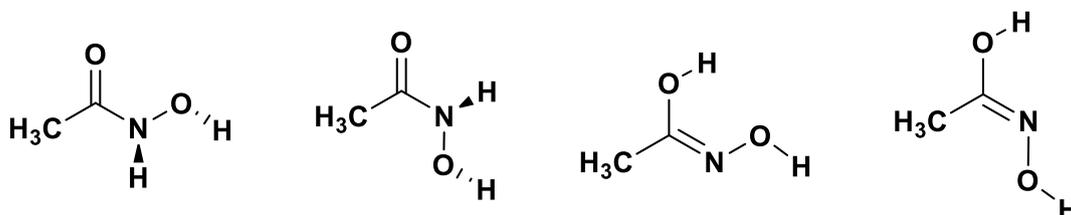


Figure 1. Neutral forms of AHA

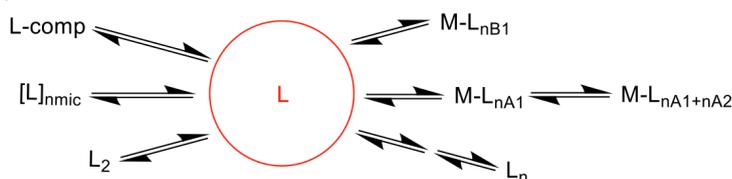
I2CITC : Modular Deconvolution of ITC Data for Complex Equilibrium Systems

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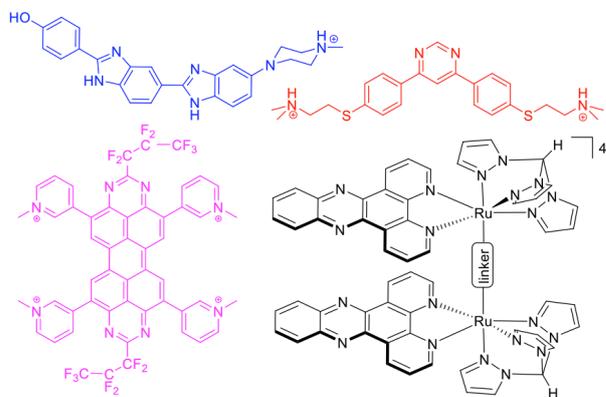
Isothermal titration calorimetry (ITC) is a popular technique for studying (bio)molecular interactions which measures heat effects resulting from interactions being broken and interactions being formed – that is the heat effects of all interactions being broken and formed. For complex equilibrium systems involving multiple binding events in combination with ligand self-aggregation (Scheme 1), this results in complex data which cannot be analysed using the analysis software provided with commercial instrumentation.



Scheme 1

Interactions of small molecules with nucleic acids frequently involve competition between binding and self aggregation because typical nucleic-acid binders (Scheme 2) are relatively hydrophobic flat compounds.

From our previous data analysis software ICITC,^{1,2} we have developed I2CITC which allows modular numerical analysis of ITC data for complex equilibrium systems. In addition to providing best fit parameters, I2CITC allows the visual evaluation of error margins and parameter correlation. Case studies involving a DNA*RNA hybrid-duplex binder,³ a quadruplex DNA binder,⁴ and dinuclear metallo intercalators^{5,6} illustrate the versatility of I2CITC in analysis of complex calorimetric data and the importance of a full analysis of error margins and parameter covariance in identifying appropriate interaction models. Although the examples from our work primarily reflect interactions between small molecules and nucleic acid structures, I2CITC works for data across supramolecular and systems chemistry. For example, we similarly obtained and analysed data for thiols binding to gold nanoparticles,⁷ and for DNA binding to cationic magnetic nanoparticles.⁸



Scheme 2

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Synthesis and Characterization of a New Coumarin-Derivative Chemosensor to Detect Mercuric Ions

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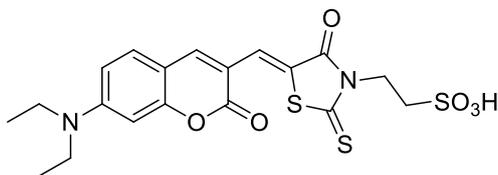
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The detection of heavy and transition metal ions is a task that is attracting a considerable amount of attention, mainly for biological or environmental applications. Among the heavy metals, Mercury is considered one of the most toxic and dangerous elements. Such element has high affinity for sulfhydryl groups such as those present in enzymes, other proteins and endogenous thiols. In the last decades, many sensitive fluorescent probes based on fluorophores such as; rhodamine, coumarin or squaraine derivatives, have been developed to detect mercury ions.¹

In the present work, a new colorimetric and fluorescent chemosensor (Z)-2-(5-((7-(diethylamino)-2-oxo-2H-chromen-3-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl)ethanesulfonic acid (**1**) was synthesized in four steps. Compound **1** was examined by UV-Vis absorption, showing a strong band at 525 nm, molar extinction coefficient (ϵ) of 148518 M⁻¹ cm⁻¹ and fluorescence spectra 630 nm.



1

Interestingly, upon addition of Hg²⁺ ions to the solution of **1**, the absorption band at 525 nm decreases and, a new blue band is formed at 485 nm, with a color change from dark to light pink. The fluorescence spectra of **1**, after the addition of mercuric ions shown, increases to 580 nm. The disappearance of band 630 nm and the formation of a new band could be attributed to the interaction of mercuric ions with the thiocarbonyl group present in the probe, leading to a chemical desulfurization reaction. A clear isosbestic point at 505 nm is observed in the absorption spectra, indicating that the reaction of **1** with Hg²⁺ produces a single component. The latter is verified with the C¹³-NMR spectra and ESI-MS analyses.

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Towards Catalytic Metalated Covalent Organic Frameworks through Supramolecular Strategies

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The increasing demand for chemical products results in the need of chemical catalysts, crucial for the efficient synthesis of chemical products. Heterogeneous catalysis has the advantage over homogeneous catalysis of allowing the separation and possible reuse of the catalyst material, especially important in the case of precious metals.

Covalent organic frameworks (COFs) are crystalline nanoporous materials obtained by crystallization of organic building blocks into a two- or three-dimensional (2D or 3D) structure.¹ 2D COFs consist of planar organic layers which stack with each other in order to form a 3D structure held together by non-covalent interactions contrary to the 3D COFs which are held purely by covalent bonds. In 2D COFs the interlayer interactions play a major role and have great influence in the properties of these COFs.

2D COFs make excellent candidates for heterogeneous catalysis due to their regular porosity, high surface area, and high chemical and thermal stability. In addition, the pore surface can be designed to contain metal-complexation sites by careful choice of the constituent building blocks.

Dipole-moment introduction to COF building blocks has been shown to result in an increase of the surface area and crystallinity of the material by enhancing the interaction between the COF layers and favouring their columnar stacking.²

Following this strategy, we design COFs using dipole-moment-bearing building blocks, which simultaneously contain a metal-complexation site. We foresee regularly placed catalytically active sites in the resulting materials, and as a consequence a high catalytic activity that may open new frontiers in chemical synthesis.

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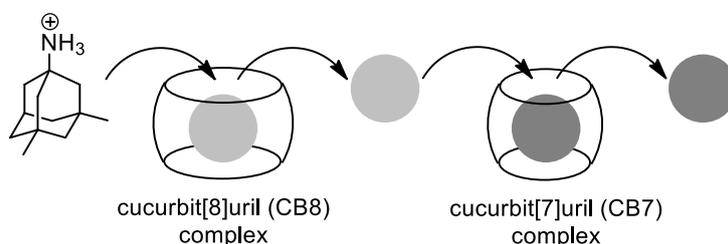
Chemical Communication in a Supramolecular Cascade

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Nowadays, molecular information processing is a field in constant development.¹ One of the bottleneck problems is the question: how can we achieve molecular communication between functional entities?² Many researchers noticed already the importance of improving the knowledge about complex supramolecular systems that can communicate a signal along a cascade of concatenated output and input events.³⁻⁵ Herein, we propose a supramolecular system, formed by a mixture of cucurbituril macrocycles as hosts and three carefully chosen guest molecules. The performance of the system can be monitored by optical and ¹H NMR spectroscopies.



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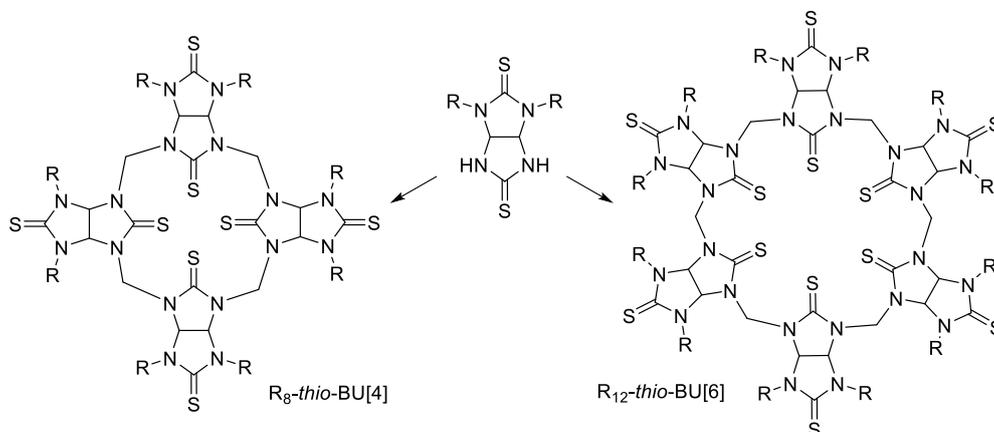
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Glycoluril is a useful building block for the design of supramolecular systems with concave structures, which have been utilized in many applications, including catalysis, sensor devices, molecular recognition and self-assembly. In 2010, a new family of macrocycles known as bambus[n]urils (BU[n]s; n=4,6) have been prepared from N,N-dialkyl glycoluril and since then the larger homolog and its derivatives were studied extensively as a class of anion receptors.¹ We have been involved in glycoluril modifications² and predicted that replacement of oxygen atoms in BUs by other heteroatoms could significantly modify their binding properties.³ We confirmed these predictions experimentally by synthesizing semithio- and semiaza-BUs and showed that semithio-BU[6] is an effective transmembrane transporter capable of polarizing lipid membranes through selective anion uniport whereas semiaza-BUs exhibit simultaneous accommodation of three anions, linearly positioned along the main symmetry axis, which is reminiscent of natural chloride channels in *E. coli*.⁴⁻⁶

Here we report the synthesis of thio-bambusurils using N,N-dialkyl thio-glycoluril building block, and demonstrate unique binding properties at their sulfur edged portals as well as molecular encapsulation within their cavity.

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Poster 113

From Peroxides to Hypohalites: Towards a General Understanding of the Reactivities of Anionic Oxygen Nucleophiles

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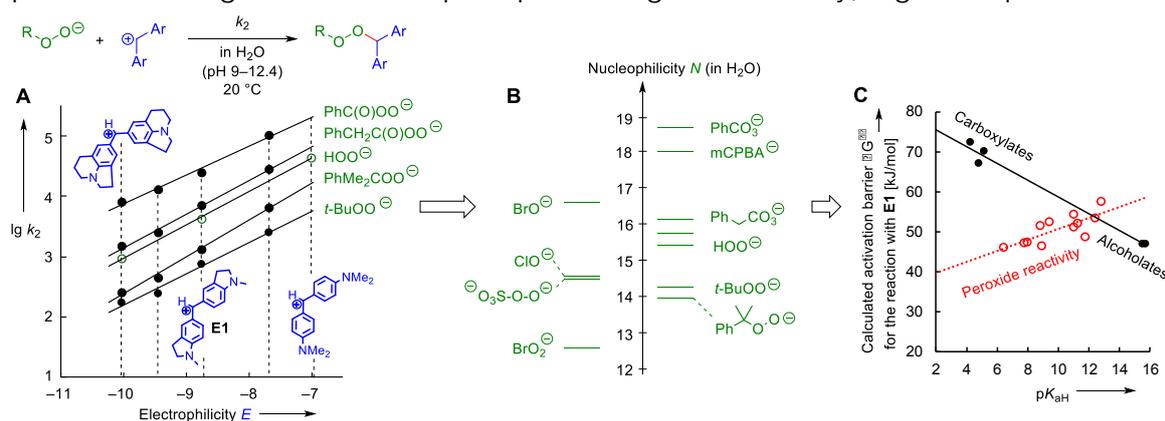
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Various nucleophilic oxidants have found application in both organic synthesis and, even more frequently, for bleaching purposes in industry or on consumer scale.¹ We have now quantified the nucleophilic reactivities (N , s_N) of the anions of various organic peroxides, halogen-oxygen anions, peroxomonosulfate and hydroperoxide (generated from different solid adducts of hydrogen peroxide) by studying the kinetics of their reactions with a series of benzhydrylium ions (Ar_2CH^+) as reference electrophiles in alkaline, aqueous solutions at 20 °C (Fig. A).²⁻³ Subsequently, analysis of the second-order rate constants by the linear free energy relationship eq. (1) furnished the nucleophile-specific parameters N and s_N (Fig. B),⁴ which could successfully be applied to predict the rates of nucleophilic epoxidations of electron-deficient olefins in aqueous solution.

$$\lg k_2 = s_N(N + E) \quad (1)$$

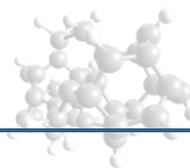
We found that the commonly assumed relationship of nucleophilicity and basicity does not hold for these systems: Peroxycarboxylates (RCO_3^-) are stronger nucleophiles than the anions generated from aliphatic hydroperoxides (ROO^-) even though the latter ones are significantly stronger bases (Fig. C).² Quantum-chemical calculations revealed that not product-stabilizing effects but intrinsic barriers and especially anion desolvation account for the observed ordering of reactivity.

A combination of experimental and theoretical data for a large variety of oxygen nucleophiles is applied to challenge fundamental principles of organic reactivity, e.g. the alpha-effect.



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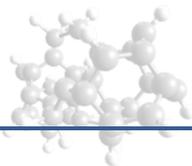
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