

**Physical Organic  
Chemistry:  
Recent developments in  
instrumentation, structure,  
theory, and mechanisms**

**691. WE-Heraeus-Seminar**

**February 18 - 21, 2019  
at the Physikzentrum Bad Honnef/Germany**

**WILHELM UND ELSE  
HERAEUS-STIFTUNG**



# Introduction

The Wilhelm und Else Heraeus-Stiftung is a private foundation that supports research and education in science with an emphasis on physics. It is recognized as Germany's most important private institution funding physics. Some of the activities of the foundation are carried out in close cooperation with the German Physical Society (Deutsche Physikalische Gesellschaft). For detailed information see <https://www.we-heraeus-stiftung.de>

## Aims and scope of the 691. WE-Heraeus-Seminar:

Physical organic chemistry aims at a better understanding of complex organic reactions or structures of organic compounds or catalysts thereby frequently using methods of physical chemistry. A special focus lies on relative chemical stabilities, the isolation and spectroscopy or spectrometry of reaction intermediates, transition states, selectivities, product distributions, non-covalent interactions, and solvation. Often, a series of measurements is performed on a set of similar compounds such that their reactivity and structures change systematically to determine trends in reactivity and structure. These changes are then correlated with the variation of functional groups and the properties and reactivities of new compounds can be predicted. These empirically derived "rules" are then collected in what is called the "mechanism" of the reaction that describes our current understanding of how reactions proceed. Physical-organic chemistry therefore defines the empirical backbone for modern synthesis and thrives on the combination of experiment and theory.

The enormous developments in physical hardware becoming available only recently allow for investigations that have not been possible before. The aim of the current seminar thus is to bring together scientist working in these quite diverse areas of physics and chemistry, such that the enormous potential of methods available today is presented and becomes more generally known. We expect that the exchange between scientists from different communities will lead to extremely stimulating discussions and that conceptionally new approaches will be identified.

The seminar focusses on the most recent developments in instrumentation, structure, theory, and mechanism:

- **Spectroscopic and spectrometric methods for the detection of reactive intermediates** (especially including novel approaches in NMR-, IR and rotational spectroscopy as well as mass spectrometry)
- **Photochemistry** (including photocatalysis and photoswitches)
- **Chirality and transfer of chirality** (including novel multidimensional chromatographic separations, Coulomb-explosion, determination of absolute configurations, enantioselective catalysis and chiral amplification)
- **Reaction kinetics for the elucidation of reaction mechanisms** (including high throughput methods, tunneling control, kinetic isotope effects, and matrix isolation)
- **Electron microscopy** (especially also cryo electron microscopy)
- **Theoretical methods and computational chemistry** (especially for the evaluation of spectra and the elucidation of reaction mechanisms)

**Program**

# Program

**Monday, February 18, 2019**

08:00 – 10:00 Registration and *BREAKFAST*

10:30 – 10:40 Scientific organizers **Welcome words**

Chair: AnnMarie O'Donoghue

10:40 – 11:25 Martin Oestreich **The subtle mechanisms of deceptively simple carbonyl hydrosilylations**

11:25 – 11:50 Jens Bredenbeck **Subensemble-selective photochemistry by mixed IR/VIS two-dimensional spectroscopy**

11:50 – 12:15 Christian Merten **VCD spectroscopy as tool to investigate substrate binding in asymmetric catalysts**

12:15 – 12:40 Martin Pitzer **Coulomb explosion imaging and coincidence**

12:40 – 14:15 *LUNCH*

Chair: Boris Rybtchinski

14:15 – 15:00 Stephen Fletcher **Asymmetric additions to racemates**

15:00 – 15:45 Rui Fausto **IR-induced chemistry: from conformational changes to bond-breaking processes**

15:45 – 16:15 *COFFEE BREAK*

# Program

**Monday, February 18, 2019**

Chair: Ryan Gilmour

16:15 – 17:00 **Poster flash talks** (10 Posters / 3 min)

Chair: Dorota Gryko

17:00 – 17:45	Sebastian Kozuch	<b>Energy span model: building bridges between computational and experimental catalysis</b>
17:45 – 18:30	Jonathan Goodman	<b>Making molecules better</b>
18:45	<i>DINNER</i>	

# Program

**Tuesday, February 19, 2019**

07:30            *BREAKFAST*

*Chair: Martin Oestreich*

08:30 – 09:15    David Procter            **Mechanism-based approach to new radical cyclisation cascades**

09:15 – 09:40    Julia Rehbein            **Beyond conventions and comfort zones: NHC stabilized radicals**

09:40 – 10:25    AnnMarie O'Donoghue            **Mechanistic understanding of chemoselectivity in NHC and BAC organocatalysis**

10:25 – 11:00    *COFFEE BREAK*

*Chair: Ruth Gschwind*

11:00 – 11:25    Alexander Breder            **Aerobic functionalization of carbonous  $\pi$ -bonds by means of rationally designed Selenium-catalysis**

11:25 – 11:50    Anke Krüger            **Electrons from diamond surfaces: Functionalized nanodiamond for photocatalytic applications**

11:50 – 12:15    Derek Pratt            **Resolving the mechanism of peroxidative cell death using physical organic chemistry**

12:15 – 12:40    Artur Mardiyukov            **Triplet Phenylphosphinidene: Synthesis, structure, and reactivity**

# Program

**Tuesday, February 19, 2019**

12:40            *LUNCH*

14:15 – 16:15   **Poster Session** and *COFFEE BREAK*

*Chair: Peter Chen*

16:15 – 17:00   Ryan Gilmour            **Exploiting physical organic principles in reaction design**

17:00 – 17:25   Josef Michl                    **Conformational dependence of sigma-delocalization**

17:25 – 18:10   Jonathan Clayden           **Dynamic foldamers as biomimetic communication devices**

18:10 – 18:25   Stefan Jorda                   **About the Wilhelm and Else Heraeus Foundation**

18:45            *DINNER*

# Program

Wednesday, February 20, 2019

07:30            *BREAKFAST*

*Chair: Stephen Fletcher*

- 08:30 – 09:15    Ruth Gschwind            **Intermediates, interactions and transition states in photo- and organocatalysis**
- 09:15 – 09:40    Ulrich Hintermaier        **Mechanistic insight into homogeneous catalysis from multi-nuclear high resolution flowNMR spectroscopy**
- 09:40 – 10:05    Ann-Christin Pöppler      **Structural insights into polymer micelles from solid-state NMR and complementary tools**
- 10:05 – 10:30    Kirsten Zeitler            **Tuning redox potentials in photocatalysis: Strategies for C O-bond activation and broadly applicable metal-free photoredox catalysts**

10:30 – 11:00    *COFFEE BREAK*

11:00 – 11:15    **Conference Photo** (in the front of the lecture hall)

*Chair: Oliver Trapp*

- 11:15 – 11:40    Michael Schmittel        **Multicomponent catalytic machinery: How the machine speed impacts catalytic activity**
- 11:40 – 12:05    Hendrik Zipse            **Transient intermediates in the phosphane-mediated trimerization of isocyanates**
- 12:05 – 12:30    Eoghan Mc Garrigle      **On the mechanism of organocatalytic glycosylations**



# Program

Wednesday, February 20, 2019

12:30            *LUNCH*

14:15 – 16:15    **Poster session and COFFEE BREAK**

*Chair: Jonathan Clayden*

16:15 – 17:00    Oliver Trapp            **Early pathways to life: Mechanisms to molecular evolution and homochirality**

17:00 – 17:25    Thomas Wirth           **Memory of chirality in flow electrochemistry**

17:25 – 18:10    Boris Rybtchinski       **Elucidating crystallization mechanisms by cryogenic electron microscopy**

18:45            *HERAEUS DINNER*  
*(social event with cold & warm buffet with complimentary drinks)*

# Program

Thursday, February 21, 2019

07:30            *BREAKFAST*

*Chair: Jonathan Goodman*

- 08:30 – 09:15    Peter Chen            **Quantifying dispersion effects on structure and bond strengths in the gas phase and in solution**
- 09:15 – 09:40    Urs Gellrich            **Reversible hydrogen activation by a Pyridonate Borane complex: Combining frustrated Lewis pair reactivity with Boron-Ligand cooperation**
- 09:40 – 10:25    Dorota Gryko            **Photoinduced porphyrinoid catalysis - the need to elucidate the mechanism**

10:25 – 11:00    *COFFEE BREAK*

*Chair: David Procter*

- 11:00 – 11:45    Melanie Schnell            **Deciphering the structure, dynamics, and chirality of complex molecules**
- 11:45– 12:30    Daniel Singleton            **Electrostatic gating and solvent holes in the mechanism of carbocation reactions**
- 12:30 – 12:45    Scientific organizers    **Closing remarks**
- 12:45            *LUNCH*

**End of the seminar and departure**

*NO DINNER for participants leaving on Friday morning*

## Posters

## Posters

- Marija Aleskovic      **From polycyclic diazirines to carbenes: Supramolecular control of photoreactivity**
- Moritz Bensberg      **Reaction energies from automated "Exact" DFT embedding**
- Jan-Philipp Berndt      **Postfunctionalization of Rhodium(II) complexes and their application as bifunctional catalysts for site-selective nitrenoid reactions**
- Bastian Bernhardt      **First generation of cis-cis-dihydroxycarbene by NIR excitation in solid Nitrogen and its disappearance through tunneling**
- Pol Besenius      **Transient supramolecular assemblies mediated by redox-responsive subunits**
- Melanie Börner      **Computational studies on NHC-ligands on metal surfaces**
- Martin Breugst      **Activation of carbonyl electrophiles by molecular iodine**
- Matthias Breuning      **Enantioselective, Cu-Catalyzed Henry reactions: Unravelling the mechanism**
- André K. Eckhardt      **Gas-phase sugar formation using hydroxymethylene as the reactive formaldehyde isomer**
- Sebastian Engl      **Visible light mediated copper catalyzed chlorosulfonylation of alkenes and alkynes**
- Shadi Fatayer      **Electrochemistry of single molecules by atom manipulation**
- Melania Gómez-Martínez      **Helical multi-coordination anion-binding catalysts enable highly enantioselective dearomatization of Pyrylium derivatives**

## Posters

- Johannes Gramüller **Brønsted acid catalysis – structural preferences and hydrogen bonding in imine•phosphoric acid complexes**
- Jens Hartung **On steric stabilization**
- Andreas H. Heindl **Tuning the switching properties of macrocyclic azobenzenes by ring strain**
- Dominik Herold **Structural and kinetic study of two photo- and electrically responsive dithienylethenes**
- Jiri Kaleta **Stereoelectronic effects in bicyclo[1.1.1]pentanes: Radical chlorination and hydrodechlorination**
- Lukas Kaltschnee **High-resolution pure shift NMR techniques for solution state structure determination**
- Iveta Klimánková **Fluoroalkylated hypervalent iodine reagents and their reactivity with thiols in water solutions**
- Kateryna Kuznetsova **Study of the oxidation reaction of cyclohexanone and its derivatives**
- Simon Malcherek **One step beyond: C–C bond activation by *N*-heterocyclic carbenes**
- Boris Maryasin **Computational chemistry and organic synthesis: Let us build a bridge**
- Anna McConnell **Reductive coupling of *N*-aryl iminoboronates and B–N dynamic covalent chemistry**
- Grzegorz Młostoń **Non-concerted cycloadditions with the *S*-centered 1,3-dipoles**
- Dominik Niedek **Switching site-selectivity with light in the acetylation of sugars with azo-peptide catalysts**

## Posters

Jochen Niemeyer	Mechanistic investigations on interlocked catalysts
Gülce Ögrüç Ildız	Large-scale matrix-site changing mediated by conformational conversion
Jenny Phan	The open-shell twin of the Breslow intermediate
Dariusz Piekarski	Theoretical insights into helical multi-coordination anion-binding catalysis
Johann Primožic	Mechanistic insight into the anion-initiated gem-difluorocyclopropanation of alkenes by TMSCF <sub>3</sub>
Henrik Quanz	TUNNEX: An easy-to-use Wentzel-Kramers-Brillouin (WKB) implementation for computing tunneling half-lives
Prince Ravat	CETHRENE: A journey from reactive biradicaloid to effective chiroptical photoswitch
Igor Rončević	Fragmentation of CB11 anions: Evidence for a charged carbonyne intermediate
Felix Andreas Roth	Travel to MARS: Constructing the space around your stereogenic centers
Alexej Scheremetjew	Electrooxidative Rhodium-catalyzed cross-dehydrogenative alkenylation
Alexander Seitz	Oligopeptide catalyzed site-selective acetylation of pyranosides
Mustafa Uygur	Metal-free desilylative C-C bond formation by visible light photoredox catalysis
Katarina Varga	Alkylation of Gold surfaces with long-chain alkylstannanes

## Posters

- Ivan Vilotijevic      **Latent nucleophiles in synthesis: Improving the scope and selectivity in Lewis base catalysis**
- Kateryna Volianiuk      **Fluorine-alkyl and oligonucleotide containing polyamphiphiles for cell and bacteria labeling**
- Jan Philipp Wagner      **Gauging stability and reactivity of carbonyl O-oxide Criegee intermediates**
- Andrii Yakymovych      **Synthesis and thermal stability of maleimide moiety containing arylalkyl peroxides and peroxyesters**

# **Abstracts of Talks**

(in chronological order)

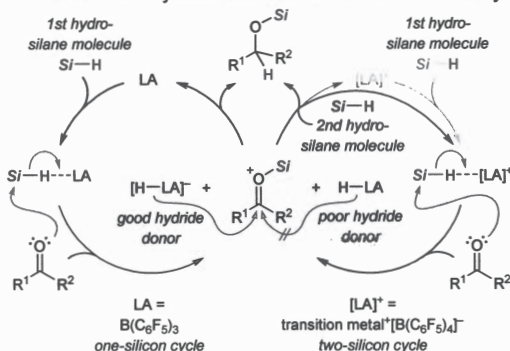


# The subtle mechanisms of deceptively simple carbonyl hydrosilylations

**M. Oestreich**

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Ionic outer-sphere mechanisms are documented for both main-group- and transition-metal-catalyzed carbonyl hydrosilylation.<sup>1</sup> Examples include contributions by Piers<sup>2</sup> and Brookhart<sup>3</sup> employing either neutral  $B(C_6F_5)_3$  or a cationic iridium(III) pincer complex as catalysts. These processes share electrophilic Si–H bond activation through  $\eta^1$ - or  $\eta^2$ - $\sigma$  coordination of the Si–H bond to the Lewis acid (LA) followed by silyl transfer from the activated hydrosilane to the carbonyl oxygen atom. Their difference lies in the reduction step (gray box). For neutral transition-metal hydrides another hydrosilane molecule is required to boost the hydride delivery. We believe that this is a general phenomenon and recently also verified this for Nikonov's system.<sup>4</sup>



## References

- [1] T. Robert, M. Oestreich, *Angew. Chem. Int. Ed.* **52**, 5216 (2013).
- [2] a) D. J. Parks, J. M. Blackwell, W. E. Piers, *J. Org. Chem.* **65**, 3090 (2000); b) S. Rendler, M. Oestreich, *Angew. Chem. Int. Ed.* **47**, 5997 (2008); c) K. Sakata, H. Fujimoto, *J. Org. Chem.* **78**, 12505 (2013); d) J. Hermeke, M. Mewald, M. Oestreich, *J. Am. Chem. Soc.* **135**, 17537 (2013); e) A. Y. Houghton, J. Humalainen, A. Mansikkamäki, W. E. Piers, H. M. Tuononen, *Nat. Chem.* **6**, 983 (2014).
- [3] a) J. Yang, P. S. White, C. K. Schauer, M. Brookhart, *Angew. Chem. Int. Ed.* **47**, 4141 (2008); b) T. T. Metsänen, P. Hrobárik, H. F. T. Klare, M. Kaupp, M. Oestreich, *J. Am. Chem. Soc.* **136**, 6912 (2014).
- [4] a) D. V. Gutsulyak, S. F. Vyboishchikov, G. I. Nikonov, *J. Am. Chem. Soc.* **132**, 5950 (2010); b) Y.-F. Yang, L. W. Chung, X. Zhang, K. N. Houk, Y.-D. Wu, *J. Org. Chem.* **79**, 8856 (2014); c) J. Fuchs, H. F. T. Klare, M. Oestreich, *ACS Catal.* **7**, 8338 (2017).

# Subensemble-Selective Photochemistry by Mixed IR/VIS Two-Dimensional Spectroscopy

**J. Bredenbeck**<sup>1</sup>

<sup>1</sup>*Institute of Biophysics, Goethe-University, Frankfurt am Main, Germany*

In the visible spectral range it is often difficult due to band overlap to distinguish between molecular species such as different conformers, isomers or molecules involved in different intermolecular interactions and to selectively excite them. IR spectroscopy is usually more selective, however, IR excitation does not offer the possibility to trigger photochemistry of the selected species. The VIPER 2D-IR experiment,<sup>1</sup> where VIPER stands for Vibrationally Induced Electronic Resonance, is a mixed IR/VIS two-dimensional spectroscopy<sup>2</sup> that combines IR selectivity with electronic excitation and the investigation of subsequent dynamics. To achieve this goal, the VIPER 2D-IR pulse sequence uses a selective narrow-band IR pulse to vibrationally tag a molecular species, followed by an off-resonant VIS pulse and a broadband IR probe pulse. Only molecules that have been vibrationally excited by the first IR pulse will be transferred to the electronically excited state, because the IR pulse shifts the molecule into resonance with the Vis pulse.<sup>3</sup> In this fashion, one can select even between molecules with identical UV/VIS spectrum by exploiting differences in the IR spectrum. Vibronic coupling between initially excited vibration and electronic transition is not essential for VIPER, because a modulation of the VIS cross-section can be achieved by energy redistribution into Frank-Condon-active modes. We report several applications of the VIPER 2D-IR experiment, such as (1) probing chemical exchange processes on time scales that are slower than the vibrational lifetime<sup>1</sup> and (2) selecting one species for electronic excitation and photochemistry out of a mixture of molecules with virtually identical UV/VIS spectra.<sup>4</sup>

## References

- [1] L. J. G. W. van Wilderen, A. T. Messmer, J. Bredenbeck, *Angew. Chem. Int. Ed.* **53**, 2667–2672 (2014)
- [2] L. J. G. W. van Wilderen, J. Bredenbeck, *Angew. Chem. Int. Ed.* **54**, 11624–11640 (2015)
- [3] J. von Cosel, J. Cerezo, D. Kern-Michler, C. Neumann, L. J. G. W. van Wilderen, J. Bredenbeck, F. Santoro, I. Burghardt, *J. Chem. Phys.* **147**, 164116 (2017)
- [4] D. Kern-Michler, C. Neumann, N. Mielke, L. J. G. W. van Wilderen, M. Reinfelds, J. von Cosel, F. Santoro, A. Heckel, I. Burghardt, J. Bredenbeck, *J. Am. Chem. Soc.* **140**, 926–931 (2018)

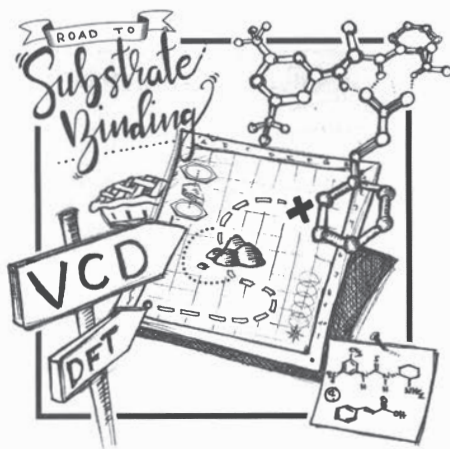
# VCD spectroscopy as tool to investigate substrate binding in asymmetric catalysts

Christian Merten<sup>1</sup>

<sup>1</sup> Ruhr University Bochum, Faculty of Chemistry and Biochemistry, Organic Chemistry 2, christian.merten@rub.de

Vibrational Circular Dichroism (VCD) spectroscopy measures the small difference in the absorption of left- and right circular polarized infrared light by a chiral sample. It allows the unambiguous assignment of absolute configurations by comparison of experimental and computationally predicted spectra,<sup>[1]</sup> but it is also highly sensitive to even very subtle differences in structures, such as conformational changes induced by solute-solvent interactions.<sup>[2]</sup> In our work, we take advantage of this conformational sensitivity and use VCD spectroscopy to probe intermolecular interactions of interest in catalysis<sup>[3]</sup> and supramolecular chemistry.

Following a short introduction to the technique itself, we will focus on some of our recent studies on the use of VCD spectroscopy to understand the interactions of asymmetric catalysis. A particular focus will be placed on hydrogen bonding interactions in thiourea catalysis.<sup>[4]</sup> First, it will be shown that VCD spectroscopy can give additional insight into the influence of solvents on the conformational preferences of a chiral thiourea model compound and its interactions with reactants will also be discussed. Afterwards, we discuss the role of dispersive interactions in the correct description of the binding of carboxylic acids to Takemoto's catalyst and show that VCD spectra can be used as valuable experimental reference for the correct structure.



## References

- [<sup>1</sup>] C. Merten, V. Smyrniotopoulos, D. Tasdemir, *Chem. Commun.* **51** (2015) 16217-16220 [<sup>2</sup>] C. Merten *PCCP* **19** (2017) 18803-18812 [<sup>3</sup>] C. Merten, C. H. Pollok, S. Liao, B. List, *Angew. Chem. Int. Ed.*, **54** (2015) 8841-8845. [<sup>4</sup>] a) N. Kreienborg, C. H. Pollok, C. Merten, *Chem. Eur. J.*, **22** (2016) 12455-12463; b) N. Kreienborg, C. Merten, *PCCP* (2018) 10.1002/chem.201804230; c) N. Kreienborg, C. Merten, *Chem. Eur. J.* (2018) 10.1002/chem.201804230

# Coulomb Explosion Imaging and Coincidence Spectroscopy for Chemistry Applications

**M. Pitzer**

*Department of Chemical and Biological Physics,  
Weizmann Institute of Science, Rehovot, Israel*

In the last decades, techniques have been developed that can remove several electrons from a molecule in a time window that is short compared to nuclear motion. The most important of these ionization techniques are presumably femtosecond laser pulses.

When molecules undergo multiple ionization, the remaining atomic cores repel each other via the Coulomb force, leading to a so-called Coulomb Explosion. Due to the short timescale of the process, the velocity vectors of the atomic or molecular fragments retain information of the initial structure.

Coincidence techniques like COLTRIMS (Cold Target Recoil Ion Momentum Spectroscopy) [1,2] are able to record these fragment velocities for single-molecule break-ups. Collecting many Coulomb Explosion events allows reconstructing structural properties of the molecular species under investigation. While this approach is widespread for diatomic and triatomic systems, it was extended to determine the stereochemical configuration of simple chiral species only a few years back [3,4].

This contribution explains the fundamentals of the Coulomb Explosion Imaging technique and discusses experiments on various chiral species and different ionization processes (for a detailed introduction, see [5]). In addition to the structural analysis, the dynamics of chiral light-matter interaction can be probed [6,7].

The second part of the talk will consider additional topics in chemistry that might benefit from multi-coincidence and Coulomb Explosion measurements in chemistry. Since the current experimental setups are restricted to small molecular species, new impulses can arise from combining the coincidence measurement scheme with different sample preparation and detection techniques.

## References

- [1] R. Dörner, et al., *Phys. Rep.* **330**, 95 (2000)
- [2] J. Ullrich, et al., *Rep. Prog. Phys.* **66** 1463 (2003)
- [3] M. Pitzer, et al., *Science* **341**, 1096 (2013)
- [4] P. Herwig, et al., *Science* **342**, 1084 (2009)
- [5] M. Pitzer, *J. Phys. B.* **50**, 153001 (2017)
- [6] M. Tia, et al., *J. Phys. Chem. Lett.* **8**, 2780 (2017)
- [7] K. Fehre, et al., *Sci. Adv.*, under review

# Asymmetric additions to racemates

S. P. Fletcher

<sup>1</sup>University of Oxford, Oxford, UK

The asymmetric addition of sp<sup>3</sup>-hybridized alkylzirconium reagents<sup>[1,2]</sup> and sp<sup>2</sup>-hybridized vinyl and (hetero)aryl boronic acids<sup>[3,4]</sup> to cyclic racemic allyl halides will be described. As will mechanistic studies of these reactions.

## References

- [1] H. You et al, *Nature*, **517**, 351 (2015)
- [2] E. Rideau et al, *J. Am. Chem. Soc.* **139**, 5614 (2017).
- [3] M. Sidera et al, *Nature Chem.* **7**, 935 (2015)
- [4] P. Schafer et al, *Nature Comm.* **8**, 15762 (2017)

# IR-Induced Chemistry: From Conformational Changes to Bond-Breaking Processes

**R. Fausto, I. Reva, S. Góbi and C. M. Nunes**

*CQC, Department of Chemistry, University of Coimbra, Portugal*

Infrared-induced chemistry has been a relatively unexplored field of research, though its roots may be traced back to the historical paper by Hall and Pimentel [1], published in 1963, where the relative populations of the two conformers of matrix-isolated nitrous acid could be varied by *in situ* IR broadband irradiation within the  $\nu\text{OH}$  stretching fundamental region. Because of lack of efficient selectivity, however, this type of chemistry did not collect, at that time, too much interest among the scientific community. Only 34 years later, the subject gained importance, when high-selectivity in controlling the chemical reactions could be achieved by introduction of narrowband IR excitation [2,3]. Since then, IR-induced chemistry has been developing and, nowadays, it can be used to control the molecular conformation with both high selectivity and efficiency. Furthermore, more recently IR excitation has also been shown to be usable to induce (or facilitate) other types of chemistry [4,5]. Our Laboratory has been involved in this type of investigations for more than 20 years, and in this talk we would present a summary of some of our most relevant achievements in the field:

- Efficient control of the molecular conformations by means of narrowband tunable IR excitation, including the generation of rare, elusive conformers otherwise inaccessible to experimentation;
- Application of the research strategy to more complex systems, like dimers;
- Controlling the conformation of selected fragments in a molecule by vibrationally exciting remotely located in space antennas;
- Using vibrational excitation to facilitate tunneling reactions, including processes involving cleavage of chemical bonds;
- Generation of novel high-energy crystals built from high-energy conformers.

## References

- [1] R. T. Hall and G. C. Pimentel, *J. Chem. Phys.*, **38**, 1889 (1963)
- [2] M. Pettersson, J. Lundell, L. Khriachtchev and M. Räsänen, *J. Amer. Chem. Soc.*, **119**, 11715 (1997).
- [3] E. M. S. Maçôas, L. Khriachtchev, M. Pettersson, R. Fausto and M. Räsänen, *J. Amer. Chem. Soc.*, **125**, 16188 (2003).
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- [5] A. J. Lopes Jesus, C. M. Nunes, R. Fausto and I. Reva, *Chem. Comm.*, **54**, 4778 (2018).

# **Energy span model: building bridges between computational and experimental catalysis**

**S. Kozuch**

*Ben-gurion University of the Negev, Beer Sheva, Israel*

With the development of computational tools the calculation of reaction pathways for catalytic systems has become a routine job. But still, a missing link between the calculated reaction profile and the kinetics of a catalytic cycle makes it impossible to resolve the basic question: What makes for a good catalytic cycle?

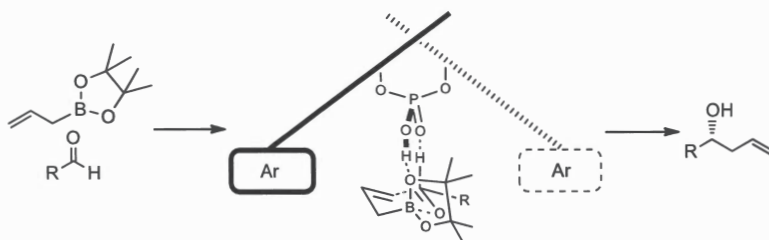
With the aid of the energy span model we will be able to calculate the TOF (turn-over frequency) and TON (turn-over number) of catalytic cycles from their energy representation in a simple, physically correct and elegant manner. In this way we can seamlessly bridge experimental and computational outcomes of catalytic cycles, explain their efficiency, and even suggest improvements.

# Making Molecules Better

K. Ermanis and J. M. Goodman

Centre for Molecular Informatics, Department of Chemistry, University of Cambridge,  
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The elucidation of reaction mechanisms and the prediction of reactivity requires three things: (i) precise calculation of reaction pathways; (ii) effective extraction of knowledge from analytical data; (iii) FAIR access of experimental data. In the first area, we have developed methods for the understanding of asymmetric catalysis using BINOL-derived phosphoric acids.[1] In the second, we are developing the DP4 method for quantifying the confidence we can have in the interpretation of NMR spectra.[2] , Finally, we are developing the RInChI reaction identifier, which will help make reaction data Findable, Accessible, Interoperable, and Reusable.[3] Using these approaches together we are making it possible to foresee the outcome of new reactions with greater confidence.



## References

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# Mechanism-based approach to new radical cyclisation cascades

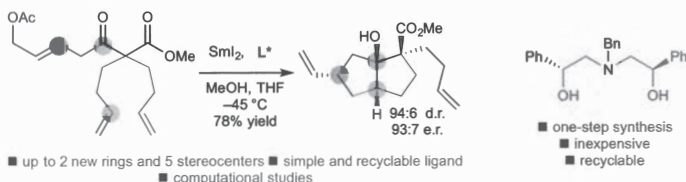
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Samarium(II) iodide ( $\text{SmI}_2$ ) is a reductive, single electron transfer (SET) reagent, that is used widely in synthetic chemistry.<sup>[1]</sup> We have discovered how to use the reagent to generate unusual ketyl radical anions by SET to esters and amides and we have used the resultant radicals in new cyclizations and cyclization cascades.<sup>[2]</sup> The first part of the lecture will describe recent work on ester-<sup>[3]</sup> and amide-alkene<sup>[4]</sup> radical cyclizations and the development of *folding cascades* that follow intriguing mechanistic pathways and deliver complex polycyclic 3D products with high control.<sup>[5]</sup> While the ability of  $\text{SmI}_2$  to generate ketyl radical anions from aldehydes and ketones is well-established,<sup>[1]</sup> up to now, attempts to render subsequent radical couplings either enantioselective or catalytic have met with little success. The second part of the lecture will describe the development of the first chiral ligand-controlled, enantioselective cyclizations mediated by  $\text{SmI}_2$ <sup>[6]</sup> and recent studies on the development of cyclization cascades that are catalytic in  $\text{SmI}_2$ .<sup>[7]</sup>



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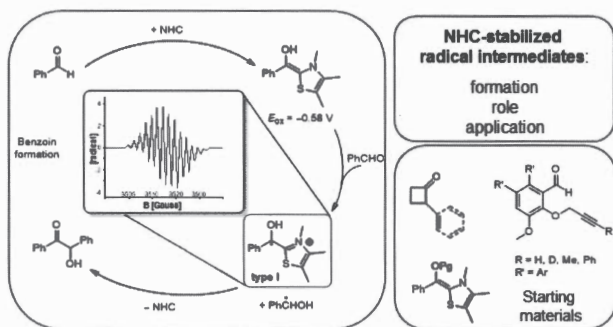
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# Beyond Conventions and Comfort Zones: NHC-Stabilized Radicals

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Understanding reaction mechanisms in great detail and taking these insights further to enable the design of new chemistry or to develop predictive models are at the heart of physical organic chemistry. Within this respect, we are especially interested in the stabilization of radicals by *N*-heterocyclic carbenes (NHCs) and re-thinking the associated reaction mechanism evolving around the Breslow intermediate (Figure).



Elucidating the formation and role of the Breslow-type radicals and their potential of being harnessed in chemistry beyond standard umpolung approaches will be discussed. In addition to the surprising ease of radical formation associated concepts of reaction path bifurcations will be highlighted in one of the transformations.

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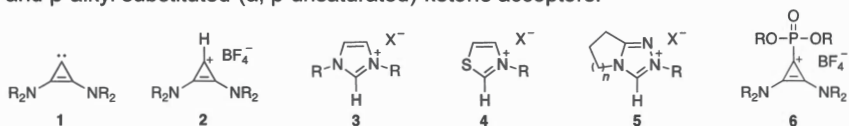
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# Mechanistic Understanding of Chemoselectivity in NHC and BAC Organocatalysis

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Bis(amino)cyclopropenylidenes (BACS) **1** are highly promising as organocatalysts for acyl anion and extended umpolung reactions, and demonstrate orthogonal chemoselectivity to N-heterocyclic carbenes (NHCs). BACS **1** (R = Et) efficiently promote the Stetter reaction with minimal contribution from a competing benzoin reaction even with more 'difficult' Stetter acceptors such as electron rich aldehydes and  $\beta$ -alkyl substituted-( $\alpha$ ,  $\beta$ -unsaturated)-ketone acceptors.<sup>1</sup>



We will discuss our kinetic evaluation of the proton transfer reactions of the bis(amino)cyclopropenium ion conjugate acids **2** of BACs **1** and will compare with kinetic acidities and pK<sub>a</sub>s for NHCs. Our results reveal cyclopropenium ions **2** have comparable acidities to *N,N*-dialkylimidazolium ions **3** (R = alkyl), however, are substantially less acidic than commonly used thiazolium **4** and triazolium organocatalysts **5**.<sup>2</sup> We will also report our structural and kinetic evaluation of BAC-catalysed benzoin and Stetter reactions including the isolation of the common first intermediate on the reaction pathway of both transformations. In the course of these studies, novel BAC-phosphonium adducts **6** were isolated (R = alkyl), which could be hydrolysed under basic conditions to access cyclopropenium ions **2**. These data provide mechanistic insight into the orthogonal reactivity of BACs relative to NHCs for competing benzoin and Stetter transformations.

If time permits, we will also report our kinetic and structural studies of the first NHC catalyst-controlled chemoselective coupling reaction between aromatic and aliphatic aldehydes. Comparatively small changes in fused ring size **5** (n = 1-3) dramatically alter the product outcome in aryl-alkyl cross benzoin reactions.

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# Aerobic Functionalization of Carbonous $\pi$ -Bonds by Means of Rationally Designed Selenium-Catalysis

S. Ortgies,<sup>1</sup> C. Depken,<sup>1</sup> F. Krätzschar,<sup>1</sup> R. Rieger,<sup>1</sup> K. Rode,<sup>1</sup> K. Koszinowski,<sup>1</sup> I. Siewert,<sup>2</sup> and A. Breder<sup>2</sup>

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The oxidative functionalization of non-polarized olefinic and acetylenic  $\pi$ -bonds using ambient air as the terminal oxidant arguably ranks among the most challenging organic transformations. While the use of air as a gratuitous and environmentally benign reagent has been well established in a variety of catalytic large-scale industrial processes for the conversion of petrochemical feedstocks into commodity chemicals (e.g., Wacker oxidation),<sup>[1]</sup> its application in synthetic regimes for the selective construction of diversely functionalized small molecules derived from simple alkenes or alkynes is far from being fully exploited.<sup>[2]</sup> Until this day, the majority of catalytic aerobic  $\pi$ -bond oxidation methods is mediated by certain transition metal compounds, such as palladium or copper complexes.<sup>[3,4]</sup> In sharp contrast, cognate processes enabled by non-metallic catalysts are notably less well developed. This circumstance is insofar remarkable and – to some degree – surprising, as certain p-block elements such as sulfur- and selenium have been shown to exhibit high catalytic activity in the oxidative functionalization of non-activated C–C  $\pi$ -bonds.<sup>[5]</sup> In this context, our research group has recently disclosed the first examples of a selenium-reliant photoredox catalysis regime that allows for the use of mere air as the terminal oxidant in the allylic coupling of non-activated alkenes with simple heteroatomic nucleophiles.<sup>[6]</sup> On the basis of mechanistic investigations,<sup>[6b,7]</sup> we have been able to emphasize the importance of oligomeric Se-cations as active catalysts.

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# Electrons from diamond surfaces: Functionalized nanodiamond for photocatalytic applications

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Carbon nanomaterials have been used in a variety of catalytic processes.

Their properties strongly depend not only on the type of hybridization ( $sp^2$  vs.  $sp^3$ ) but also on the size of the carbon nanoobject and the actual orientation and morphology of its surface. Additionally, the surface termination plays a major role in the surface chemistry that is subsequently accessible for the respective carbon nanomaterial.

Diamond is a wide-bandgap semiconductor with unique electronic properties. Using the inherent negative electron affinity of the diamond surface, the barrier free emission of electrons from the materials' conduction band into the surrounding medium, i.e. water is possible. These electrons can be used to initiate highly demanding reduction processes such as the reduction of  $CO_2$  or nitrogen. However, due to the large bandgap of diamond (5.5 eV) this is normally possible only with short wavelength UV light.<sup>[1]</sup>

Here we discuss the production of differently terminated nanodiamond particles for the application of visible light for the population of the diamond conduction band and their physicochemical properties. Furthermore, the functionalization of different types of nanodiamond and its influence on the materials properties will be presented. Such efforts aim at the synthesis of tailored functional diamond materials for application in (photo)catalysis, energy transformation, storage and solar fuel production.

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

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# Resolving the Mechanism of Peroxidative Cell Death Using Physical Organic Chemistry

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Lipid peroxidation, the free radical mediated autoxidation of lipids, has long been implicated in a wide variety of degenerative diseases, but only recently has it been unambiguously associated with a specific mechanism of cell death: ferroptosis.<sup>1</sup> Ferroptotic cell death can be cleanly initiated by pharmacological inhibition or genetic deletion of glutathione peroxidase 4, the enzyme responsible for the detoxification of (phospho)lipid hydroperoxides. Various types of compounds have been demonstrated to rescue cells from ferroptosis, including ferrostatins and liproxstatins, lipoxygenase inhibitors, mitochondria-targeted nitroxides and deuterated polyunsaturated fatty acids. The cytoprotective properties of these compounds have prompted various confounding hypotheses regarding the mechanism of ferroptosis.<sup>2</sup>

Enabled by our understanding of the mechanisms and kinetics of radical reactions relating to hydrocarbon autoxidation and its inhibition, and methods that we have developed to study them, we have worked to clarify the steps involved in the initiation and execution of ferroptosis. In doing so, we have elucidated the mechanism of cytoprotection of ferrostatins/liproxstatins,<sup>3,4</sup> resolved the debate surrounding the role of lipoxygenases in cell death,<sup>5</sup> advanced a reasonable mechanism for nitroxide-based cytoprotectants,<sup>6</sup> and attempted to clarify the role of mitochondria in ferroptosis. The physical organic chemistry that underlies these developments will be presented.

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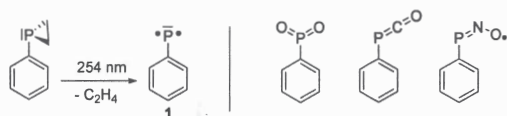
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# Triplet Phenylphosphinidene: Synthesis, Structure, and Reactivity

A. Mardyukov

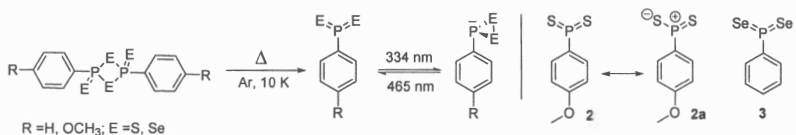
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Phosphinidenes (R-P:) are a class of reactive intermediates, which are of considerable importance in a variety of organic reactions.<sup>1</sup> Due to their high reactivity, the chemical properties of phosphinidenes have been deduced almost exclusively from trapping or complexation experiments.<sup>2</sup> The talk reports the first synthesis, IR, and UV/Vis spectroscopic characterization of parent phenylphosphinidene (**1**) and its reactions with small molecules. As products of these reactions, we have been able to identify a series of elusive intermediates using matrix isolation spectroscopy (Scheme 1).<sup>3,4</sup> We illustrate that the chemical transformations involved are distinctly different from those observed with triplet nitrenes.



## Scheme 1.

Moreover, the first spectroscopic (IR and UV/Vis) characterization of (4-methoxy)phenyl phosphine disulphide (**2**) and phenyl phosphine diselenide (**3**) together with their unexplored photochemistry (Scheme 2) will be presented.<sup>5,6</sup> These hitherto unreported molecules have been postulated as key intermediates derived from Lawesson's and Woollins' reagents that are extremely useful in sulfur and selenium transfer reactions.



## Scheme 2.

## References

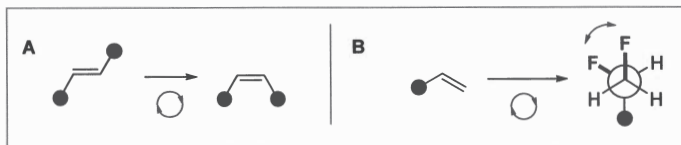
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# Exploiting Physical Organic Principles in Reaction Design

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Controlling molecular space in 2- and 3-dimensions is a challenge that continues to be intensively pursued. In this lecture, *contra*-thermodynamic  $E \rightarrow Z$  isomerization via energy transfer catalysis (A) will be discussed together with our latest contributions to the field of stereoelectronic conformational control using fluorine (B).



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# Conformational Dependence of sigma-Delocalization

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We have examined the effect of chain conformation on the delocalization of sigma-electrons in saturated catenanes of group 14 elements from carbon to lead, with focus on regular helices of finite to infinite length. We have employed both density functional theory and simple model calculations for which algebraic solutions can be written down to answer some fundamental questions: (i) Is there a simple intuitive explanation of the strong delocalization of a hole in the HOMO when the helix is loose (backbone dihedral angles close to 180 deg) and hardly any delocalization when the helix is tight (backbone dihedral angles close to 0 deg)? (ii) Can one explain simply why the effects of sigma-electron delocalization are so much more pronounced in the chains of the heavier elements than in the chains of carbon (hydrocarbons)?

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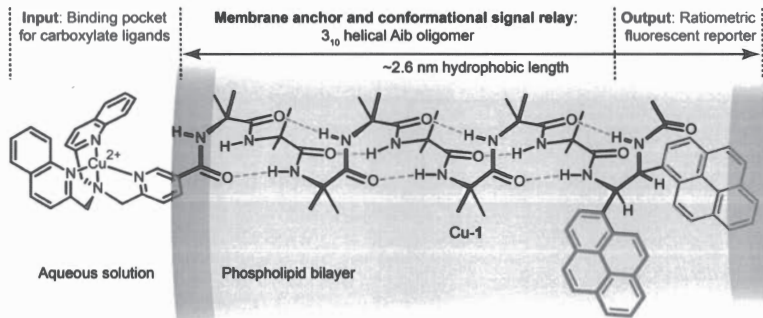
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# Dynamic foldamers as biomimetic communication devices

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Biology solves the problem of communicating information through cell membranes by using conformationally switchable proteins such as GPCRs.[1] Synthetic dynamic foldamers built from 2-aminoisobutyric acid (Aib) display switchable conformational preferences[2] that propagate over long ranges.[3] Biological receptors adjust their conformation in response to non-covalent interactions with ligands, and by using competitive boronate ester formation, ion pairing, hydrogen bonding, or metal-ligand interactions it is possible to induce the communication of information through foldamer-based receptor mimics.[4,5] The construction of an artificial GPCR requires molecules that will incorporate themselves into a membrane, and also necessitates the extension of solution state analytical tools[6] to the study of conformation in the membrane phase. Methods employing the tools of solid-state  $^{19}\text{F}$  NMR and of fluorescence spectroscopy will be described, along with their application to the development of functioning membrane-bound switchable GPCR [7] (below) and photosensitive rhodopsin mimics.[8]



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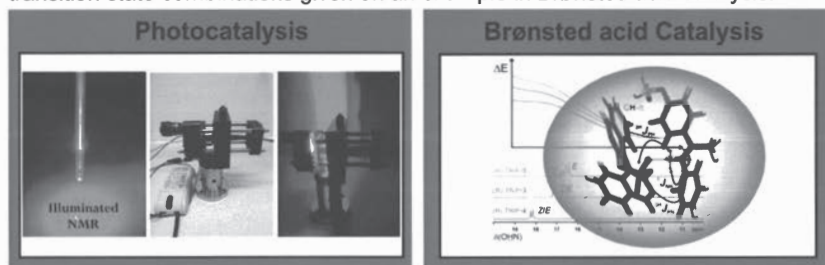
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# Intermediates, Interactions and Transition States in Photo- and Organocatalysis

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The detection and characterization of intermediates in catalytic reactions and the understanding of their key intermolecular interactions is crucial for the rational optimization of reaction conditions. However, in many rapidly expanding fields of asymmetric catalysis, mechanistic studies as well as structural investigations on intermediates or intermolecular interactions are scarce. In this talk I will present results in the field of photocatalysis and Brønsted acid catalysis. First our LED based NMR illumination device will be introduced together with the new triple combination illumination/NMR/UV<sup>1,2</sup> and an NMR access to intermediates below the detection limit.<sup>3</sup> Next applications to photocatalytic reactions show that NMR allows for new mechanistic insights into one- versus two-electron processes or proton transfer mechanisms usually inaccessible to UV/Vis.<sup>4,5</sup> In Brønsted acid catalysis the first detailed ion pair structures of chiral phosphoric acids will be presented.<sup>6,7</sup> Combining NMR data and theoretical calculations the intermolecular interaction pattern and the hydrogen bond properties are used to explain the great success of this class of catalysts.<sup>6,7</sup> Last but not least we merge illumination and Brønsted acid catalysis and present the DTS-hv method (decrypting transition states by light), the first experimental access to active transition state combinations given on an example in Brønsted acid catalysis.<sup>8</sup>



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# Mechanistic Insight into Homogeneous Catalysis from Multi-Nuclear High Resolution FlowNMR Spectroscopy

Catherine Lyall,<sup>1</sup> John Lowe<sup>2</sup> and Ulrich Hintermair<sup>1,2,3</sup>

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The development and optimization of homogeneous catalysts is often hampered by limited insight into the kinetics of the reaction and the transformation of the catalyst during turnover, in many cases enforcing empirical optimization in practice. Rational catalyst and reaction development is only possible through thorough understanding of catalyst activation and de-activation mechanisms, potential resting or dormant states, and the kinetics of the productive cycle (i.e. rate-limiting steps).

We have built a setup in which a reaction vessel is coupled to a NMR flow tube via air-tight small diameter HPLC tubing. With this we can continuously circulate a reaction mixture through the spectrometer, thereby follow the reaction progresses and catalyst transformation under catalytically relevant conditions in real time.

We have characterised the hydrodynamic characteristics of the setup and measured flow effects on continuous NMR acquisition to quantify changes in  $T_1$ ,  $T_2$  and signal intensity as function of volumetric flow velocity.<sup>1</sup> Application in real-time reaction and catalyst monitoring under strictly inert conditions has been demonstrated, and multiple solvent suppression and selective excitation techniques allow the detection of minor intermediates even in non-deuterated solvents.<sup>2</sup>

Importantly, the setup also allows monitoring reactions that require continuous delivery of a driving force for turnover, which are difficult to investigate by traditional techniques. For instance, we have recently demonstrated facile monitoring and mechanistic interrogation of a photocatalytic reaction.<sup>3</sup>

Other ongoing projects exploit multi-nuclear techniques, 2D correlation, DOSY, EXSY, pure shift and other advanced pulse sequences for even deeper levels of insight into complex catalytic reaction networks.

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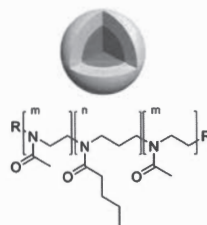
# Structural Insights into Polymer Micelles from Solid-state NMR and Complementary Tools

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Approximately 40% of the currently marketed drugs and even up to 75% of the compounds under development display poor aqueous solubility.<sup>[1]</sup> Thus, transporting them through the body and improving their bioavailability is a major challenge. Polymeric micelles encapsulating the drug molecules represent one possibility to do so.<sup>[2]</sup> However, structural information on these materials is difficult to obtain due to their low degree of order.



Solid-state NMR in general and proton detected experiments in particular are very sensitive to changes in the local environment and intermolecular interactions as well as to solid-state dynamics. Furthermore, the analysis is possible for a broad range of materials, especially because it is not limited to crystalline forms.

In the presented project, we analyze polymer formulations with varying amounts of encapsulated molecules by using different solid-state NMR experiments and complementary techniques. This data is compared to the respective pure compounds in both the crystalline and the amorphous state. It can be shown that a higher loading of the micelles results in a lower degree of order in the micellar core. Changes in chemical shift and line shape contain information on the arrangement and dynamics of drug and polymer, while contacts in 2D NMR can help to improve the picture we are starting to paint.

We now work on correlating the structural information with properties in more physiologically relevant conditions.

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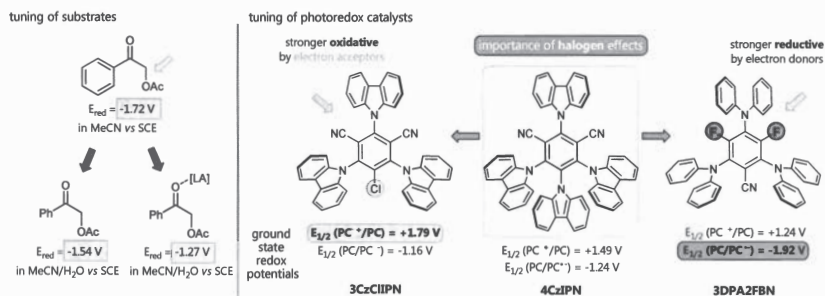
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# Tuning redox potentials in photocatalysis: Strategies for C-O-bond activation and broadly applicable metal-free photoredox catalysts

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Redox properties of substrates and photocatalysts are often critical elements for the successful realization of a proposed photocatalytic transformation. While the choice of a specific photo(redox) catalyst is important for the mechanistic course of the reaction with respect to reductive or oxidative quenching cycles, additional tuning is available by the implementation of multicatalytic procedures.<sup>[1]</sup> LUMO lowering strategies, such as Brønsted acid catalysis, Lewis acid catalysis or the activation by 2c3e- or hydrogen bonds, can contribute to e. g. facilitate the reduction of carbonyl groups. We have used a multicatalytic approach for a C-O bond activation-based cross coupling of  $\alpha$ -acetoxy ketones with styrenes.<sup>[2]</sup>



We further show that deliberate structural manipulations of cyanoarene derivatives including halogen core substitutions can be used to predictably modify the redox potentials of such donor-acceptor type catalysts in a broad range to provide strongly reducing to highly oxidative photocatalysts that additionally stand out due to their remarkably balanced redox potentials.<sup>[3]</sup>

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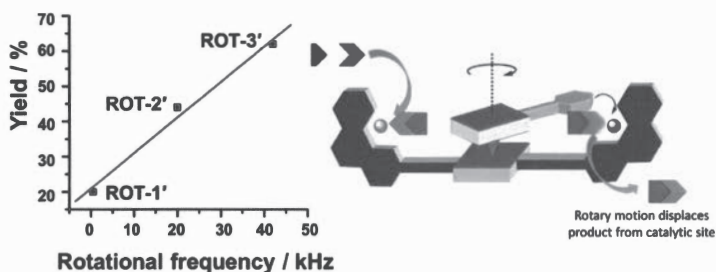
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# Multicomponent Catalytic Machinery: How the Machine Speed Impacts Catalytic Activity

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While nature has built and optimized rotating catalysts (e.g. ATP synthase) over millions of years with the purpose to improve catalytic conversion for instance by eliminating product inhibition, abiotic examples using analogous nanomechanical action in catalysis have been lacking. Recently, we have developed examples of multicomponent machinery that operate by two distinct novel mechanisms. The first machinery operates by dynamic allosteric effect that leads to an increasing liberation of catalyst into solution the higher the rate of machine motion.<sup>[1]</sup> In the second example, product inhibition is increasingly reduced at augmented machine speed.<sup>[2]</sup> The complete mechanism of action in both catalytic machinery has been clarified by a variety of physical organic methods, including VT-NMR to determine the machine speed, evaluation of the catalytic rate at zero conversion ( $v_0$ ), binding constants, speciation analysis and product liberation studies.



**Figure 1.** Cartoon representation of the multicomponent catalytic machinery that increases conversion due to reduction of product inhibition at higher machine speed.

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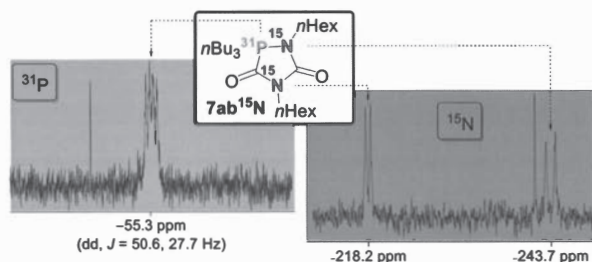
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# Transient Intermediates in the Phosphane-Mediated Trimerization of Isocyanates

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The Umpolung reaction of electrophiles through addition reaction with common Lewis bases such as phosphanes and amines represents a key step in many Lewis base-mediated addition reactions.<sup>[1-3]</sup> For the example of the phosphane-catalyzed oligomerization of isocyanates, the structure of a transient catalytic intermediate has now been re-assigned using <sup>15</sup>N-labeled isocyanates in combination with low temperature <sup>1</sup>H/<sup>13</sup>C/<sup>15</sup>N NMR measurements. Structural assignment of the five membered ring intermediate is largely facilitated through comparison of experimentally measured and theoretically calculated NMR chemical shifts.<sup>[3]</sup>



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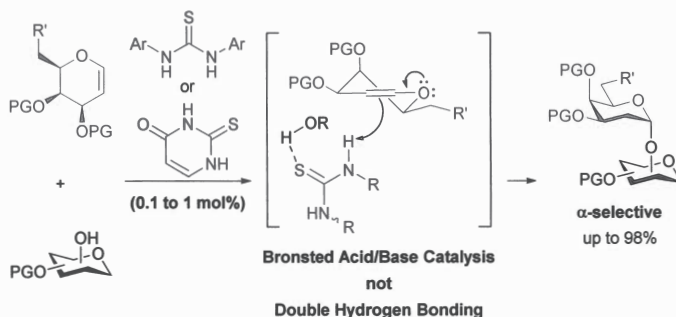


# On the Mechanism of Organocatalytic Glycosylations

A. C. Colgan, G. A. Bradshaw, I. Pongener, N. P. Allen, M. B. Boland, Y. Ortin and E. M. McGarrigle

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Thiouracil, and structurally related molecules, catalyze stereoselective glycosylations with galactals in loadings as low as 0.1 mol%.[1] It is proposed that in these glycosylations thiouracil, monothiothalamide, and the previously reported catalyst,[2] Schreiner's thiourea, do not operate via a double H-bonding mechanism but rather by Brønsted acid/base catalysis. Evidence to support this proposal will be presented. Our results are in line with calculations by Varga, Pápai and co-workers[3] on the THP protection of alcohols catalyzed by thioureas.[4] In the course of our studies we uncovered a catalyst poison arising from the benzylation of alcohols in DMF in the preparation of our glycal substrates.[5]



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# Early Pathways to Life: Mechanisms to Molecular Evolution and Homochirality

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Mechanisms leading to a molecular evolution and the formation of homochirality in nature are interconnected and a key to the underlying principles that led to the Origin of Life. In this presentation I will focus on mechanisms that lead to the formation of homochirality by creation of self-amplifying and auto-catalytic molecular networks. The most prominent example of an autocatalytic process that leads to high amplification of chirality is the Soai reaction, where aldehydes are transformed into the corresponding alcohols by addition of dialkylzinc reagents. Mechanistic investigations and a novel mechanism of the Soai reaction will be presented with a focus to transfer the knowledge to reactions that are relevant in the context of Origin of Life. The understanding of such complex mechanisms leading to amplification of chirality is important to identify potential catalysts and active species in molecular networks that are formed under prebiotic reaction conditions. Furthermore, an autocatalytic system that is able to show molecular evolution will be discussed.

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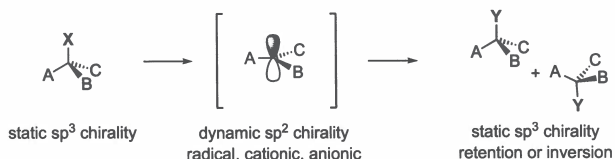
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# Memory of Chirality in Flow Electrochemistry

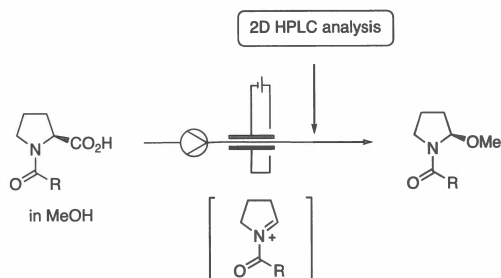
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Memory of chirality is describing a principle where the chirality of the starting material is preserved in a reactive intermediate for a limited time, while the original stereocenter is functionalized through a cationic, anionic or radical intermediate.<sup>[1]</sup>



First successful reactions to capitalize on this principle were designed by Fuji.<sup>[2,3]</sup> We use a reaction of proline derivatives<sup>[4]</sup> employing a recently developed flow electrochemical reactor to demonstrate the memory of chirality in flow chemistry.<sup>[5]</sup> The combination with inline 2D HPLC allows rapid stereochemical analysis and therefore a fast optimization of reaction conditions.



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# Elucidating crystallization mechanisms by cryogenic electron microscopy

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Obtaining a comprehensive picture of how molecular or atomic order evolves during crystallization is a long-standing challenge. It has been recognized recently that nonclassical crystallization from solution involving transient amorphous precursor phases is common. Understanding the morphological and structural properties of these precursors, and how they evolve into crystals is a key challenge in inorganic, protein, and organic crystallization. We will describe our recent studies on crystallization of organic molecules and proteins by cryo-TEM imaging and cryo-STEM tomography. We show that crystallization involves initial densification of various pre-nucleation aggregates, followed by gradual ordering concomitant with continuous densification and change in morphology. This mechanistic picture reveals that density, molecular ordering, and morphology are intimately connected and develop gradually, providing a unifying view on how different amorphous precursors convert into crystals.

# Quantifying Dispersion Effects on Structure and Bond Strengths in the Gas Phase and in Solution

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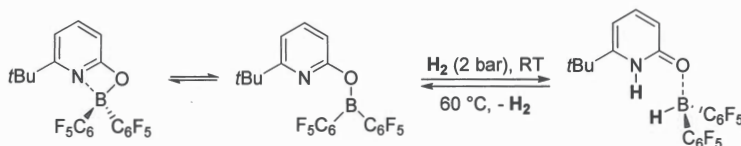
Van der Waals attractive forces have often been neglected because each individual interaction is small. Nevertheless, for organic and organometallic molecules of distinctly moderate size, e.g. 100-200 atoms, the large number of small, attractive interactions can add up to a significant contribution to the bond dissociation energy, in the range of tens of kcal/mol, or a different gross structure. We report experimental measurement of bond dissociation energies for large molecules in the gas phase, as well as solution measurements for the same molecules, that quantify the interactions and provide the data for intuitive interpretation of how dispersion works in organic reactions. We accompany the experimental work with extensive quantum chemical calculations using DFT and DLPNO-CCSD(T) methods taken to the CBS limit. We furthermore show structural determinations for large organic and organometallic ions using vibrational predissociation spectroscopy of electrosprayed ions at temperatures as low as 10K. The IR spectra provide an independent experimental measurement of dispersion interactions. Lastly, we treat solvation with dispersion-corrected PCM models. 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.

# Reversible Hydrogen Activation by a Pyridonate Borane Complex: Combining Frustrated Lewis Pair Reactivity with Boron-Ligand Cooperation

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In recent years, metal-ligand cooperation has emerged as a powerful tool for sigma-bond activation by transition-metal complexes.<sup>[1]</sup> In this work, a pyridone borane complex that liberates dihydrogen under mild conditions is described.<sup>[2]</sup> The reverse reaction, dihydrogen activation by the formed pyridonate borane complex, is achieved under moderate H<sub>2</sub> pressure (2 bar) at room temperature. The reversible dihydrogen activation was monitored by *in situ* <sup>1</sup>H and <sup>11</sup>B NMR spectroscopy.



**Figure 1:** Reversible hydrogen activation by a pyridonate borane complex via boron-ligand cooperation.

DFT and DLPNO CCSD(T) computations reveal that the active form of the pyridonate borane complex is a boroxypyridine that can be described as a single component Frustrated Lewis Pair (FLP). Our investigations show that the boroxypyridine undergoes a chemical transformation to a neutral pyridone donor ligand in the course of hydrogen activation. This mode of action may thus, in analogy to metal-ligand cooperation, be regarded as an example of boron-ligand cooperation. First applications of the pyridone borane complex that rely on the concept of boron-ligand cooperation in metal-free catalytic transformations will be presented.

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# Photoinduced porphyrinoid catalysis - the need to elucidate the mechanism

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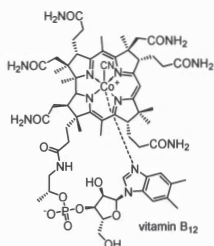
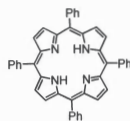
*"Look deep into nature, and then you will understand everything better."*

*Albert Einstein*

Our life depends on porphyrinoids and these tetrapyrroles are referred as pigments of life. Among them are chlorophylls, which in the first instance are responsible for transforming light energy into the chemical reactivity with the ultimate production of starch (**photosynthesis**). Following nature, we have been exploiting potential of porphyrinoids and the unlimited source of solar energy in catalytic reactions.

Over the years, impressively divers range of photochemical reactions has been developed, they are mainly catalyzed by ruthenium and iridium complexes. On the other hand organic dyes exhibiting considerable advantages have been also shown to act as photocatalysts with eosin Y being the most widely studied.

The presentation will highlight a successful application of porphyrinoids (porphyrins, vitamin B<sub>12</sub>) as photosensitizers and as photoredox catalysts for visible-light induced selective functionalizations, including photooxidation of aldehydes,<sup>[1]</sup> alkylation of carbonyl compounds,<sup>[2]</sup> olefins,<sup>[3]</sup> and indoles, arylation of heteroarenes,<sup>[4]</sup> acylation of olefins,<sup>[5]</sup> deallylation of allyloxyarenes<sup>[6]</sup>. Mechanistic aspects of these transformations will be discussed.



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# Deciphering the structure, dynamics, and chirality of complex molecules

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The precise knowledge of the structures of molecules and their ability to form dedicated non-covalent intermolecular interactions is of fundamental use for understanding their function. High-resolution rotational spectroscopy provides an outstanding tool to determine accurate molecular structures in the gas phase and thus free of solvent and crystal effects. These conditions allow for a direct comparison and benchmarking with quantum-chemical experiments.

Of particular interest for us are the roles of conformational flexibility, non-covalent interactions, and chirality in molecular processes. We use broadband rotational spectroscopy (complemented by quantum-chemical calculations and other spectroscopy techniques) to evaluate how molecules bind to each other and to establish a hierarchy of intermolecular interactions. These studies are also relevant with respect to the first steps of aggregation, such as in soot and grain formation, and can thus provide important insight into the transition from the isolated molecule to the bulk.

In a related branch of research, we focus on characterizing, controlling, and finally manipulating chirality. Using the new microwave three-wave mixing approach, which is non-linear and resonant, we can differentiate enantiomeric pairs of chiral molecules using tailored microwave pulses. The technique is uniquely mixture-compatible and allows for enantiomer separation, as will be discussed.



# Electrostatic Gating and Solvent Holes in the Mechanism of Carbocation Reactions

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Mechanisms in solution are generally viewed as completely defined by a sequence of transition states and intermediates connecting the reactants to the products. In recent years, however, there has been an explosion in the recognition of reactions that are not describable so simply. The regular mechanistic paradigm fails when the understanding of experimental observations requires the consideration of additional information, such as the multifurcating shape of an energy surface, the excess energy in an intermediate and its distribution, or the non-equilibrium solvation of structures. We describe all such reactions as involving “dynamic effects” in that they possess experimental characteristics that can be understood by allowance for the motions and momenta of atoms, if not for now by the standard statistical theories of chemistry. The common denominator for dynamic effects is *time*. That is, when an experimental observation is associated with the evolution of a sufficiently short-lived structure, whether it is a formal intermediate or simply on the slope of an energy surface, then the inaccuracy or inapplicability of statistical theories is unsurprising.

Carbocations are generally short lived, making their reactions ripe for dynamic effects, but the abundant observations in classical carbocation chemistry have usually been fit by implicit assumption into a normal mechanistic model in which the carbocations act as ordinary intermediates and their reactions are controlled statistically by barrier heights. We describe were the failure of such models to account for a textbook observation, the preferential kinetic formation of 1,2-adducts in the addition of acids to 1,3-dienes. We find that simplified models for such additions are inadequate to account for product mixtures, but QM/QM simulations of additions in explicit solvent perform well in predicting experimental observations.

These simulations describe a reaction in which solvation dynamics are paramount. Very few trajectories started from the apparent free-energy transition state cross from starting material to product. Instead, they recross the TS, either because the solvation prohibits the formation of charge or, in the opposite direction, stabilizes charge so greatly that reversion to uncharged starting materials is prohibited. Once an ion pair is formed, the solvation dictates what happens next. Part of the time, the ion pair is relatively unstabilized and the ions are forced for form an uncharged product immediately. Alternatively, the solvation may so stabilize the ion pair that it becomes long-lived and must await thermal activation to complete the reaction. A final portion of the time, the solvation forces immediate dissociation of the ion pair. Experimental observations then reflect the combination of these events.

# **Abstracts of Posters**

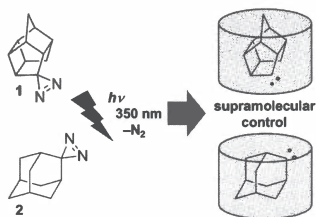
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# From polycyclic diazirines to carbenes: supramolecular control of photoreactivity

**M. Alešković, T. Šumanovac, M. Matković, K. Mlinarić-Majerski,  
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Photochemical elimination of nitrogen from diazirines leading to carbene intermediates is a valuable tool for investigating carbene reactivity.[1] Platz *et al.* reported spectroscopic studies on adamantane diazirine **2**,[2] whereas Bonneau, Wirz *et al.* indirectly proved the formation of carbenes by trapping them with pyridine and obtaining the corresponding ylides.[3] However, photochemical reactivity of pentacycloundecane (PCU) diazirine **1** has not been explored in such detail.



As part of our interest in the chemistry of carbenes and synthesis of strained molecules,[4] we prepared diazirines **1** and **2** and studied their photochemical reactivity in different solvents and in different supramolecular host molecules. We found that the presence of supramolecular hosts indeed affects the photochemical reaction pathways, *e.g.*, complexation of diazirines with cyclodextrins ultimately changes the relative ratio

of singlet and triplet carbene products. Furthermore, we found that product formation from singlet carbenes involves protonation and formation of carbocations, experimentally confirmed by the observed rearrangement of the PCU skeleton. We additionally corroborated our results by performing DFT computations on the starting diazirines as well as on the formed carbene intermediates.

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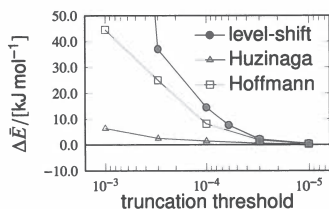
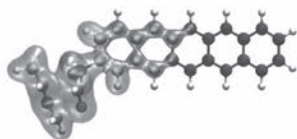
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# Reaction Energies from Automated “Exact” DFT Embedding

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Describing the reaction energetics of large molecules can be a demanding task for correlated wavefunction (WF) methods or (double) hybrid functionals. Embedding approaches like WF-in-density functional theory (WF-in-DFT) [1, 2, 3] can help reducing this cost. Exact embedding (within a DFT context) of the desired method can be achieved using projection-based embedding (PbE) [4]. However, the computational cost of the embedded calculation is only reduced significantly if PbE is used in combination with a basis set truncation scheme [5, 6]. Furthermore, the results of the embedding ansatz depend highly on the choice of the embedded region [7].



In this work the effect of basis set truncation in DFT-in-DFT embedding in combination with different approaches [4, 8, 9] to PbE is investigated and an automatization scheme for the selection of the active region for chemical reactions is presented. Example reactions are investigated based on this novel approach.

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# Postfunctionalization of Rhodium(II) Complexes and their Application as Bifunctional Catalysts for Site-Selective Nitrenoid Reactions

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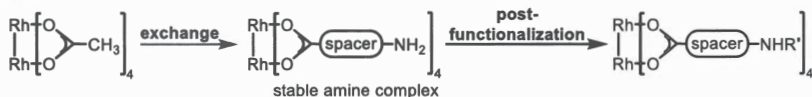
We present a new synthesis of dirhodium(II) carboxylates, which are catalysts for carbene<sup>[1]</sup> and nitrene<sup>[2]</sup> transfer reactions. Rhodium carboxylates are typically prepared in two steps, including the synthesis of the ligand and a ligand exchange with rhodium(II) acetate.<sup>[3]</sup> These ligand exchange conditions do not tolerate a large variety of functional groups such as double bonds, triple bonds or nucleophilic atom containing moieties.<sup>[4]</sup> By reversing the traditional approach, we were able to isolate a stable rhodium carboxylate complex containing a free amine. The postfunctionalization of this amino complex enables the incorporation of a great variety of functional groups, thus paving the way to new classes of polymeric catalysts, polymetallic complexes, and bifunctional catalysts.

As a demonstration of the power of this novel approach, we prepared a bifunctional catalyst capable to perform site-selective nitrenoid insertions by remote hydrogen bonding control.

previous work:



this work:



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# First Generation of *cis-cis*-Dihydroxycarbene by NIR Excitation in Solid Nitrogen and its Disappearance through Tunneling

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While quantum-mechanical tunneling (QMT) was recognized early in the emerging field of quantum theory as an accelerating effect in chemical reactions,<sup>[1]</sup> its fundamental importance beyond kinetic and thermodynamic control for chemical reactions was demonstrated only recently.<sup>[2,3]</sup> As a means to an end, matrix isolation was utilized to generate, trap, and identify reactive intermediates that undergo spontaneous QMT.<sup>[4]</sup> In case of higher-energy conformers, selective excitation with near-infrared light (NIR) is suitable to prepare one desired conformer.<sup>[6-9]</sup> Such experiments provide insights into medium effects<sup>[10]</sup> and conformation dependent QMT.<sup>[11]</sup> Here we show the results of our reinvestigation of dihydroxycarbene, an activated isomer of formic acid,<sup>[12]</sup> that displays an intricate QMT process.

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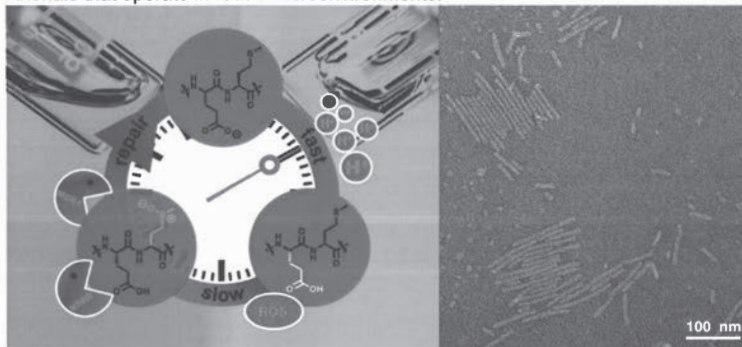
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# Transient Supramolecular Assemblies Mediated by Redox-Responsive Subunits

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Spatial and temporal control are critical properties to advance and optimize functional (macro)molecular materials in order to mimic key features of living systems. [1] In my lecture, I will discuss our methodology in developing non-equilibrium states in supramolecular polymers and materials. We have expanded our concept of charge regulated  $\beta$ -sheet self-assembly [2] of alternating hydrophilic and hydrophobic amino acids in order to introduce redox-switchable properties. An interplay of pH- and oxidation-stimuli, promoted by the production of reactive oxygen species (ROS) thus leads to transient supramolecular polymerizations of methionine containing amphiphiles, with tuneable lifetimes and stabilities of the hydrogels. [3] The incorporation of triethylene glycol chains introduces thermoresponsive properties to the materials, which operates in a biomedically relevant temperature range of 30 - 40 °C. Repair enzymes are able to reverse the oxidative damage in the methionine-based thioether side chains and thus reinitiate supramolecular polymerization. Reactive oxygen species play an important role in signal transduction cascades, and our strategy therefore offers great potential for applications in dynamic biomaterials that operate in redox microenvironments.



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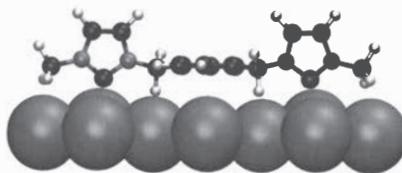
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# Computational Studies on NHC-Ligands on Metal Surfaces

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N-heterocyclic carbenes (NHCs) have emerged as valuable ligands for the functionalization of metal surfaces [1, 2]. Such modified surfaces show enhanced stability compared to their thiol-modified equivalents [3, 4] and were successfully utilized in biosensing [5] and catalysis [6, 7]. Lately, it has been shown that multidentate NHCs can be employed to achieve improved material stability as well as enhanced catalytic activity for selected reactions, taking advantage of the chelate effect [6, 8]. However, the influence of the nature of the linker connecting the NHC-units remains to be investigated in order to access the full potential of applications. Density functional theory (DFT) is a powerful tool to characterize and design new materials [9, 10], which has already provided important insights into the interactions between NHCs and surfaces [3, 11–13]. Here, we compare the adsorption geometries of bidentate NHC-ligands connected by various linkers and examine how the structure of the linker affects the adsorption properties on different metal surfaces.



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# Activation of Carbonyl Electrophiles by Molecular Iodine

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In the last years, halogen bonds have been shown to catalyze different organic transformations.<sup>[1]</sup> In this context, we have analyzed the reaction mechanisms of iodine-catalyzed Michael additions and were able to show that indeed a halogen-bond activation of the carbonyl group is most likely.<sup>[2]</sup> Other modes of activation such as a hidden Brønsted-acid catalysis could for the first time be ruled out experimentally.

Subsequently, we have investigated experimentally and computationally whether molecular iodine can be employed in other reactions and whether other monodentate halogen-bond donors like halogenated azolium salts or imides can replace iodine to activate carbonyl electrophiles (Figure 1).<sup>[3]</sup> Interestingly, many halogen-bond donors turned out to be catalytically active albeit with lower reactivities.

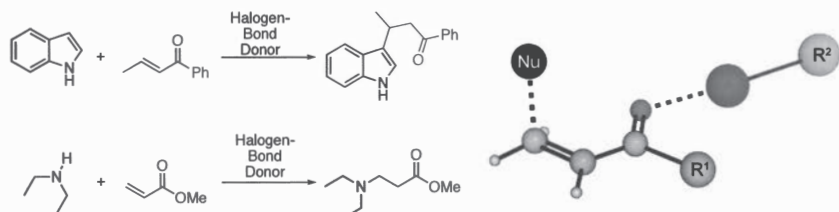


Figure 1: Halogen-bond activation of carbonyl electrophiles in Michael additions.

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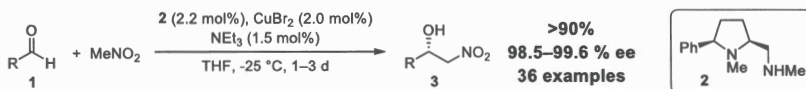
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# Enantioselective, Cu-Catalyzed Henry Reactions: Unravelling the Mechanism

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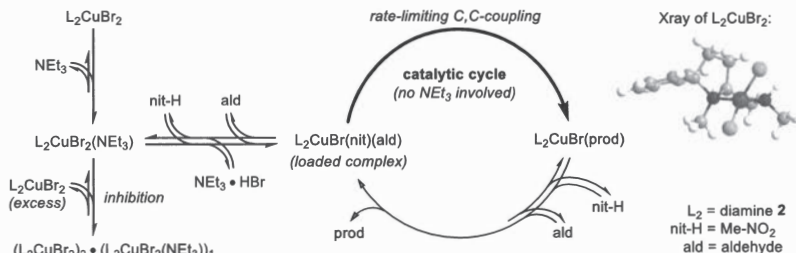
The Cu-catalyzed, enantioselective Henry (nitro aldol) reaction is a powerful asymmetric C—C bond forming reaction. In 2014, we introduced the chiral diamine ligand **2**,<sup>1</sup> which is still unrivalled and permits  $\geq 98\%$  ee in the addition of nitromethane to a series of aromatic, heteroaromatic, vinylic, and aliphatic aldehydes **1** (36 examples).<sup>2</sup>



**1**, **3**: R = aryl, hetaryl, vinyl, alkyl (for R = alkyl, a 4-fold amount of **2**, CuBr<sub>2</sub>, and NEt<sub>3</sub> was used)

Cu-catalyzed Henry reactions are supposed to follow an uneventful mechanism. Our investigations<sup>3</sup> (competition, deuteration, and NLE experiments, <sup>1</sup>H NMR studies, kinetic measurements by react-IR), however, revealed a more complex mechanism, in which the ancillary base NEt<sub>3</sub> is not part of catalytic cycle. An unusual, reversible inhibition of the catalytically active species in the presence of an excess catalyst (L<sub>2</sub>CuBr<sub>2</sub> > NEt<sub>3</sub>) was observed.

## Proposed Mechanism



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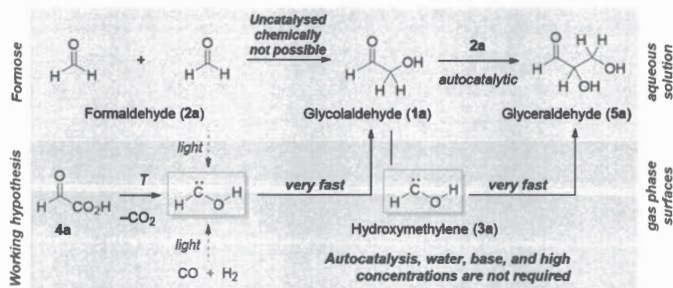
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# Gas-phase sugar formation using hydroxymethylene as the reactive formaldehyde isomer

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Carbohydrates  $(\text{CH}_2\text{O})_n$  or sugars are the formal adducts of carbon (atoms) to water with a repeating unit that structurally resembles  $\text{H}-\ddot{\text{C}}-\text{OH}$  (hydroxymethylene, **3a**). Although hydroxymethylene has been suggested as a viable building block for sugar formation, it is a reactive species that had escaped its detection until recently.<sup>[1]</sup> Here we demonstrate that formaldehyde (**2a**) reacts with its constitutional isomer hydroxymethylene to give glycolaldehyde (**1a**) in a nearly barrierless reaction.<sup>[2]</sup> This carbonyl-ene-type transformation operates in the absence of base and solvent at cryogenic temperatures similar to those found in extraterrestrial environments or interstellar molecular clouds. Hydroxymethylene acts as a building block for an iterative sugar synthesis as we demonstrate through the formation of the triose glyceraldehyde (**5a**). The results, therefore, provide a link between the well-known formose (Butlerow) reaction and sugar formation under non-aqueous conditions.<sup>[3-4]</sup>



**Figure 1:** Mechanistic hypotheses related to sugar formation from formaldehyde.

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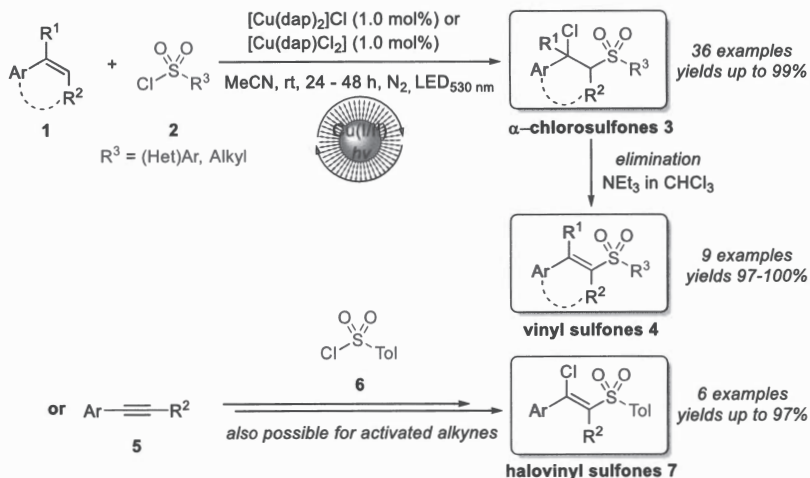
# Visible Light Mediated Copper Catalyzed Chlorosulfonylation of Alkenes and Alkynes

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A visible light mediated photocatalyzed protocol utilizing copper-phenanthroline based catalysts has been developed to convert a large variety of styrene and phenylacetylene derivatives into their chlorosulfonylated products. Besides the Cu(I)-complex [Cu(dap)<sub>2</sub>]Cl, which is now well-established in photo-ATRA processes<sup>1,2</sup>, the corresponding Cu(II)-complex [Cu(dap)Cl<sub>2</sub>] proved to be often even more efficient in the title reaction, being advantageous from an economic point of view, but also opening up new avenues for photoredox catalysis. Moreover, those outperformed commonly used ruthenium, iridium or organic dye based photocatalysts. Additionally, the obtained photoproducts can be smoothly converted in one step giving rise to the corresponding vinyl sulfones in almost quantitative yields, which are of great importance for several fields in synthetic organic as well as medicinal chemistry.<sup>3</sup>



Scheme 1. Visible light mediated copper catalyzed chlorosulfonylation of alkenes and alkynes.

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# Electrochemistry of single molecules by atom manipulation

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The charge state of an adsorbed molecule significantly affects its physical as well as its chemical properties, for example, adsorption position, molecular conformation and aromaticity. The proven capabilities of single-electron sensitivity [1,2] and atomic-resolution [3] of atomic force microscopy (AFM) make it an ideal tool to perform charge-state manipulation while atomically resolving the induced changes within the molecule. Here, we present AFM-based results that demonstrate both the control in charge-state and the capability of resolving the atomic structure of a single molecule for various chemical compounds.

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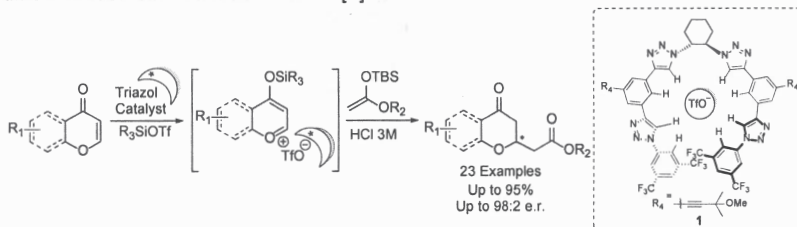
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# Helical Multi-Coordination Anion-Binding Catalysts Enable Highly Enantioselective Dearomatization of Pirylium Derivatives

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Dariusz G. Piekarski<sup>1</sup> and Olga García Mancheño<sup>1\*</sup>

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Asymmetric anion-binding catalysis,[1] which relies on the activation of the ionic substrates by the catalyst binding to their counter-anions and formation of a chiral contact ion pair, has become a powerful synthetic tool, offering new possibilities in the area of enantioselective catalysis. To contribute to the development of new multicoordination anion-binding catalysis, the C-H bond-based chiral tetrakis triazole **1** with distinct confined anion-binding pockets was designed to carry out the nucleophilic dearomatization[2] reaction of *in situ* generated pyrylium derivatives. However, they present intrinsic reactivity and selectivity issues: *i*) in most cases nucleophilic reactions to pyrylium salts lead to decomposition or ring-opening adducts, *ii*) they are less reactive than non-conjugated oxonium ions, and *iii*) it is not easy to fine-tune the stereoelectronic properties on the substrate, making enantio-differentiation difficult to be realized.[3]<sup>†</sup>



Under the optimal reaction conditions, the helical catalyst **1** shows very high catalytic activity, allowing the use of low catalytic loadings (1-5 mol%) while providing a simple access to chiral chromanones and the more challenging dihydropyrones in high enantioselectivities (up to 98:2 e.r.).[4]

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# Brønsted Acid Catalysis – Structural Preferences and Hydrogen Bonding in Imine•Phosphoric Acid complexes

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Despite the growing number of theoretical,<sup>1</sup> experimental<sup>2</sup> and spectroscopic<sup>3,4</sup> studies on activation modes and the origin of stereo induction in Brønsted Acid Catalysis, a prediction of the optimal catalyst choice often remains elusive. On the example of asymmetric transfer hydrogenation of imines with Hantzsch ester, four different chiral phosphoric acids (CPA) have been investigated together with various aromatic imines in regard of their catalyst•substrate structure to rationalize key factors for the stereoselective outcome. For each catalyst, theoretical and NMR-spectroscopic studies revealed the presence of four binary CPA•imine complex structures, two featuring an *E*-imine and two an *Z*-imine. All complexes are anchored by strong hydrogen bonds. Herein, the structural investigations of *R*-TRIM ((*R*)-3,3'-bis(2,4,6-trimethylphenyl)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate,) are presented. For all TRIM-systems, additionally a dimeric structure of the binary TRIM•*E*-imine complex was identified by characteristic high field shifts and size dependent TROSY effects (transverse relaxation optimized spectroscopy) and DOSY measurements (diffusion ordered spectroscopy). The hydrogen bond of binary TRIM•imine complexes was characterised by a <sup>1</sup>H <sup>15</sup>N chemical shift correlation in a Steiner Limbach curve<sup>5</sup> and <sup>1</sup>J<sub>NH</sub> coupling, revealing strong hydrogen bonds for the mainly ion paired complex. <sup>2</sup>J<sub>PH</sub> and <sup>3</sup>J<sub>PN</sub> trans-hydrogen bond scalar coupling constants were derived by NMR spin echo difference experiments to get insights into the hydrogen bond geometry. The results were corroborated by theoretical calculations.

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# On Steric Stabilization

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3-Hydroxy-1,3-thiazole-2(3*H*)thiones react with *O*-(*tert*-butyl)-*N,N*-diisopropyl isourea to furnish heterocyclic *O*-(*tert*-butyl) thiohydroxamates in up to 64% yield [1]. The compounds are stable crystalline solids, showing carbon-13 resonances for the thiocarbonyl group at 183±1 ppm, and vibrational combinations from the *O*-alkyl thiohydroxamate functional group, situated in the range between 950 and 1300 cm<sup>-1</sup>. 1-(*tert*-Butoxy)pyridine-2(1*H*)thione, prepared similarly, is a labile compound, quantitatively rearranging into *O*-(*tert*-butyl) pyridine-2-sulfenate. Differences in chemical behavior relate to N,O-bond strengths, as expressed for 3-(*tert*-butoxy)-1,3-thiazole-2(3*H*)thiones by a N,O-bond order of 1.4. Molecular orbital theory describes partial multiple bonding between nitrogen and oxygen as  $\sigma$ (N,O)-bond in combination with three superimposed  $\pi$ (N,O)-bonds of different strengths, with the degree of  $\pi$ -bonding increasing with the size of the bond angle at thiohydroxamate oxygen [2]. Photoexciting 3-(*tert*-butoxy)thiazole-2(3*H*)thiones or adding an initiator radical to thiocarbonyl sulfur disconnects ground state stabilizing mechanisms, inducing homolytic breaking of N,O-bond. *tert*-Butoxyl radicals liberated from heterocyclic *O*-(*tert*-butyl) thiohydroxamates in photochemical experiments furnish spin-adducts, which were detected by electron spin resonance spectroscopy, or a 1-(*tert*-butoxy)-2-bromoalkane formed by intermolecularly adding to an alkene in the presence of bromotrichloromethane.

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# Tuning the Switching Properties of Macrocyclic Azobenzenes by Ring Strain

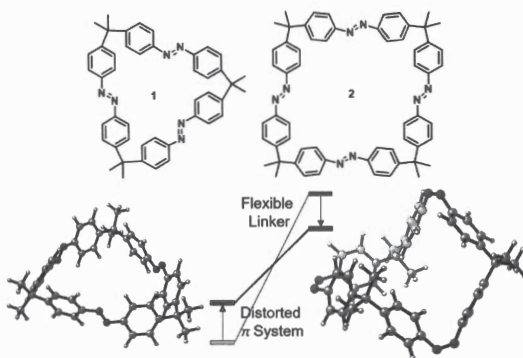
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Azobenzenes have gained increasing interest due to their applicability as molecular switches in diverse scientific fields. Macrocyclic azobenzenes exhibit unique isomerization behavior due to the influence of ring strain.<sup>1</sup> We<sup>2</sup> and others<sup>3</sup> 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.<sup>4</sup> 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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# Structural and kinetic study of two photo- and electrically responsive dithienylethenes

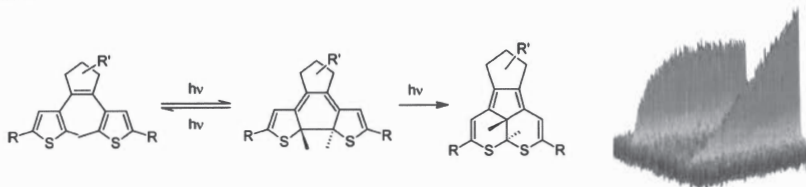
**D. Herold<sup>1</sup>, J. Kind<sup>1</sup>, F. Frieß<sup>1</sup>, J. von Irmer<sup>2</sup>, M. Gallei<sup>2</sup> and C. M. Thiele<sup>1</sup>**

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Smart materials are one of the most innovative and versatile developments during the last decades. These chemical compounds utilize an external stimulus like pH, temperature, light or electric fields to change the physical and chemical properties. Especially light is a fascinating stimulus due to its spatio-temporal controllability.<sup>[1]</sup>

The GALLEI group is investigating stimulus-responsive properties of surface-modified materials.<sup>[2-3]</sup> Recently, two photo- and electrically responsive dithienylethenes, attached to a gold surface, were synthesized and investigated. It could be shown that switchable conductivity for the use in plasmon resonance is possible; however, the rates of forming the reversible and irreversible states (scheme below) were still unknown.



In order to obtain a deeper insight into the reaction schemes not only UV/Vis- but also *in situ* irradiation NMR-spectroscopy was executed.<sup>[4]</sup> With this powerful combination we were able to determine reaction constants for the reversible and irreversible reactions as well as extinction coefficients. This allowed conclusions on possible reaction schemes for both compounds. These photochromic systems of the dithienylethene class show effectively no thermal relaxation and we present their structural and kinetic characteristics.

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# Stereoelectronic Effects in Bicyclo[1.1.1]pentanes: Radical Chlorination and Hydrodechlorination

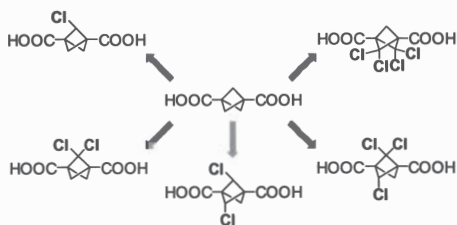
J. Kaleta,<sup>1,2</sup> I. Rončević,<sup>1</sup> I. Čisářová,<sup>3</sup> M. Dračínský,<sup>1</sup> V. Šolínová,<sup>1</sup> V. Kašička,<sup>1</sup> and J. Michl<sup>1,2</sup>

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Radical chlorination of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid is highly selective and up to four chlorine atoms can be introduced relatively easily without damage to the strained bicyclic cage. Combined with hydrodechlorination with  $\text{TMS}_3\text{SiH}$ , direct chlorination provides access to five of the 15 possible chlorinated diacids. Their stereochemistry has been established by X-ray diffraction. Their  $\text{p}K_a$  values have been measured by capillary electrophoresis and calculated at the B3LYP-D3BJ/6-311+G(d,p) level. The results are in good agreement and reflect the expected trend. Strain energy relative to the parent diacid was calculated for all 15 chlorinated diacids and shows a dramatic increase with successive chlorination, due to non-bonded Cl - Cl repulsions. The remarkable stereoselectivity in both the introduction and the removal of chlorine atoms can be understood in terms of stereoelectronic effects (sigma conjugation).



# High-Resolution Pure Shift NMR Techniques for Solution State Structure Determination

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Structure elucidation using liquid state NMR often faces the challenge of insufficient signal resolution, even at the highest field strengths available. This problem is particularly pressing for <sup>1</sup>H spectral dimensions, which feature a narrow chemical shift range, usually paired with complex signal multiplicity patterns originating from homonuclear couplings.

In an attempt to circumvent such limitations if needed, NMR experiments which collapse multiplet signals into singlets by means of homonuclear decoupling have recently attracted much attention<sup>1</sup>. By suppressing homonuclear signal multiplicity, these so-called *pure shift* approaches can provide an enhanced signal resolution, as well as a facilitated analysis, for crowded spectral regions.

This contribution will highlight a number of *pure shift* NMR experiments we have recently developed. COSY- and TOCSY-type *pure shift* experiments are covered, which can be used for <sup>1</sup>H-signal assignment in challenging cases<sup>2,3</sup>. Further, *pure shift* HSQC experiments are discussed<sup>4,5</sup>, which can be utilized for high-resolution signal assignment purposes, as well as for the accurate extraction of residual dipolar couplings (RDCs). These examples shall illustrate the broad potential of *pure shift* techniques for high-resolution NMR studies.

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# Fluoroalkylated Hypervalent Iodine Reagents and their Reactivity with Thiols in Water Solutions

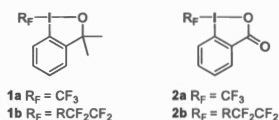
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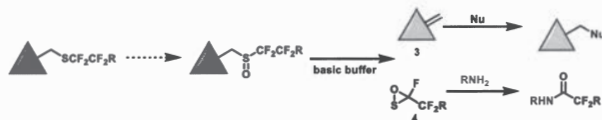
Incorporation of fluorine in biomolecules has many potential applications, such as the study of their structure and conformational changes by <sup>19</sup>F NMR<sup>[1]</sup> or modulation of their function and properties.<sup>[2]</sup> Post-translation selective functionalization is one of the strategies for the introduction of fluorine group, such as CF<sub>3</sub> in proteins.<sup>[3]</sup>

Fluoroalkylated hypervalent iodine reagents **1** and **2** transfer the trifluoromethyl<sup>[4]</sup> or tetrafluoroalkyl groups<sup>[5]</sup> to various nucleophiles, especially reactions with thiols are high-yielding and thiol selective. This exclusive reactivity led us to consider use this reagent for thiol bioconjugation.



Scheme 1. Fluoroalkylated hypervalent iodine reagents

The aim of my work is to optimize conditions for clean and mild thiol modification. Model reactions with cysteine and small peptide were carried out and the influence of pH, amount of cosolvent, reaction time and concentration was investigated. The side products formation (Scheme 2) and mechanism of the reaction was also studied. The limiting factor for the thiol modification seems to be the water solubility of the reagent; therefore synthesis of water soluble analogue of **1** is in progress.



Scheme 2. Side products formation through the reactive intermediates 3 and 4

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# Study of the oxidation reaction of cyclohexanone and its derivatives

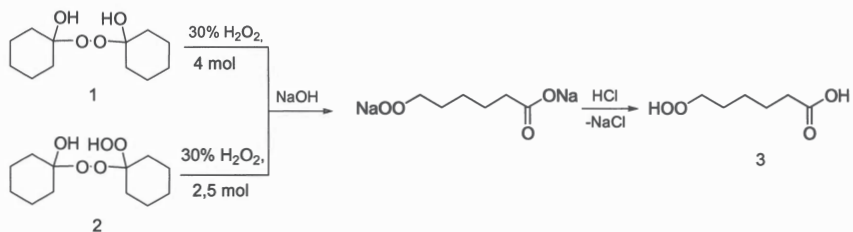
Kateryna Kuznetsova, Natalia Shuliga, Roman Fleychuk, Orest Hevus  
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Therefore, a series of publications describing the synthesis of lactones of  $\omega$ -hydroxycarboxylic acids resulted from oxidation of cyclic ketones with 30% hydrogen peroxide in the presence of various catalysis have been appeared recently [2-5].

The aim of the work was to study the conditions for the oxidation of cyclohexanone and its derivatives - 1,1'-dioxycyclohexanol and 1-[(1-hydroperoxycyclohexyl) peroxy]cyclohexanol.

We have found that the optimal molar ratio of reagents - cyclohexanone, hydrogen peroxide and alkali is 1: 3: 2.1, and the optimum temperature of the process is 20 ... 25 ° C.

It was established that under the above conditions in a similar reaction come not only cyclic ketones but also hydroxyhydroperoxides and dihydroxyperoxides of cyclic ketones:



We study the kinetics of reactions of oxidation cyclohexanone, 1,1'-dioxycyclohexanol (1) and 1-[(1-hydroperoxycyclohexyl) peroxy]cyclohexanol (2). The structure of the synthesized substances has been confirmed by IR- and NMR-spectroscopy data, functional analysis.

## References

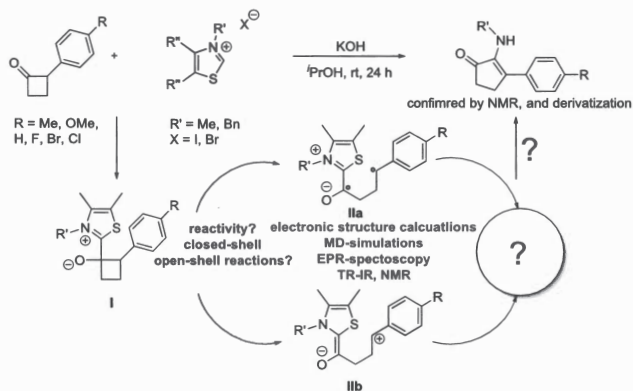
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# One Step Beyond: C–C Bond Activation by N-Heterocyclic Carbenes

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Usually, N-heterocyclic carbenes (NHCs) are the organocatalyst to achieve various 1,2-functionalization of carbonyls, especially aldehydes [1]. What has not been investigated in great detail so far are NHC-catalyzed C–C bond cleavages [2]. Originally being interested in the potential radical species [3] arising from the NHC-adduct **I** (Scheme) we found an interesting ring-enablement reaction providing nitrogen functionalized cyclopentenes.



Mechanistic aspects that will be discussed on the poster are touching the concept of reaction path bifurcations, radical vs. ionic pathways and detailed analysis of the impact of catalyst structure and reaction conditions on the product scope. All data and conclusions are based on experiments, (time-resolved) EPR, NMR and IR spectroscopy and computational chemistry.

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# Computational Chemistry and Organic Synthesis: Let Us Build a Bridge

**B. Maryasin<sup>1,2</sup>, D. Kaldre<sup>1</sup>, D. Kaiser<sup>1</sup>, I. Klose<sup>1</sup>, S. Ruider<sup>1</sup>, G. Di Mauro<sup>1</sup>, A. Pinto<sup>1</sup>, S. Shaaban<sup>1</sup>, M. Drescher<sup>1</sup>, H. Kählig<sup>1</sup>, I. D. Jurberg<sup>3</sup>, L. González<sup>2</sup>, N. Maulide<sup>1</sup>**

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Progress in quantum chemistry and computational techniques allows chemists to understand and predict the outcome of organic reactions in a very efficient fashion. Hereby we demonstrate the power of bridging experiment and theory on some recent examples from our lab.

The Claisen rearrangement is a classical textbook reaction.<sup>1</sup> However, it still holds the potential to provide new experimental results and a series of novel Claisen-type rearrangements have recently been developed by the Maulide group.<sup>2</sup> Our combined theoretical/experimental study of these transformations reveals a diversity of possible pathways and products. The calculations clarify the experimental results and predict new reactions.<sup>3</sup>

The Maulide Group has also discovered a new synthetic approach leading to imidazoles with concomitant observation of an unusual sulfonyl migration.<sup>4</sup> Our in-depth theoretical analysis of possible intermediates and transition states shed more light on this rearrangement.

Moreover, some reactions can even proceed via several different unclear mechanisms. One of those examples is our TEMPO-mediated aminoxylation ofynamides.<sup>5</sup> The calculations explain the experimentally observed phenomena.

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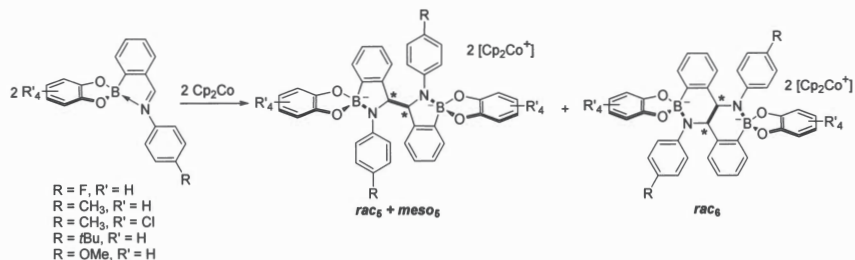
# Reductive Coupling of *N*-Aryl Iminoboronates and B-N Dynamic Covalent Chemistry

Evan N. Keyzer,<sup>1</sup> Alexandru Sava,<sup>1</sup> Tanya K. Ronson,<sup>1</sup> Jonathan R. Nitschke,<sup>1</sup> and Anna J. McConnell<sup>1,2</sup>

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*N*-Aryl iminoboronates are appealing platforms for the investigation of reductive coupling reactions as they are readily self-assembled from an amine, 2-formylphenyl boronic acid and a diol, enabling tuning of their electronic and steric properties. We recently reported the reductive coupling of a series of iminoboronates using cobaltocene gave three isomeric products following the C-C bond formation: the diastereomeric *rac*<sub>5</sub> and *meso*<sub>5</sub> products with coupled five-membered rings and the enantiomeric *rac*<sub>6</sub> with fused six-membered rings (Figure 1).<sup>[1]</sup> The *rac*<sub>5</sub> and *rac*<sub>6</sub> isomers were observed to interconvert through a rearrangement of the dynamic covalent B-N bonds. Investigations into the mechanism for the C-C bond formation and this unusual B-N bond rearrangement will be presented.



**Figure 1.** Reductive coupling of *N*-aryl iminoboronates giving the three *rac*<sub>5</sub>, *meso*<sub>5</sub> and *rac*<sub>6</sub> isomeric products from C-C bond formation (bold) and in the case of the *rac*<sub>6</sub> isomer, rearrangement of the dynamic covalent B-N bonds (also bold).

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# Non-concerted cycloadditions with the S-centered 1,3-dipoles

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Thiocarbonyl S-methylides appears as transient species, which can be conveniently generated via thermal [3+2]-cycloelimination of 2,5-dihydro-1,4,5-thiadiazoles [1]. They belong to the group of the most prominent, so called S-centered 1,3-dipoles with great importance for the synthesis of sulfur heterocycles and olefination reactions (Barton-Kellogg reaction) [2]. Their [3+2]-cycloadditions with electron deficient dipolarophiles demonstrated, that they occur via a zwitterionic intermediates and both 5- and 7-membered cycloadducts, resulting from competitive reactions can be formed [3].

In a series of recent publications, intermediacy of delocalized diradicals was postulated to rationalize the course of some formal [3+2]-cycloadditions of hetaryl thioketones (C=S dipolarophiles) with CH<sub>2</sub>N<sub>2</sub> and its derivatives (as 1,3-dipoles) [4]. Unusual 'head-to-head', step-wise dimerization of chlorinated thiocarbonyl S-imides, leading unexpectedly to 6-membered dimers will be also discussed [5].

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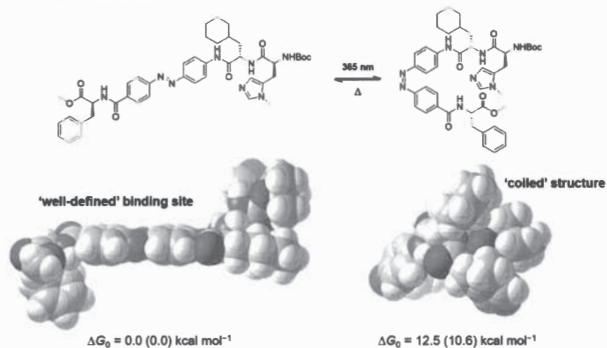
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# Switching Site-Selectivity with Light in the Acetylation of Sugars with Azo-Peptide Catalysts

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Polyols like, e.g., saccharides and polyphenols, are highly important building blocks for the molecules of life and there are numerous protocols for their functionalization. Usually each target structure requires a specific catalyst and well balanced reaction conditions. Therefore, we developed a novel strategy for the design of catalysts that enable the site-selective acylation of a variety of substrates. Inspired by the fundamental work of Feringa *et al.*,<sup>[1]</sup> we used azobenzene-based<sup>[2]</sup> photoswitches to enable peptide catalysts. As catalytic moiety for acylations we chose well established  $\pi$ -methyl-L-histidine (L-Pmh).<sup>[3-6]</sup> The azobenzene backbone itself was synthesized using Mills conditions.<sup>[7]</sup> Photoisomerization of the *E*- to the *Z*-azobenzene catalyst (monitored *via* NMR) with an LED ( $\lambda = 365$  nm) drastically changes the environment around the Pmh moiety and substrate recognition. Thus, catalyst shape allows differentiation of the acylation positions, while the regioselectivity can be controlled through an external stimulus.



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# Mechanistic investigations on interlocked catalysts

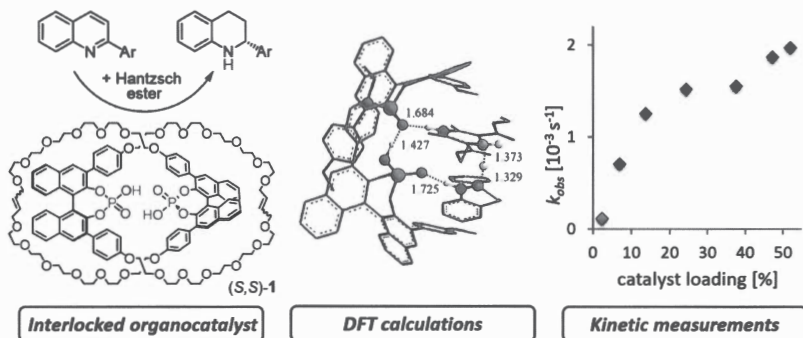
D. Jansen<sup>1</sup> and J. Niemeyer<sup>1</sup>

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The development of highly efficient organocatalysts, for example chiral Brønsted-acids, has revolutionized chemical catalysis in the last decade.<sup>[1]</sup>

Our group has recently developed a chiral bifunctional [2]catenane based on 1,1'-binaphthyl-phosphoric acids.<sup>[2]</sup> We have now investigated the application of this bifunctional organocatalyst for the transfer-hydrogenation of 2-substituted quinolines to the corresponding chiral tetrahydroquinolines. While the catenane-catalyst (*S,S*)-1 gave excellent enantioselectivities, significantly lower selectivities were found for the macrocyclic and acyclic reference systems.<sup>[3]</sup> This works highlights the possible advantages of using interlocked molecules in catalysis and shows that the mechanical bond can be used as a novel design element in catalyst synthesis.

In order to develop a better understanding of the observed stereoselectivities, we have developed a mechanistic model based on DFT-calculations.<sup>[3]</sup> This suggests a cooperative interaction of the phosphoric acids in the stereodetermining reaction step, leading to the observed higher stereoselectivities for the catenated catalyst. To obtain experimental proof for the suggested mechanism, we are currently performing an extensive mechanistic investigation by NMR-analysis of the reaction kinetics.



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# Large-Scale Matrix-Site Changing Mediated by Conformational Conversion

**G. Ogruc-Ildiz,<sup>a,b</sup> G. Tarczay,<sup>c</sup> G. Bazsó,<sup>c</sup> R. Apóstolo<sup>a</sup> and R. Fausto<sup>a</sup>**

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The control of the molecular shape in a very effective way, through selective infrared-induced conformational isomerization in matrix-isolated molecules, has been receiving great attention in our laboratories, since the pioneer studies on formic acid [1,2]. In this communication we report on the first observation of the higher-energy conformer of tribromoacetic acid (*trans*-TBAA) and on a noteworthy phenomenon of matrix-site changing mediated by conformational conversion [3].

The *trans*-TBAA conformer was produced in different cryogenic matrices (Ar, Kr, N<sub>2</sub>) by *in situ* selective narrowband near-infrared excitation of the lower-energy *cis*-TBAA conformer, and characterized both structurally and vibrationally. The novel *trans*-TBAA conformer is shown to spontaneously decay to the most stable *cis*-TBAA form in all studied matrix media, by tunneling, and the measured decay rates in the different matrices were compared with those of the *trans* conformers of other carboxylic acids in similar experimental conditions. In the N<sub>2</sub> matrix, where *trans*-TBAA establishes a specific stabilizing intermolecular interaction with the host N<sub>2</sub> molecules *via* its OH group and is about 11 times more stable than in rare gases matrices, the effect of changing the irradiation wavenumber within the 2νOH absorption profile was investigated in details. A fascinating phenomenon of matrix-site changing mediated by conformational conversion was observed in this matrix: vibrational excitation of *cis*-TBAA predominantly converts the molecules located in a specific “matrix site” into *trans*-TBAA; then, relaxation (by tunneling) of the produced higher-energy conformer back to the *cis* form populates almost exclusively another “matrix site”. The experimental studies received support from quantum chemistry calculations, which allowed a detailed characterization of the relevant regions of the potential energy surface of the molecule and the detailed assignment of the infrared spectra of the two conformers in the various matrices.

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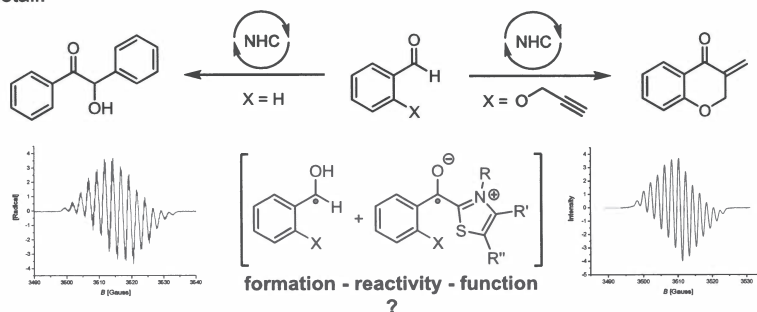
# The Open-Shell Twin of the Breslow Intermediate

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N-heterocyclic carbene catalyzed reactions are the way to realize a 1,2-functionalization of carbonyl compounds. Over the last decades mechanistic studies<sup>[1]</sup> have evolved around the identification and reactivity of the key intermediate - the enaminol or Breslow-intermediate<sup>[2]</sup>.

In our computational and EPR-spectroscopy investigations of the benzoin and hydroacylation reaction<sup>[3-5]</sup> of alkynes we came across an open-shell reactivity of the Breslow-Intermediate leading to NHC-stabilized radicals. The radicals' reactivity, formation and function within the catalytic cycles will be discussed on the poster in detail.



Based on the mechanistic analysis, an outlook on the independent generation of such NHC-stabilized ketyl radicals will be provided and by that shining light on their synthetic potential.

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# Theoretical insights into helical multi-coordination anion-binding catalysis

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Asymmetric anion-binding catalysis<sup>[1]</sup> has become a powerful synthetic tool in the past few years. However, only a limited number of catalyst's motifs are available i.e. based on chiral bidentate N-H and, more recently, O-H hydrogen-donor catalysts such as thioureas<sup>[2]</sup> and silanediols,<sup>[3]</sup> respectively. Additionally, while anion-binding offers a high flexibility and tunability, the non-covalent interactions involved are experimentally more difficult to control compared to the covalent approaches. Therefore, theoretical approaches are necessary to get a complete picture of the many-body reactions and the nature of these weakly interacting complex systems. The outstanding catalytic activity of the Tetrakistriazoles recently developed in our group<sup>[4]</sup> has been investigated with the density functional (DFT-M062X/6-31G(d,p)) and COSMO-RS (sigma surfaces and potentials) theories with Gaussian09 and COSMOtherm programs, respectively. An extensive analysis for model catalyst:guest systems has been performed focussing on their structures, energetics and binding mechanism. Together with NMR experiments, the docking analysis suggests a high order complexation of the catalyst with the ionic substrates.<sup>[5]</sup> Moreover, the calculations confirm the excellent binding properties of the tetrakistriazole catalyst and shed a light on a robust and effective H-donor catalyst design methodology.<sup>[6]</sup>

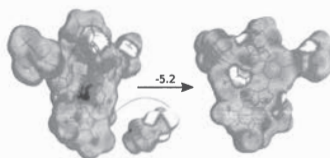


Fig.1 Docking on  $\sigma$ -surfaces (black and white matching).

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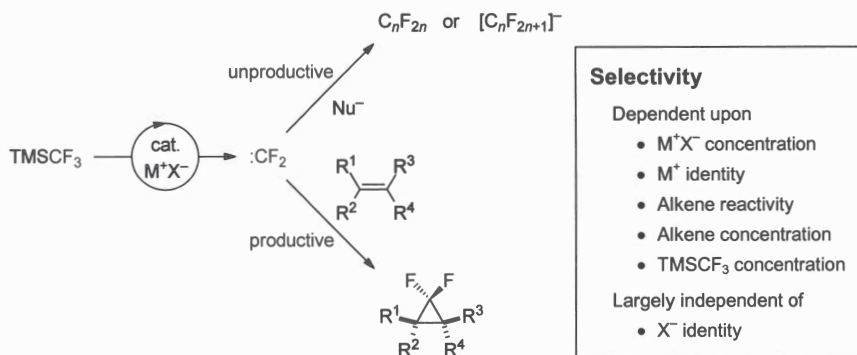
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# Mechanistic Insight into the Anion-Initiated *gem*-Difluorocyclopropanation of Alkenes by TMSCF<sub>3</sub>

Johann J. Primozic,<sup>1</sup> Thomas H. West,<sup>1</sup> and Guy C. Lloyd-Jones<sup>1</sup>

<sup>1</sup>EaStCHEM, University of Edinburgh, Joseph Black Building, David Brewster Road, Edinburgh, EH9 3FJ, U.K.

The mechanism of the anion-initiated *gem*-difluorocyclopropanation of alkenes by TMSCF<sub>3</sub>,<sup>[1]</sup> a versatile reagent in fluoroorganic synthesis,<sup>[2-4]</sup> has been investigated by means of kinetic analysis, stability studies and variation of the initiator M<sup>+</sup>X<sup>-</sup>. The reaction is proposed to proceed via difluorocarbene<sup>[5,6]</sup> (:CF<sub>2</sub>) as an intermediate, generated by an anionic chain mechanism<sup>[7]</sup> from TMSCF<sub>3</sub> with CF<sub>3</sub><sup>-</sup>, [TMS(CF<sub>3</sub>)<sub>2</sub>]<sup>-</sup> and [TMS(CF<sub>3</sub>)F]<sup>-</sup> as chain carriers. Our results suggest that :CF<sub>2</sub> can either undergo a productive [2+1] cycloaddition with the alkene to give the desired product, or an unproductive reaction with CF<sub>3</sub><sup>-</sup> forming various oligomers of :CF<sub>2</sub>. The selectivity of this partition was found to be dependent on the concentration of M<sup>+</sup>X<sup>-</sup>, the identity of M<sup>+</sup>, the concentration and reactivity of the alkene as well as the concentration of TMSCF<sub>3</sub>.



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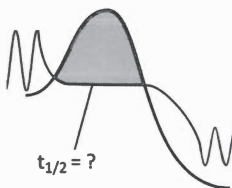
# TUNNEX: An easy-to-use Wentzel-Kramers-Brillouin (WKB) implementation for computing tunneling half-lives

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The outcome of chemical reactions are determined by two factors: the relative stability of the products, and the rate of formation (kinetic *versus* thermodynamic control<sup>[1]</sup>). Usually, the barrier with the lowest energy is the reaction with the highest kinetic rate. Recent experimental findings<sup>[2-6]</sup> imply that the product with the lowest barrier is not always the preferred kinetic product, because the rate is changed by quantum mechanical tunneling (QMT). As QMT is affected by several factors (barrier height and width, mass, temperature, pre-exponential factor) it is difficult hard to intuitively predict whether tunneling plays a role in a given reaction.

We developed tunneling in experiments (TUNNEX), a free open-source program with an easy-to-use graphical user interface to simplify the process of WKB computations.<sup>[7-9]</sup> TUNNEX aims at experimental chemists with basic knowledge of computational chemistry offering the computation of tunneling half-lives, visualization of data, and exporting of graphs. TUNNEX is open source and available at <https://github.com/prs-group/TUNNEX>. As the WKB approximation usually overestimates tunneling half-lives, it can be used to screen tunneling processes before proceeding with elaborate kinetic experiments or higher-level tunneling computations such as instanton theory and small curvature tunneling approaches.



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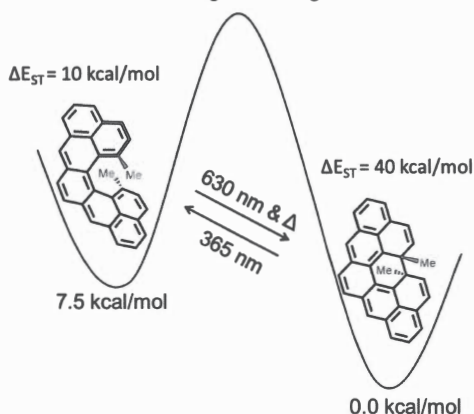
# CETHRENE: A Journey from Reactive Biradicaloid to Effective Chiroptical Photoswitch

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13,14-Dimethylcethrene represents an unprecedented chiral biradicaloid switch. This photochemical switch can be transformed reversibly via conrotatory electrocyclozation to its more stable close form by visible light (630 nm) or heat and switched back to open form by UV light (365 nm), following the Woodward-Hoffmann rules. Upon transformation from open form to the close form the electronic and structural properties such as HOMO–LUMO gap, Singlet–Triplet (ST) gap, and helical twist changes significantly. This allowed us to probe the switching behavior by variety of spectroscopic techniques namely, NMR, UV-vis, and CD. The UV-vis kinetic measurements in toluene and DCM indicated the reaction barrier is solvent dependent and the mechanism of switching is investigated.



In this study we demonstrate how the chemical reactivity of a biradicaloid molecule can be translated into a switching function. Moreover, the DFT calculations revealed that the ST gap of cethrene can be tuned by altering the degree of helical twist. The dimethylcethrene or related structures can be used in design of magneto-chiral switches operated by light.

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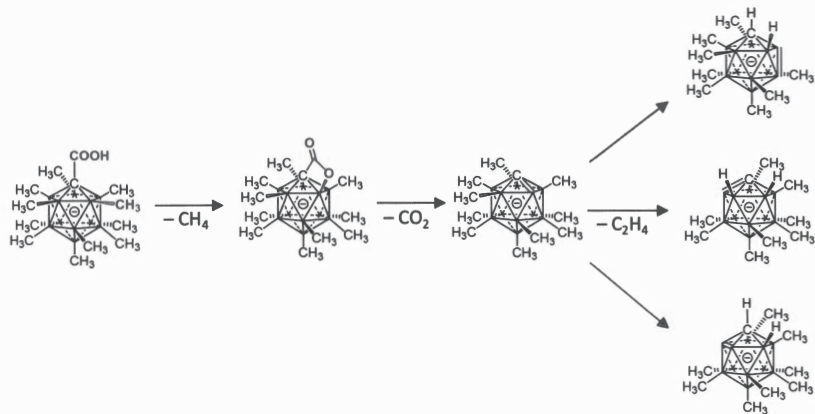
# Fragmentation of CB<sub>11</sub> Anions: Evidence for a Charged Carbyryne Intermediate

Jiří Kaleta,<sup>a,b</sup> Igor Rončević,<sup>a</sup> Josef Cvačka,<sup>a</sup> and Josef Michl<sup>a,b</sup>

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<sup>b</sup>Department of Chemistry, University of Colorado, Boulder, United States

The fragmentation of the HOOC-CB<sub>11</sub>Me<sub>11</sub><sup>-</sup> anion is investigated by collision-induced dissociation (CID) MS/MS and computational methods. Results from both techniques suggest the formation of a previously unreported anionic carbyryne intermediate, formed by the elimination of CO<sub>2</sub> and CH<sub>4</sub> from adjacent substituents on vertices 1 and 2. Going by the aromatic analogy,<sup>[1]</sup> this intermediate is similar to benzyne and has previously been reported to exist in uncharged carboranes.<sup>[2,3]</sup> A series of pairwise losses of adjacent methyl substituents from CB<sub>11</sub>Me<sub>10</sub><sup>-</sup> carbyryne with the missing substituents at the 1,2 positions is also extensively explored. The CID-MS/MS observed elimination of C<sub>2</sub>H<sub>4</sub> is computationally explained as a series of hydrogen transfers driven by the energetically favored saturation of the carbyryne unsaturation.



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# Travel to MARS: Constructing the space around your stereogenic centers

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Routine nuclear magnetic resonance (NMR) spectroscopy of organic compounds is commonly performed in isotropic solution due to the good spectral quality and low experimental effort. In this technique all information on the molecular orientation during acquisition, and thereby anisotropic observables, are lost. An elegant way to fuse anisotropic observables with high resolution NMR is the use of anisotropic solutions like liquid crystalline (LC) phases. This results in interactions similar to solid state NMR spectroscopy like residual dipolar couplings (RDCs), residual quadrupolar couplings (RQCs) and chemical shift anisotropy (RCSA) which all give access to the spatial arrangement of atoms in a molecule.

RDCs have an undeniable use for structure elucidation due to comparatively low effort of measuring and interpreting them.<sup>[1]</sup> A well-known protocol to do so is the singular value decomposition (SVD) based fit of the RDCs to structure proposals.<sup>[2]</sup> By varying the relative configuration or conformation of these structures the best solution can be found.

At the beginning of this millennium MEILER<sup>[3]</sup> and TOLMAN<sup>[4]</sup> derived independently alternative mathematical frameworks for *de novo* model free approaches towards the interpretation of RDCs to obtain information on the structure and dynamics of proteins. The approach introduced by MEILER was refined throughout the years and published as iterative algorithm by LAKOMEK<sup>[5]</sup> in 2006.

Here we describe the implementation (C++ code called MARS – Multiple Alignment analysis of RDCs in Small molecules) of this approach for the determination of relative configurations of organic compounds. This will boost the amount and quality of information obtained on analytes by using RDC datasets from different LC phases.



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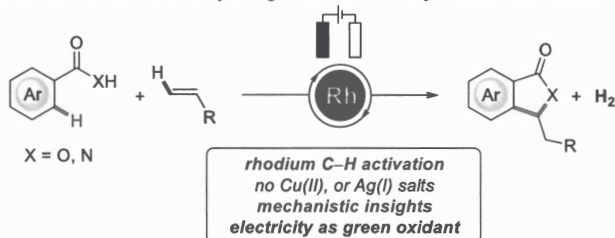
# Electrooxidative Rhodium-Catalyzed Cross-Dehydrogenative Alkenylation

A. Scheremetjew, Y. Qiu, W.-J. Kong, J. Struwe, N. Sauermann,  
T. Rogge and L. Ackermann\*

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Over last decades, rhodium(III) catalysis has enabled a plethora of oxidative C–H activations, which predominantly employ stoichiometric amounts of hazardous and/or expensive sacrificial metal oxidants such as silver(I) and copper(II) salts. At the same time, organic electrosynthesis has experienced a renaissance and has been recognized as a viable alternative to chemical oxidants.<sup>[1–3]</sup> Herein, we describe the first rhodium-catalyzed oxidative C–H activation with sustainable electricity as the sole oxidant and molecular hydrogen as the sole byproduct.<sup>[4]</sup> The reaction features twofold C–H/C–H transformation by electrocatalysis through weakly coordinating bezoic acids and benzamides. Robustness and versatility have been proven with a representative set of benzoic acids and various alkenes bearing electron donating as well as electron withdrawing substituents, as well as differently substituted acrylates. Notably, valuable electrophilic functional groups were well tolerated, including sensitive esters and enolizable ketones. Furthermore, detailed mechanistic studies were conducted and revealed key insight into the catalyst's mode of action.



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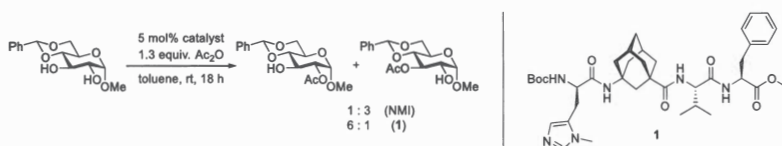
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# Oligopeptide Catalyzed Site-Selective Acetylation of Pyranosides

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Carbohydrates are omnipresent as oligosaccharides and glycoconjugates and are vital in a variety of biological processes.<sup>[1,2]</sup> Their synthesis usually requires protection of the desired monosaccharide building blocks.<sup>[3]</sup> One possibility to do that is the site-selective acylation of monosaccharides;<sup>[3]</sup> Miller *et al.* showed that oligopeptides are capable to perform such acylation reactions.<sup>[4]</sup> With our expertise using oligopeptide catalysts for selective acylation of a variety of diols,<sup>[5-7]</sup> we envisioned the catalysts to be capable of performing site-selective acylations of pyranoside derivatives as well.



The depicted peptide catalyst (**1**) is able to overcome the intrinsic reactivity of the substrate (there is virtually no reaction without catalyst) and reverses the selectivity of *N*-methylimidazole as catalyst in the site-selective acetylation of methyl 4,6-*O*-benzylidene- $\alpha$ -D-glucopyranoside. We furthermore exchanged the 4,6-*O*-protecting group, the anomeric center, and the configuration of the monosaccharide to gain deeper insights into the interaction between substrate and catalyst.

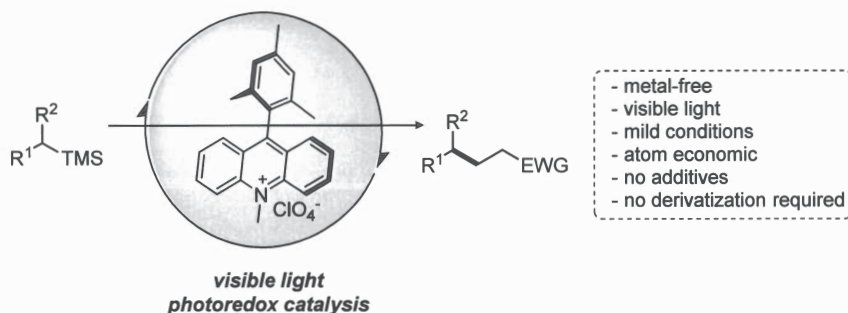
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# Metal-Free Desilylative C-C bond Formation by Visible Light Photoredox Catalysis

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The application of visible light photoredox catalysis for the activation of organosilanes is rarely explored due to the stability of these compounds. More precisely, the C-Si bond cleavage requires either UV light irradiation or a pre-derivatization of the substrates to the corresponding silicates.<sup>[1],[2],[3]</sup> A newly developed methodology for the use of organosilicon compounds as radical precursors under metal-free and visible light conditions is presented in this work. The ability of the 9-mesityl-10-methylacridinium perchlorate to form an extremely strong oxidant in its excited state enables the transformation of the organosilicon compounds to the carbon-centered radicals, which were trapped by various alkenes. Quenching experiments as well as deuterium labeling studies were performed to give a deep mechanistic insight to the first organophotocatalyst mediated desilylative C-C bond formation under remarkably mild conditions, without the need of any external additive.



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# Alkylation of Gold Surfaces with Long-chain Alkylstannanes

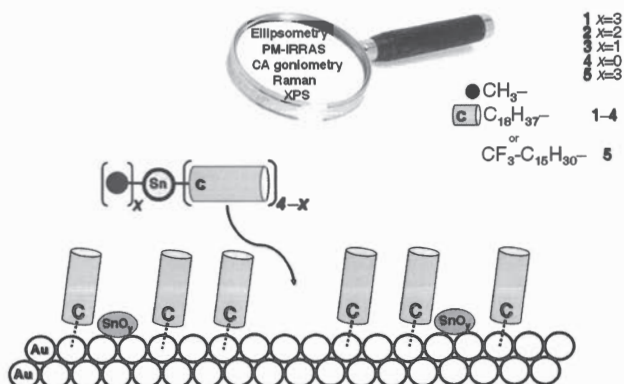
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Reaction of alkylstannane solutions with gold surfaces under ambient conditions permits a fabrication of self-assembled alkyl monolayers (SAMs) containing also tin oxide.<sup>1-4</sup> In an attempt to improve our mechanistic understanding of the process, we used ellipsometry to investigate the kinetics of the self-limiting growth of long-chain alkyl SAMs formed upon treatment of a cleaned gold surface with THF solutions of five tetraalkylstannanes. Four (1 - 4) contained one to four *n*-octadecyl moieties and three to zero methyl groups at the tin atom, and the fifth (5) carried three methyl groups and a *n*-hexadecyl group with a terminal CF<sub>3</sub> instead of CH<sub>3</sub>. In addition to ellipsometric measurements, the monolayers were also characterized by polarization modulated IR reflection absorption spectroscopy, surface-enhanced Raman spectroscopy, contact angle goniometry, and X-ray photoelectron spectroscopy. Mechanistic insight and structural information about the nature of the attachment have been obtained.



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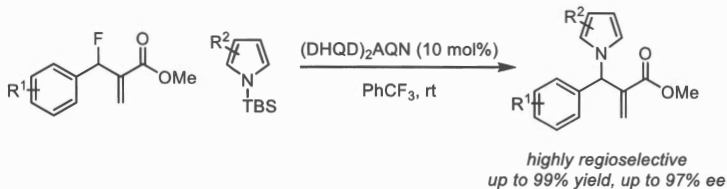
# Latent Nucleophiles in Synthesis: Improving the Scope and Selectivity in Lewis Base Catalysis

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Lewis-base-catalyzed (LB-catalyzed) reactions are often limited in scope of the nucleophilic reaction partner. For example, LB-catalyzed allylic substitutions of Morita-Baylis-Hillmann (MBH) derivatives with a nitrogen centered nucleophile are limited to those nucleophiles that feature an acidic N-H such as imides, sulfonamides and sulfoximines.<sup>[1]</sup> These nucleophiles necessarily install an amine functionality protected with groups that are typically not easily removed.<sup>[2]</sup>

We have recently introduced the concept of latent nucleophiles in LB-catalysis and defined them as molecules that are themselves not nucleophilic but could be rendered nucleophilic by a mild external activator. If the presence of activator is conditioned by the activation of the electrophilic reaction partner by a LB catalyst, the fast reaction between the activated electrophile and the activated nucleophile offers the means to better control selectivity in such reactions.



Here, we report the proof of concept study on LB-catalyzed substitution of MBH derived allylic fluorides with silylated nitrogen heterocycles (pyrroles, indoles, carbazoles) as latent nucleophiles. These reactions proceed in high yields with exquisite regioselectivity both with respect to the electrophile and nucleophile. The use of chiral cinchona alkaloid derived catalysts renders the reactions enantioselective, providing the allylation products of pyrroles, indoles and carbazoles with selectivities of up to 97% ee. In this report, we disclose the preliminary work on understanding the mechanistic aspects of these transformations.

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# Fluorine-alkyl and oligonucleotide containing polyamphiphiles for cell and bacteria labeling

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The unique properties of fluorine-containing amphiphilic polymers such as high inertness, surface activity and stability in physiological solutions, open the way to their use in biomedicine, particularly, for creation of low toxic delivery systems for drugs, nucleic acids, and proteins, cell and bacteria recognizing and labeling.

The aim of present work is purposeful synthesis of polymeric surfactants combining hydrophobic fluorine-containing and hydrophilic, including biopolymers, side chains and blocks via radical and non-radical reactions.

The fluorine-alkyl side chains and blocks were included into the structure of polymers as part of the initiating system (fluorine alcohol and Ce<sup>4+</sup> salt) or by copolymerization of fluorine-alkyl methacrylates (F-MA). Using cumene derivatives with epoxy or peroxide functional group (CGE and MP, respectively) as chain transfer agents provides controlling molecular weight characteristics and amount of telechelic polymers containing terminal functional fragment.

Radical polymerization of vinyl pyrrolidone (NVP) initiated by poly(F-MA)-MP as precursor - macroinitiator in the presence of CGE was used for obtaining water-soluble poly(F-MA)-block-poly(NVP)-CGE combining linear and comb-like blocks.

Amphiphilic block-copolymers of linear structure were obtained via radical polymerization of NVP initiated by Red-Ox system (fluorine-alkyl alcohol (F-alc) - Ce<sup>4+</sup> salt) in the presence of telogen CGE. As a result, amphiphilic water-soluble heterotelechelic polymers F-alc)-poly(NVP)-CGE were obtained by one-step process. Structures of the polymers were confirmed by IR- and NMR-spectroscopy and elemental analyses. The influence of the concentrations of the components and the length of the fluorinated fragment on the kinetic patterns was studied.

The polymers are surface active and form micelle-like structures (MLS) of different size and morphology in water, which is confirmed by the form of surface tension isotherms. Sizes of MLS were studied using DLS-technique.

The terminal epoxide group in both polymer molecules provides controlled attachment of biopolymers (proteins, peptides, oligonucleotides) and their successful biomedical application for nucleic acid and protein delivery as well as cell and bacteria labeling.

# Gauging Stability and Reactivity of Carbonyl O-Oxide Criegee Intermediates

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Carbonyl O-oxides, often referred to as *Criegee intermediates*, constitute highly reactive molecules, that form during the ozonolysis of alkenes.<sup>[1,2]</sup> Recently, these intermediates have been recognized as important oxidizers in the troposphere.<sup>[3]</sup> Considering the vast number of (unsaturated) volatile organic compounds that are emitted into the atmosphere, it is important to understand the influence of substitution on stability and reactivity of these carbonyl oxides. Therefore, we computed about 50 different Criegee intermediates at the CBS-QB3 level of theory and evaluated their intrinsic stabilization energy according to the following isodesmic reaction equation.



While  $\sigma$ -acceptors are mildly destabilizing,  $\pi$ -donor substituents are vastly stabilizing. Regarding their reactivity, it has already been demonstrated that carbonyl oxide reactions rely on mixing of the closed-shell ground state with the first excited triplet state.<sup>[4]</sup> Thus, we gauged the reactivity of the carbonyl oxides by comparison of their respective singlet-triplet gap to that of the simplest Criegee intermediate H<sub>2</sub>C=O-O. Again,  $\pi$ -donor substituents seem to hamper potential reactions substantially.

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# Synthesis and thermal stability of maleimide moiety containing arylalkyl peroxides and peroxyesters

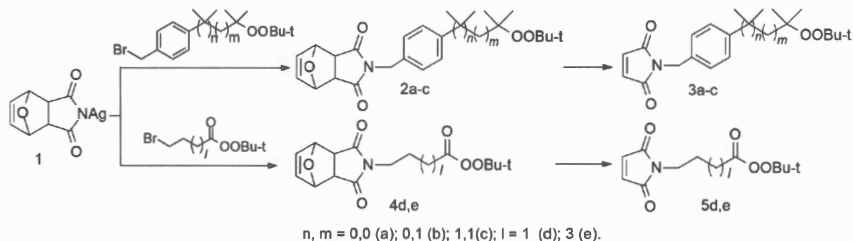
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Monomers which contain initiating centres (inimers) are used for synthesis of functional oligomers with initiating centres in side branches of macromolecular chain. The application of such the oligomers as macroinitiators allows to obtain graft-copolymers of complex architecture.

We synthesized a novel type of peroxy monomers i.e. maleimide as well as investigated their thermolysis is investigated and calculated the kinetic parameters of theirs process. The maleimide derivatives with peroxyester fragments were obtained by the interaction of the silver salt of the protected maleimide with peroxy benzyl bromides and  $\omega$ -bromocarboxylic acids peroxyesters. After removal of the furan protection the compounds were converted into peroxy maleimide monomers.



The thermolysis of the synthesized compounds was investigated by the complex thermal analysis method; the rate constants and the activation energy of the thermolysis were determined. As for compounds 2 a-c the thermolysis is occurred in two stages which corresponded to the depletion of the furan fragment (endothermic process) and the homolysis of the peroxy group (exothermic process). For peroxyesters 4 d, e the temperature range of the destruction was 363-434 K with the maximum at 413-423 K, the value of the  $E_{act}$  was within 126-138 kJ/mol. For ditertiary peroxides 3a-c the temperature range of the destruction was 394-464 K with the maximum of 429-438 K; the value of the  $E_{act}$  was within 169-180 kJ mol.

It was shown that the synthesized monomers are able to copolymerize with conventional monomers with the formation of the oligomers with the peroxy substituents in the side branches of the macrochain. The peroxy groups are preserved during an emulsion polymerization.