WWU
MÜNSTER

9th MÜNSTER SYMPOSIUM ON COOPERATIVE EFFECTS IN CHEMISTRY

2018
March 16th

Münster,
Germany

Book of Abstracts

SFB
858

Symposium Schedule

Friday, March 16th 2018
Schloss of the WWU Münster (Aula)

UPDATED PROGRAMME

9.55 am Opening — *Armido Studer, SFB 858 Spokesperson*

10.00 am **Helmut Schwarz** — *Chair: Christian Mück-Lichtenfeld*
Technische Universität Berlin, GER
The Methane Challenge:
A Cold Experimental / Computational Approach to a Hot Problem

11.00 am **Bernd Giese** — *Chair: Ulrich Hennecke*
Université de Fribourg, SUI
Respiration without Oxygen

12.00 Business Lunch
12.30 pm **Symposium Poster Session**

2.15 pm **MS_CEC Young Researcher Awards 2018** — *Chair: Frank Glorius*
Dr. Anna McConnell
Christian-Albrechts-Universität zu Kiel, Otto Diels-Institut für Organische Chemie, GER
Dr. Urs Gellrich,
Justus-Liebig-Universität Gießen, Institut für Organische Chemie, GER

3.00 pm **Tobias Ritter** — *Chair: Manuel van Gemmeren*
Max-Planck-Institut für Kohlenforschung, Mülheim a. d. Ruhr, GER
Late-Stage Functionalizations

4.00 pm **Varinder K. Aggarwal** — *Chair: Olga Garcia-Mancheño*
University of Bristol, UK
Assembly Line Sysnthesis

5.00 pm **MS_CEC Poster Prize Announcements**
Closing Remarks

Poster Contributions

in alphabetical order (presenting author's surname)

No.	Authors	Institution	Title
01.	J. E. Armstrong, J. Naapuri, J. Deska, Martin H. G. Prechtl*	Universität zu Köln	Catalytic Hydrogen Production from NADH in a Bio-Coupled System
02.	A. U. Augustin, M. Sensse, M. Busse, P. G. Jones, D. B. Werz*	TU Braunschweig	Stereospecific Reactions of Donor-Acceptor Cyclopropanes with Thioketones: A Novel Access to Highly Substituted Thiolanes
03.	L. J. Kost, A. Aust, K. Brüninghoff, P. Meyer-Ahrens, H. D. Mootz*	WWU Münster / SFB 858	Structural insight into multivalent SUMO-SIM interactions by a novel FRET sensor
04.	J. Bachmann, N. Doltsinis*	WWU Münster / SFB 858	Adaptive QM/MM simulations of metal-mediated DNA
05.	S. Behren, J. Yu, C. Pett, M. Schorlemer, U. Westerlind*	ISAS - Leibniz Institute for Analytical Sciences, Dortmund	Generation of A Mucin Glycopeptide Microarray Library for Evaluation of Host-Pathogen Interactions
06.	S. Bente, F. E. Hahn*	WWU Münster / SFB 858	Preparation of a heterobimetallic NHC complex *via* site-selective metalation of an azolium/azole precursor
07.	T. Biberger, S. Makai, Z. Lian, B. Morandi*	Max-Planck-Institut für Kohlenforschung, Mülheim	Iron-Catalyzed Ring-Closing C–O/C–O Metathesis of Aliphatic Ethers
08.	J. S. Bruchhage, K. Martinewski, W. Uhl*	WWU Münster / SFB 858	Various Novel Oligomerization and Insertion Reactions by Active Lewis Pairs
09.	K. Brüninghoff, P. Meyer-Ahrens, W. Dörner, K. F. Taupitz, H. D. Mootz*	WWU Münster / SFB 858	Stabilizing transient SIM-SUMO interactions by photoinducible crosslinking
10.	S. Ehrmann, C.-W. Chu, S. Kumari, K. Silberreis, C. Böttcher, J. Dernedde, B. J. Ravoo, R. Haag*	Freie Universität Berlin, WWU Münster	A Toolbox Approach for Multivalent Presentation of Ligand-Receptor Recognition on a Supramolecular Scaffold

Poster Contributions

in alphabetical order (presenting author's surname)

No.	Authors	Institution	Title
11.	M. Freitag, N. Möller, D. T. Nguyen, P. Tegeder, A. Rühling, S. Lamping, F. Glorius*, B. J. Ravoo*	WWU Münster / SFB 858	Innovative Ligands for Nanoparticles and Surfaces – Synergistic Effects for Stability and Reactivity
12.	A. Galstyan,* J. Putze, U. Dobrindt	WWU Münster	Turning photons into drugs: Advanced photoactive compounds and interfaces in the resistance era
13.	D. Grill, N. Heitzig, A. Kühnl, A. L. Linard Matos, K. Ludewig, S. Schloer, H.-J. Galla*, T. Grewal, V. Gerke*, U. Rescher*	WWU Münster / SFB 858	Cooperative binding promotes demand-driven recruitment of AnxA8 to cholesterol-containing membranes
14.	R. Guha, S. Engel, A. Schmidt, B. J. Ravoo, J. Müller*	WWU Münster / SFB 858	Cooperative Binding of a Pt(II) Complex to Guanine Quadruplex DNA
15.	K. S. Hagen, N. Ma, B. Koksch*	Freie Universität Berlin	Coiled-coil-based peptide hydrogels as ECM mimics for stem cell differentiation
16.	P. H. Hamming, J. Huskens*	University of Twente	Dynamics of a weakly multivalent walker
17.	M. Hayduk, J. Voskuhl*	Universität Duisburg-Essen	Novel luminophores with aggregation-induced emission properties for protein and amine recognition
18.	G. Hoffmann, A. Studer*	WWU Münster	Short and Protecting Group free Total Synthesis of (–)-Δ^8-THC, (–)-Machaeriol B, D and Analogues
19.	S. Klotzbach, S. Ivanova, P. Adamski, F. Beuerle*	Universität Würzburg	Self-Sorting of Covalent Organic Cage Compounds
20.	D. Jansen, J. Niemeyer*	Universität Duisburg-Essen	Asymmetric organocatalysis with chiral [2]catenanes

Poster Contributions

in alphabetical order (presenting author's surname)

No.	Authors	Institution	Title
21.	B. Jash, J. Müller*	WWU Münster / SFB 858	1*H*-Imidazo[*4,5-f*][1,10]phenanthroline - a versatile nucleobase surrogate in metal-modified nucleic acids
22.	P. Kiran, S. Kumari, S. Bhatia, D. Lauster, K. Ludwig, C. Böttcher, A. Hamann, A. Herrmann, R. Haag*	Freie Universität Berlin	Multivalent Sialylated Polyglycerol Derivatives Inhibit Influenza Virus Propagation
23.	K. Bojaryn, C. Hoffmann, S. Kirupakaran, R. Struth, C. Hirschhäuser*	Universität Duisburg-Essen	Iterative Preparation of Heteroatom-Rich Systems – Towards an Atom for Atom Synthesis of Carbohydrates
24.	M. Kischkewitz, A. Studer*	WWU Münster	Exploring the Scope of Radical-Polar Crossover Reactions of Vinyl Boron Ate Complexes in Three Component Couplings
25.	H. Klaasen, L. Liu, A. Timmer, H.-Y. Gao, D. Barton, H. Mönig, J. Neugebauer*, H. Fuchs*, A. Studer*	WWU Münster / SFB 858	α-Diazo Ketones in On-Surface Chemistry
26.	M. Klika Škopić, K. Jung, A. Gohla, A. Brunschweiger*	TU Dortmund	Au(I)-mediated synthesis of hexathymidine-DNA-pyrazol(in)e chimeras, an efficient entry to DNA-encoded libraries inspired by drug structures
27.	M. C. Kohlhaas, J. Niemeyer*	Universität Duisburg-Essen	Cage-like nanocapsules for molecular recognition and catalysis
28.	M. Körner, N. Krause*	TU Dortmund	Enantioselective Synthesis of Chiral Trifluoromethylated Allenes by S_N2'-Reaction
29.	F. Krätzschmar, C. Depken, R. Rieger, K. Rode, A. Breder*	Georg-August-Universität Göttingen	Aerobic Phosphatation of Alkenes via Dual Selenium Catalysis
30.	T. Kurzawa, K. Harms, U. Koert*	Philipps-Universität Marburg	Stereoselective Synthesis of the Benzodihydropentalene Core of the Fijiolides

Poster Contributions

in alphabetical order (presenting author's surname)

No.	Authors	Institution	Title
31.	R.-J. Li, G. H. Clever*	TU Dortmund	Guest-to-Host Chirality Transfer in Photoswitchable Metallocages
32.	T. Liedtke, P. Spannring, L. Riccardi, A. Gansäuer*	Rheinische Friedrich-Wilhelms-Universität Bonn	Mechanism-Based Condition-Screening for Sustainable Catalysis in Single Electron Steps by Cyclic Voltammetry
33.	A. Lücht, L. J. Patalag, A. U. Augustin, P. G. Jones, D. B. Werz*	TU Braunschweig	Reactions of Donor–Acceptor Cyclopropanes with Naphthoquinones: Redox and Lewis Acid Catalysis Working in Concert
34.	F. Lutz, J. Niemeyer*	Universität Duisburg-Essen	DNA-supported bimetallic photoredox catalysis
35.	M. Mantel, M. Brauns, J. Schmauck, M. Guder, M. Breugst*, J. Pietruszka*	Heinrich-Heine Universität Düsseldorf, FZ Jülich, Universität zu Köln	The Efficient Allylation of Ketones – Bench-Stable Reagents for the Highly Enantioselective Generation of all Stereoisomeres of Tertiary Homoallylic Alcohols
36.	B. Matarranz, G. Fernández*	WWU Münster / SFB 858	Supramolecular Polymerization of Pd(II) and Pt(II) BODIPY-based Structures
37.	D. J. Mikolajczak, J. Scholz, B. Koksch*	Freie Universität Berlin	Positive Cooperativity and Substrate Specificity of Peptide-Nanoparticle Conjugates
38.	H. Neitz, F. Thomas*	Georg-August-Universität Göttingen	Coiled-Coil Induced Assembly of Inactive hPin1 WW-Domain Fragments to Functional Protein Modules
39.	R. N. Osorio, F. E. Hahn*	WWU Münster / SFB 858	C8 Metalation of Adenine. Synthesis of Rh^{III} and Ir^{III} Complexes featuring bidentate di-NHC ligands
40.	S. Ossinger, H. Naggert, L. Kipgen, M. Bernien, W. Kuch, F. Tuczek*	Christian-Albrechts Universität zu Kiel, Freie Universität Berlin	Fe(II) SCO Complexes: Cooperativity in the Bulk and in Vacuum Deposited Films

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No.	Authors	Institution	Title
41.	N. J. Overeem, E. van der Vries, J. Huskens*	University of Twente	Surface gradients in lipid bilayers to study multivalent binding of influenza
42.	N. Pairault, J. Niemeyer*	Universität Duisburg-Essen	Heterobifunctional [2]rotaxanes based on phosphate-ammonium interactions
43.	I. Paul, A. Goswami, N. Mittal, M. Schmittel*	Universität Siegen	Catalytic Three-Component Machinery: Control of Catalytic Activity by Machine Speed
44.	T. Peez, J.-N. Luy, R. Tonner, U. Koert*	Philipps-Universität Marburg	Exploring Acenaphth(yl)ene Chemistry
45.	S. Kiontke, E. Herrmann, L. Langemeyer, C. Ungermann, D. Kümmel*	WWU Münster	Collaborative mechanism of catalysis and localization of the Rab7/Ypt7 GEF (guanine nucleotide exchange factor) Mon1-Ccz1
46.	L. Rakers, D. Grill, A. L. L. Matos, S. Wulff, D. Wang, J. Börgel, M. Körsgen, H. F. Arlinghaus, H.-J. Galla*, V. Gerke*, F. Glorius*	WWU Münster / SFB 858	Novel addressable cholesterol analogs for live imaging of cellular membranes
47.	J. Rath, N. Krause*	TU Dortmund	Synthesis of Trifluormethylated Pyridines
48.	K. Rau, A. Rentmeister*	WWU Münster / SFB 858	A new tool for sequence-specific manipulation of N^6-methyladenosine
49.	F. Reeßing, M. C. A. Stuart, R. A.J.O. Dierckx, B. L. Feringa*, W. Szymanski*	University of Groningen	Development of light-responsive MRI contrast agents for imaging and theranostics
50.	I. Regeni, B. Chen, M. Frank, G. H. Clever*	TU Dortmund	Self-assembled $[(Pd/Pt)_2L_4]$ coordination cages based on well-known organic dyes

Poster Contributions

in alphabetical order (presenting author's surname)

No.	Authors	Institution	Title
51.	A. Sadurní, R. Gilmour*	WWU Münster / SFB 858	Fluorine-Directed Glycosylation Enables the Stereocontrolled Synthesis of Selective SGLT2 Inhibitors for Type II Diabetes
52.	B. Gole, R. Sánchez-Naya, S. Rager, D. D. Medina, T. Bein, F. Würthner, F. Beuerle*	Universität Würzburg, Ludwig-Maximilians-Universität München	Microtubular Self-Assembly of Covalent Organic Frameworks
53.	J. Schieven, N. Krause*	TU Dortmund	A Gold-catalyzed Three-component Spirocyclization to Highly Functionalized
54.	C. Schwermann, N. L. Doltsinis*	WWU Münster / SFB 858	Chiral N-Heterocyclic Carbenes as Molecular Ratchets
55.	G. A. Shevchenko, G. Pupo, R. Properzi, D. Petkova, G. Bistoni, F. Neese, P. Kraft, B. List*	Max-Planck-Institut für Kohlenforschung, Mülheim	Enol Catalysis – Enantioselective Transformations via Bifunctional Brønsted Acid Promoted Enolization
56.	A. Sowa, J. Dubbert, J. Voskuhl*	Universität Duisburg-Essen	Subphthalocyanines as Model System for Supramolecular Photosensitizers in Biomedical Applications
57.	P. Stallforth*, J. Arp, S. Götze, R. Mukherji, M. Klapper	Leibniz-HKI, Jena	Synergy in and Biosynthesis of Natural Products from Pseudomonads
58.	L. M. Stratmann, D. M. Engelhard, G. H. Clever*	TU Dortmund	Programmable Ligand Environments for Transition Metal Ion Binding in DNA G-quadruplex Structures
59.	F. Strieth-Kalthoff, M. Teders, C. Henkel, A. Gómez-Suárez, K. Bergander, C. G. Daniliuc, D. M. Guldi, F. Glorius*	WWU Münster	Guided Serendipity – A Two-Dimensional Approach Towards Novel Transformations and Mechanisms in Photocatalysis
60.	N. Tsuji, J. L. Kennemur, T. Buyck, S. Lee, S. Prévost, P. S. J. Kaib, D. Bykov, C. Farès, B. List*	Max-Planck-Institut für Kohlenforschung, Mülheim	Activation of Olefins via Asymmetric Brønsted Acid Catalysis

Poster Contributions

in alphabetical order (presenting author's surname)

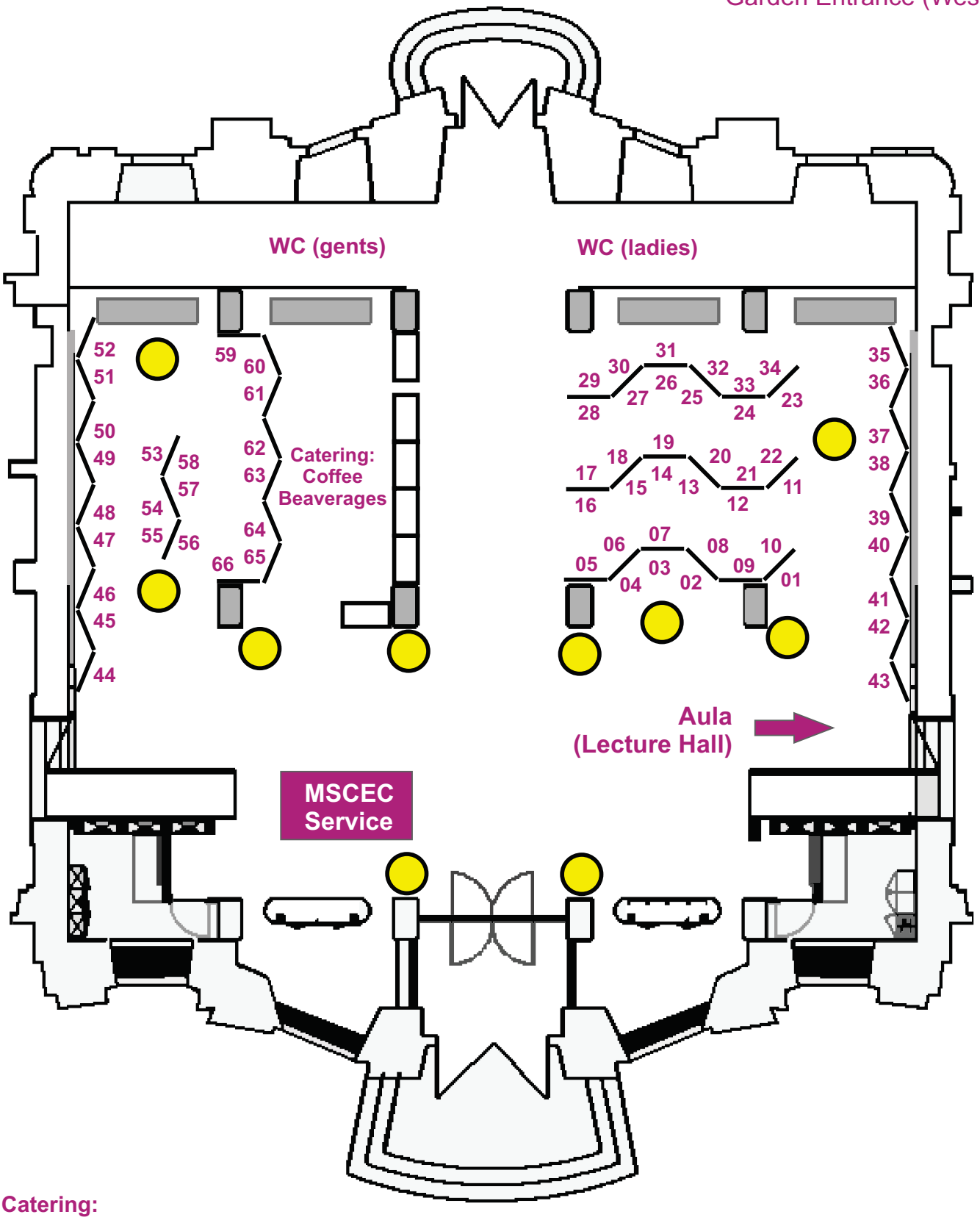
Nr.	Authors	Institution	Title
61.	D. Van Craen, M. Albrecht*	RWTH Aachen	Hierarchical Helicates – More Than Just Models
62.	W. C. de Vries, D. Grill, M. Tesch, A. Studer*, V. Gerke*, B. J. Ravoo*	WWU Münster / SFB 858	Stimulus-Responsive Degradable Nanocontainers for the Intracellular Release of Lipids
63.	H. Chen, P. Wedi, T. Meyer, G. Tavakoli, M. van Gemmeren*	WWU Münster / SFB 858, Max Planck Institut für Chemische Energie-konversion	Dual Ligand-Enabled Nondirected C–H Olefination of Arenes
64.	M. Wissing, A. Studer*	WWU Münster / SFB 858	Mixed Metal Nanoparticles as Highly Active Catalysts for Alkyne *cis*-Semihydrogenation
65.	B. Zhang, G. H. Clever*	TU Dortmund	Salen Complex-based Multicomponent Self-Assembled Cages
66.	Y. Zhang, T. Sun, N. Krause*	TU Dortmund	Total Synthesis of the Natural Product (+)-3-*O*-Feruloylcassine

SFB 858

9th MÜNSTER SYMPOSIUM ON COOPERATIVE EFFECTS IN CHEMISTRY

Poster Forum

Garden Entrance (West)



Catering: Business Lunch (external marquee)

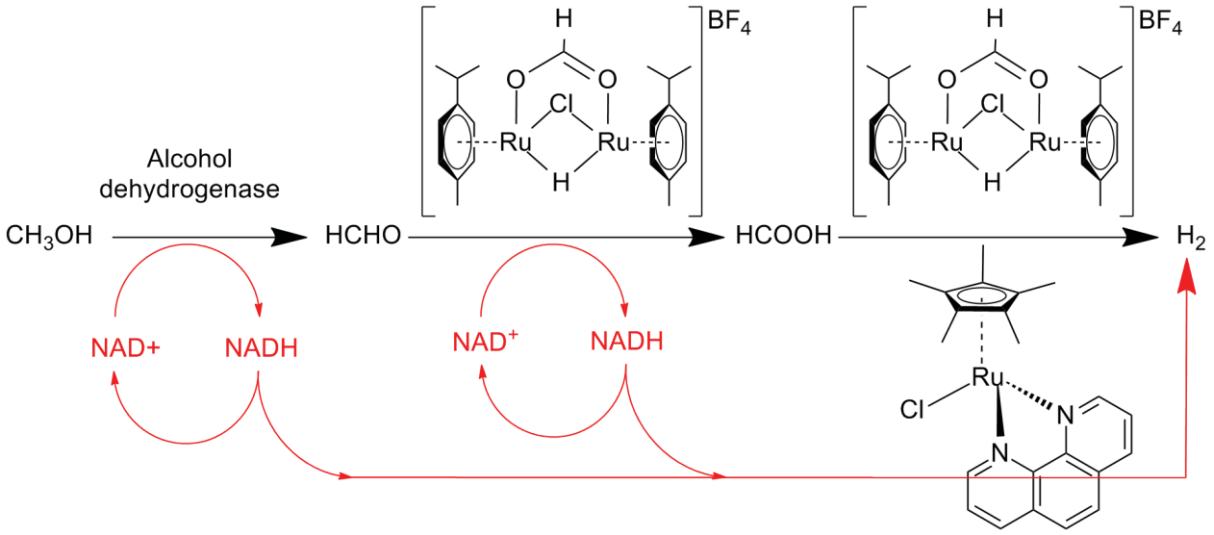
Main Entrance (East)

Title:
Catalytic Hydrogen Production from NADH in a Bio-Coupled System

Contributors:
Jessica E. Armstrong,[a] Janne Naapuri,[b] Jan Deska,[b] Martin H. G. Prechtl[a,*]
[a]*Department of Chemistry, University of Cologne, Cologne, Germany, www.h2.bio*
[b]*Department of Chemistry, Aalto University, Espoo, Finland, www.deskalab.com*

Abstract:
With a rise in global population, worldwide demands for efficient energy storage systems are growing dramatically. Hydrogen gas presents an alternative to fossil fuels but is limited in mobility. In Nature, hydrogen is enzymatically transferred from formaldehyde to NAD^+, yielding NADH.[1,2] We have studied biomimetic catalysts for the oxidation of NADH to form NAD^+. These catalysts will be incorporated into a chemoenzymatic system using methanol, NAD^+, and NADH to generate H_2.[1,2] This system exploits the redox cycle of NADH/NAD^+ to produce H_2 as a clean fuel.

Scheme for illustration:



References:
[1] Heim, Leo E.; Thiel, Daniel; Geding, Christian; Deska, Jan; Prechtl, Martin H. G. *Angew. Chem. Int. Ed.* **2015**, 54, 10308-10312.
[2] Shen, Yangbin; Zhan, Yulu; Li, Shuping; Ning, Fandi; Du, Ying; Huang, Yunjie; He, Ting; Zhou, Xiaochun. *Chem. Sci.* **2017**, 8, 7498-7504.

Stereospecific Reactions of Donor-Acceptor Cyclopropanes with Thioketones: A Novel Access to Highly Substituted Thiolanes

André U. Augustin, Maximilian Sensse, Marius Busse, Peter G. Jones, Daniel B. Werz*

Technical University Braunschweig, Institute of Organic Chemistry,
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In recent years the use of donor-acceptor (D-A) cyclopropanes as easy available building blocks in organic synthesis has flourished and rushed more and more in the focus of synthetic methodology due to their 1,3-zwitterionic character. [1] Their high ring strain of about 115 kJ/mol make them a powerful reagent able to generate a broad scope of compounds reaching from polyfunctional open-chained structures to carbocyclic and heterocyclic scaffolds.[2]

During our work on cyclopropanes, we subjected higher homologs of ketones, such as thioketones to a Lewis-acid catalyzed formal [3+2]-cycloaddition process to synthesis 2,5-disubstituted tetrahydrothiophene derivatives. Our initial studies paved the way to diverse thiolanes by using symmetric and non-symmetric thioketones bearing various alkyl and aryl groups in a stereospecific manner. Moreover, an intramolecular approach was successfully implemented to gain access to sulfur-bridged [*n*.2.1] bicyclic ring systems. Inspired by these results we could extend our investigations to the formation of tetrahydroselenophenes by using capricious selenoketones. [3a] Finally, we finished our studies by a formal thioketene insertion catalyzed by $Sc(OTf)_3$. (Figure 1)[3b]

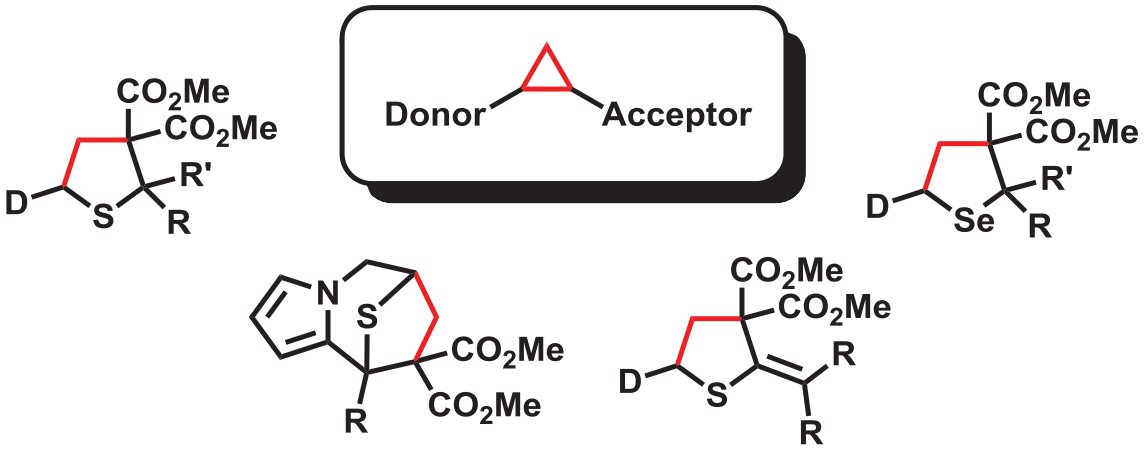

Figure 1. Lewis-acid catalyzed cycloaddition of Donor-Acceptor Cyclopropanes with thio- and selenoketones.

[1] a) H.-U. Reissig, R. Zimmer, *Rev. Chem.* **2003**, *103*, 1151; b) T. F. Schneider, J. Kaschel, D. B. Werz, *Angew. Chem. Int. Ed.* **2014**, *53*, 5504; *Angew. Chem.* **2014**, *126*, 5608.

[2] Recent examples from our group: a) J. Wallbaum, L. K. B. Garve, P. G. Jones, D. B. Werz, *Org. Lett.* **2017**, *19*, 98; b) L. K. B. Garve, P. G. Jones, D. B. Werz, *Angew. Chem. Int. Ed.* **2017**, *56*, 9226; *Angew. Chem.* **2017**, *129*, 9354; c) A. Lücht, L. J. Patalag, A. U. Augustin, P. G. Jones, D. B. Werz, *Angew. Chem. Int. Ed.* **2017**, *56*, 10587; *Angew. Chem.* **2017**, *129*, 10723.

[3] a) A. U. Augustin, M. Sensse, P. G. Jones, D. B. Werz, *Angew. Chem. Int. Ed.* **2017**, *56*, 14293; *Angew. Chem.* **2017**, *129*, 14481; b) A. U. Augustin, M. Busse, P. G. Jones, D. B. Werz, *Org. Lett.* **2018**, 20, 820.

Structural insight into multivalent SUMO-SIM interactions by a novel FRET sensor

Lisa J. Kost, Annika Aust, Kira Brüninghoff, Pascal Meyer-Ahrens
and Henning D. Mootz
Westfälische Wilhelms-Universität Münster, Institut für Biochemie,
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Posttranslational protein modifications by ubiquitin or Ubl (ubiquitin-like) proteins like SUMO (small ubiquitin-related modifier) can alter stability, location and activity of substrate proteins. SUMO regulates many cellular processes, including transcription, DNA repair, signal transduction and cell-cycle control. Misregulation of the SUMO pathway is related to many diseases like carcinogenesis, Alzheimer's, Parkinson's or Huntington's disease.
SUMOylation of a target protein can provide a new binding site that enables non-covalent interactions between SUMO and an interaction partner containing a SIM (SUMO-interacting motif). Most of the known target proteins are conjugated with SUMO monomers, but there is growing evidence that modification with SUMO chains also plays an important role in cellular regulation. Proteins with multiple SIMs like RNF4 (RING finger protein 4) have a high affinity towards SUMO chains which is driven not by one single high affinity interaction but by the combination of multiple low affinity interactions.
Our aim is to investigate the structure and dynamics of SUMO chains. Therefore, we developed a linear SUMO dimer which is labeled with two organic dyes using bioorthogonal reactions.[1] By employing FRET (Förster-resonance energy transfer), we are studying the influence of different interaction partners on the conformation of the SUMO dimer.

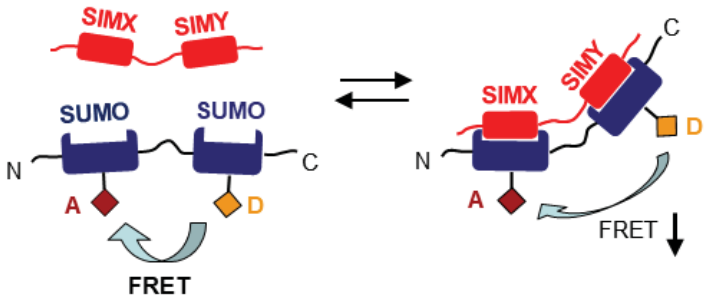

Figure 1: Conformational change of SUMO dimer due to multiple SUMO-SIM interactions

References
[1] Kost L., Mootz H. D., ChemBioChem, 2017, 19(2), 177-184

Adaptive QM/MM simulations of metal-mediated DNA

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[1]) Westfälische Wilhelms-Universität Münster

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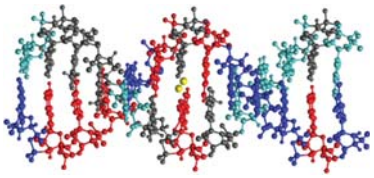
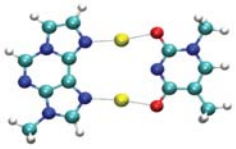
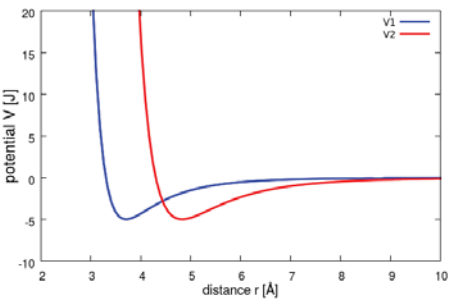
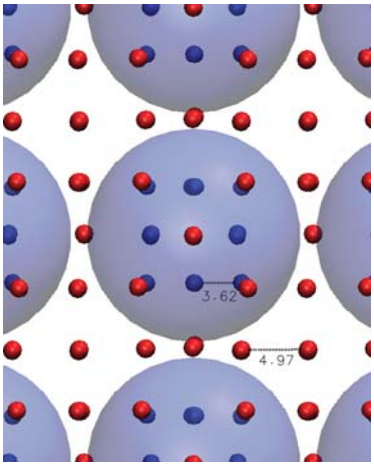
Metal mediated DNA seeks to combine the stability and extendability of DNA with the conductive properties of metals[1]. In this work, the structure and dynamics of metal-mediated DNA is investigated by quantum-chemical calculations and QM/MM simulations. To model and understand the fundamental processes governing the metal inclusion, it is necessary to employ an adaptive QM/MM partitioning scheme, which allows metal ions to be treated by classical force fields in solution and by ab initio methods as they enter the DNA.





Here we develop a new adaptive QM/MM method based on a fully energy conserving scheme proposed by M. Böckmann, N. Doltsinis, and D. Marx [2] for switching between different potentials in the time-domain. The new method is tested for a fictitious argon gas in which a selected atom interacts with other atoms by a Lennard-Jones potential V_1 within a defined cut-off distance and by a Lennard-Jones potential V_2 beyond this distance, where the potentials differ in the location of the minimum.





[1]Y. Takezawa, M. Shionoya, Acc. Chem. Res. **2011**, 113, 33
[2]M. Böckmann, N. Doltsinis, D. Marx, J. Chem. Theory Comput., **2015**, 11, 2429-2439

Generation of A Mucin Glycopeptide Microarray Library for Evaluation of Host-Pathogen Interactions

Sandra Behren, Jin Yu, Christian Pett, Manuel Schorlemer, Ulrika Westerlind*
Synthetic Biomolecules, Department of Bioanalytics,
ISAS - Leibniz Institute for Analytical Sciences,
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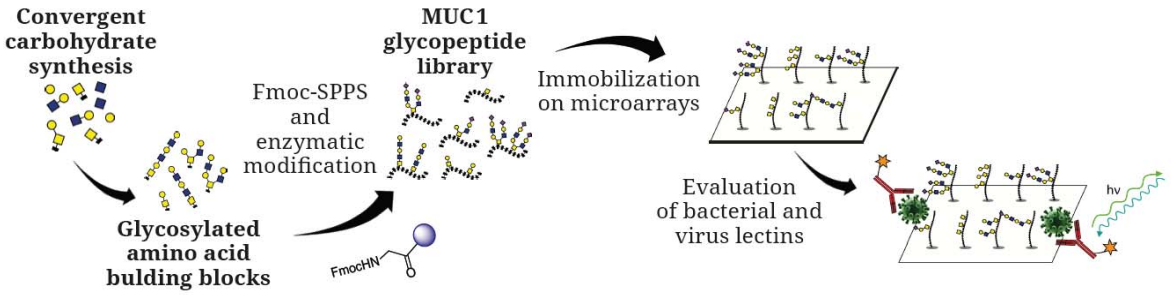
Mucins are heavily glycosylated proteins ubiquitously found on the epithelial cell surface in a membrane-bound or secreted form.[1] They contribute among other things to mucociliary clearance, an innate immune defense system which protects the airways against invading pathogens and chemical or physical stress factors.[2] Mucins exhibit extracellular tandem repeat (TR) regions rich in proline, threonine and serine (PTS) that form a scaffold for the attachment of *O*-linked glycans. Mucin *O*-linked glycans are often arranged in a multivalent fashion and function as ligands to different pathogens, which are cleared by the mucus under normal flow properties.[3] In airway diseases, mucin overexpression and altered terminal glycosylation, e.g. sialylation and fucosylation, as well as binding of pathogens to carbohydrate ligands, which leads to inflammatory-infective responses in the respiratory tract, occur.[4-7] This contributes to defect flow properties of the mucus and airway obstruction.

To better understand the role of mucin-type *O*-glycosylation in host-pathogen interactions, a synthetic glycopeptide library, immobilized onto microarray slides, was generated. For this purpose, a synthesis strategy was established to build-up diverse amino acid building blocks glycosylated with common mucin-type *O*-glycan core structures, which were subsequently introduced into mucin tandem repeat peptides by Fmoc-SPPS. To increase the diversity and generate specific glycan motifs, the glycan structures were further modified by chemoenzymatic elongation with *N*-acetyllactosamine structures, termination by 2,3- and 2,6-sialylation and fucosylation. The obtained glycopeptide library was then immobilized on microarray slides. The generated glycopeptide microarrays are currently employed in studies of bacterial and virus lectin binding preferences.



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Preparation of a heterobimetallic NHC complex *via* site-selective metalation of an azolium/azole precursor

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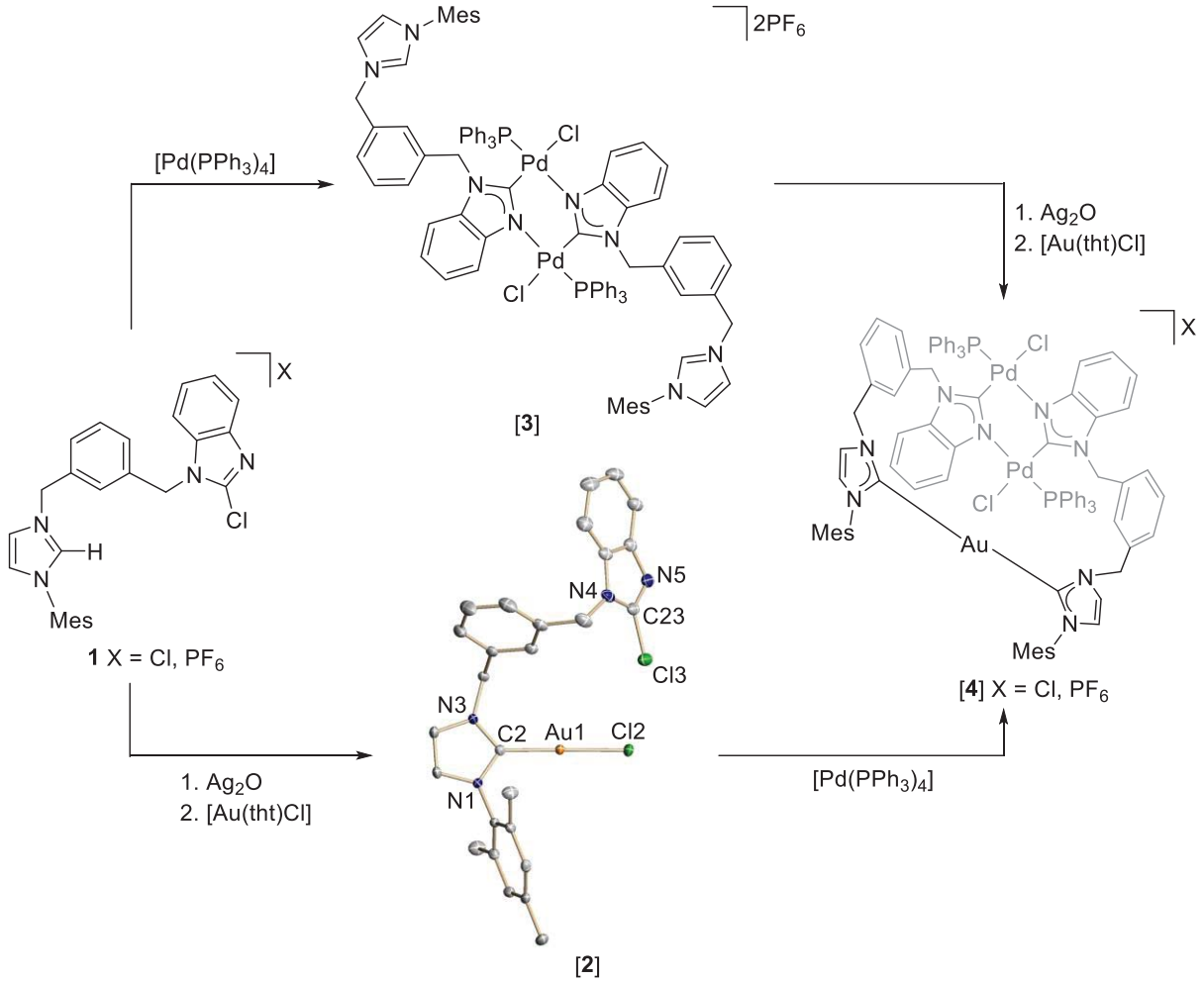
The interest in heteronuclear metal complexes bearing N-heterocyclic carbene ligands (NHCs) has been increasing over the last years due to their application in cooperative catalysis.[1,2] The most prominent method for the preparation of such complexes is the sequential metalation of diazolium salts.[2] We aim to exploit the difference in reactivity between C–H- and C–Cl-bonds to build heterobimetallic complexes using a chemoselectivity approach. Ligand precursor **1** posseses two reactive sites, which can be addressed selectively to gold(I) (deprotonation, metalation) and palladium(0) (oxidative addition) to yield complex [**4**] independent of the order in which the two reaction steps are performed.



Scheme 1. Two step synthesis of complex [**4**] *via* deprotonation and oxidative addition.

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Title of the poster:

Iron-Catalyzed Ring-Closing C–O/C–O Metathesis of Aliphatic Ethers

Names:

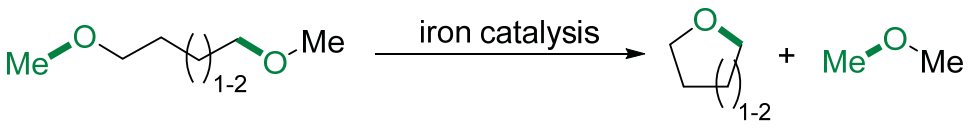
Tobias Biberger, Szabolcs Makai, Zhong Lian, Bill Morandi*

Abstract:

Among all metathesis reactions known to date in organic chemistry, the metathesis of multiple bonds such as alkenes and alkynes has evolved into one of the most powerful methods to construct molecular complexity. In contrast, metathesis reactions involving single bonds are scarce and far less developed, particularly in the context of synthetically valuable ring-closing reactions. Herein, we report an iron-catalyzed ring-closing metathesis of aliphatic ethers for the synthesis of substituted tetrahydropyrans and tetrahydrofurans, as well as morpholines and polycylic ethers. This transformation is enabled by a simple iron catalyst and likely proceeds through cyclic oxonium intermediates.

Scheme:

C(sp^3)–O/C(sp^3)–O metathesis of ethers (single bonds)



- *rare example of C(sp^3)–X metathesis*
- *sustainable iron catalysis*
- *synthesis of THFs, THPs, morpholines and dioxanes*
- *mechanistic study*

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Various Novel Oligomerization and Insertion Reactions by Active LEWIS Pairs

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Monomeric aluminium/nitrogen-based active LEWIS pairs (ALPs) were obtained by hydroalumination of ynamines (**1**) or hydrazones (**4**) with different dialkylaluminium hydrides. These bifunctional LEWIS pairs are able to coordinate and activate small molecules or can be used as catalysts for unprecedented oligomerization reactions.[1,2]

Current investigations showed the formation of an unprecedented five-membered heterocycle **2** with three N atoms, one vinylic C atom and an Al atom after treatment the ALP **1** with azides. Four equivalents of benzophenone reacted with **1** by isobutene elimination and formation of compound **3**. Both allyl groups attached to the Al atom of **1** are replaced by alcoholate groups and a C=O bond inserted into the Al-C(vinyl) bond. An intact benzophenone molecule completes the coordination sphere of Al.

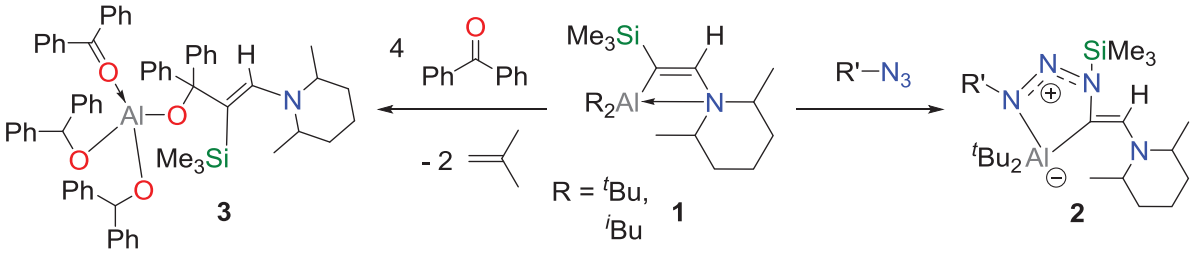

Figure 1: Reaction of ALPs with benzophenone and different azides.

ALP **4** reacted with phenyl isocyanate by the twofold of isocyanate groups in to an Al-N bond and formation of **5**. **5** reacted as a nucleophile with carboxylic acid chlorides to afford new highly functionalized organic compounds (**6**). Interesting oligomerization reactions were observed with suitable monomers (**7**).

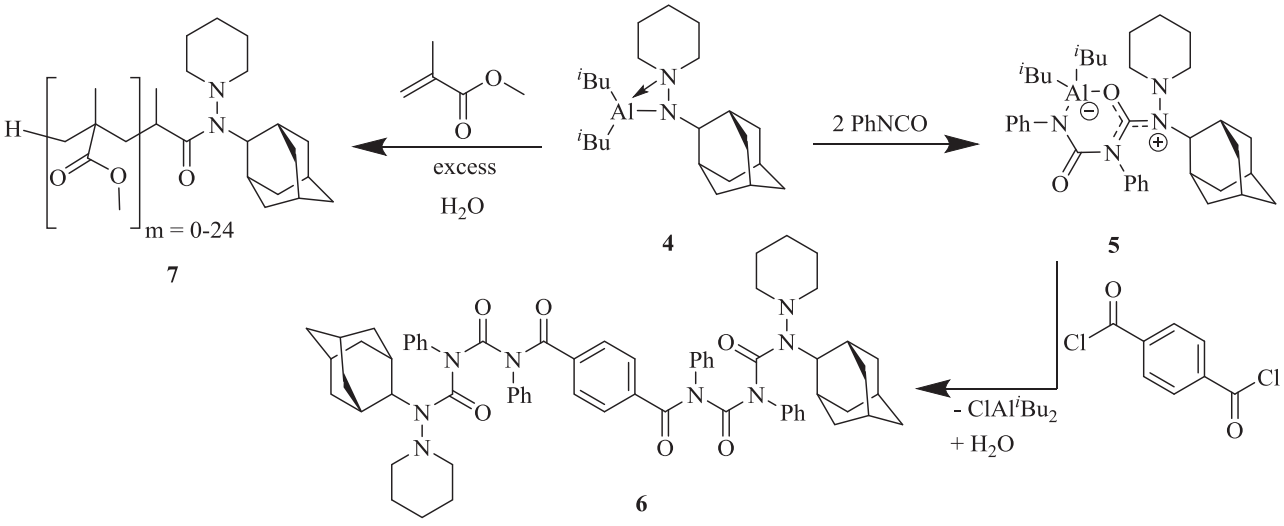

Figure 2: Generation of **5** and reactions with electrophiles to afford oligo-functional secondary products. Oligomerization reactions were observed for suitable monomers.

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Stabilizing transient SIM-SUMO interactions by photoinducible crosslinking

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Posttranslational modifications represent one option for cells to react rapidly on external and internal stimuli. They have a direct influence on the activity, conformation, intracellular localization and protein-protein interaction pattern of the modified protein. Besides the conjugation of small chemical moieties like phosphate groups, a protein can also be covalently modified by small proteins such as ubiquitin or ubiquitin-like proteins (Ubls), e.g. SUMO (small ubiquitin-related modifier). Thousands of proteins are SUMOylated in human cells. It has been shown that a misregulation of the SUMO conjugation / deconjugation cycle is related to the emergence of neurodegenerative diseases such as carcinogenesis, Alzheimer's or Parkinson's disease.

Aside from the covalent attachment, SUMO can interact non-covalently with proteins that possess a SIM (SUMO-interacting motif) and thereby affect new protein-protein interactions. However, due to the relatively weak SIM-SUMO interaction, the study of the precise role of SUMOylation is challenging.

This work aims on a further investigation of the SIM-SUMO interaction by application of photoinducible chemical crosslinkers. These are introduced into the SIM interaction surface in SUMO and provide an experimental tool to stabilize a protein complex upon a SIM-SUMO interaction covalently by irradiation with UV light for further investigation. [1]

This approach will be applied to the identification of SIM-mediated SUMO binding partners from cell extracts by tandem mass spectrometry. In regards to this, proteins interacting with conjugated SUMO probes are of special interest.

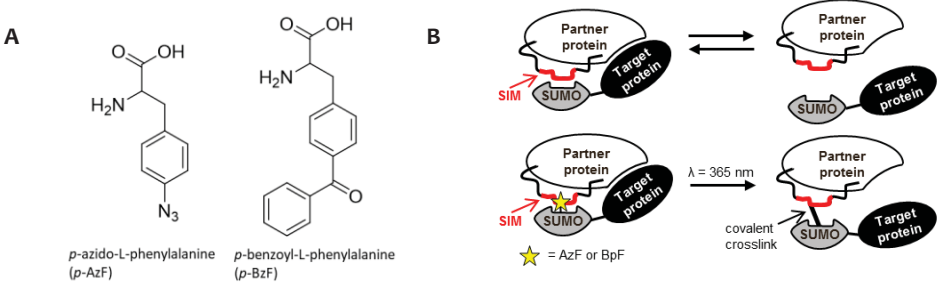

Figure 1: A. Unnatural amino acids incorporated for photocrosslinking. **B.** Concept of photoinducible crosslinking as a tool to study SIM-SUMO mediated interactions in multi protein complexes.

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A Toolbox Approach for Multivalent Presentation of Ligand-Receptor Recognition on a Supramolecular Scaffold

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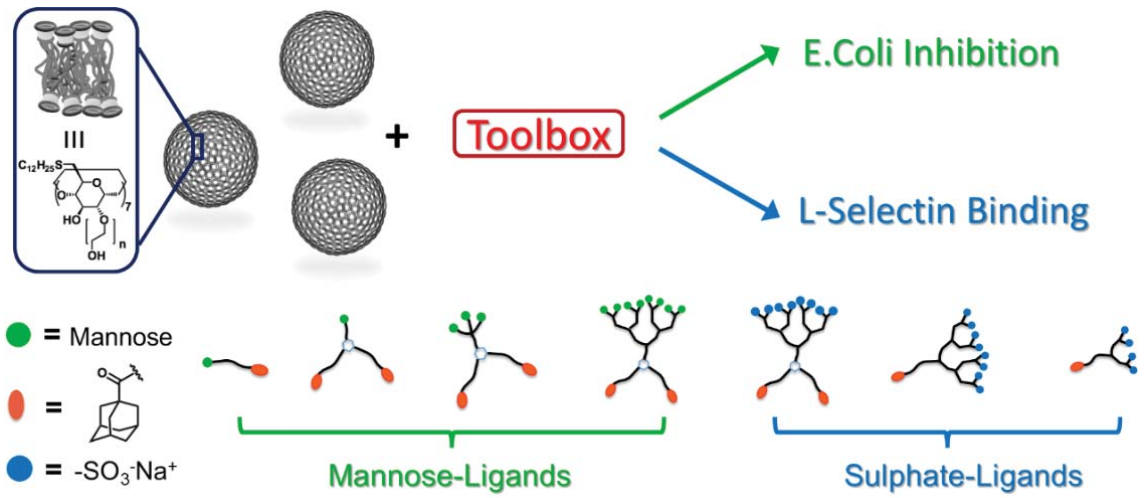
Understanding lectin-carbohydrate recognition at cell surfaces during bacterial adhesion processes is of high relevance for the development of artificial cell systems. Different factors and their specific influences including valency, topology, carbohydrate-ligand density and glyco-cluster effects are currently under investigation. In particular, non-ionic bilayer vesicles based on amphiphilic β-cyclodextrin can be used as model compounds for biological membranes. By decoration with ligands, these supramolecular complexes are suitable as mimic of an artificial glycocalyx.[1]

In this work[2], we synthesized and investigated supramolecular functionalized β-cyclodextrin vesicles (CDV). In order to show the versatility of our approach we synthesized carbohydrate-based ligands including mono-, tri-, and octavalent mannose as well as ligands functionalized with sulphate groups. Besides the physicochemical analysis of our complexes, we performed surface plasmon resonance (SPR) and microscale thermophoresis (MST) measurements to analyze the lectin binding affinity to Concanavalin A (ConA) and L-selectin, respectively. A competitive *in vitro* assay with uroepithelial cells, *E.Coli* and our carbohydrate-vesicle system revealed cell-bacteria adhesion inhibition and showed the applicability of our systems in biologically relevant problems.



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Innovative Ligands for Nanoparticles and Surfaces – Synergistic Effects for Stability and Reactivity

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In the past few years the modification of surfaces and nanoparticles with innovative, tailor-made ligands has gained in importance due to their promising application in fields such as biochemistry, heterogeneous catalysis, chip-based biosensors and materials science.
A major challenge for these purposes is the coverage of nanoparticles or surfaces by suitable ligands. An emerging class of ligands in this research area are N-heterocyclic carbenes, which has the additional advantage of being easily structurally adapted on demand.[2] Herein, we present on the one hand the broad applicability of N-heterocyclic carbenes as ligands for gold surfaces, noble metal alloy- and upconversion-nanoparticles.[3] One the other hand photo-catalytically active ligands were used as innovative ligands for upconversion nanoparticles. Additionally, catalytic hydrogenation reactions and photo-induced transformations were studied, which benefit in selectivity or reactivity from the adsorbed N-heterocyclic carbene ligands. Furthermore, the structuring of gold surfaces with NHCs could lead to the development of novel nanodevices.

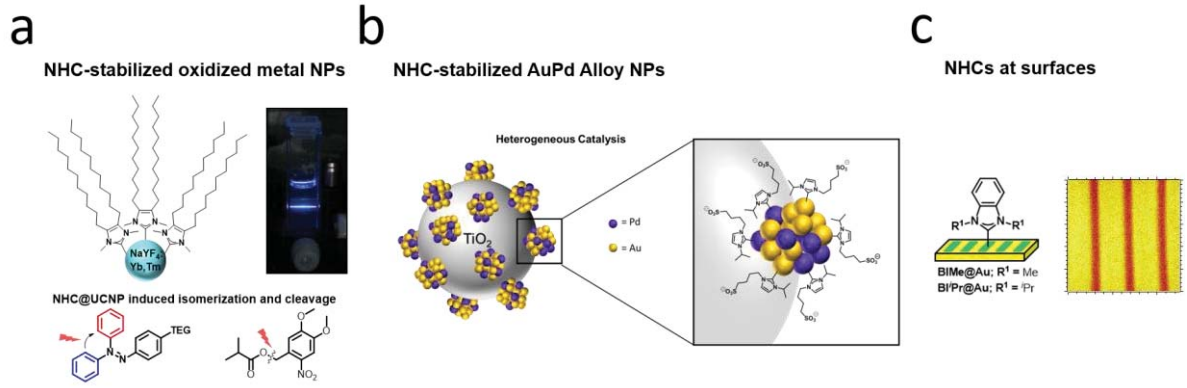

Figure 1: Schematic illustration of N-heterocyclic carbenes as ligands for gold surfaces, noble metal alloy- and upconversion-nanoparticles. **a, b** Different metal nanoparticle systems stabilized by diverse NHC ligands. **c** Gold surface functionalized with NHCs.

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Turning photons into drugs: advanced photoactive compounds and interfaces in the resistance era

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The increasing resistance of many bacteria to antibiotics demands development of alternative treatment methods. In this regard, compounds capable to (photo) eradicate pathogenic microorganisms are of particular value for a range of clinical and other applications. Design of photosensitizers (PS) that can be employed in antimicrobial photodynamic therapy commonly should fulfill many different criteria. Overall photosensitization efficiency of PS can be significantly influenced by the nature of the conjugated moiety[1] and readily tuned via host-guest complexation with supramolecular construct (Fig. 1).[2] One of the favorable attributes for a PS to be used in an antimicrobial photodynamic therapy is the possibility to implement it in formulations for delivery or for antibacterial coatings.[1]

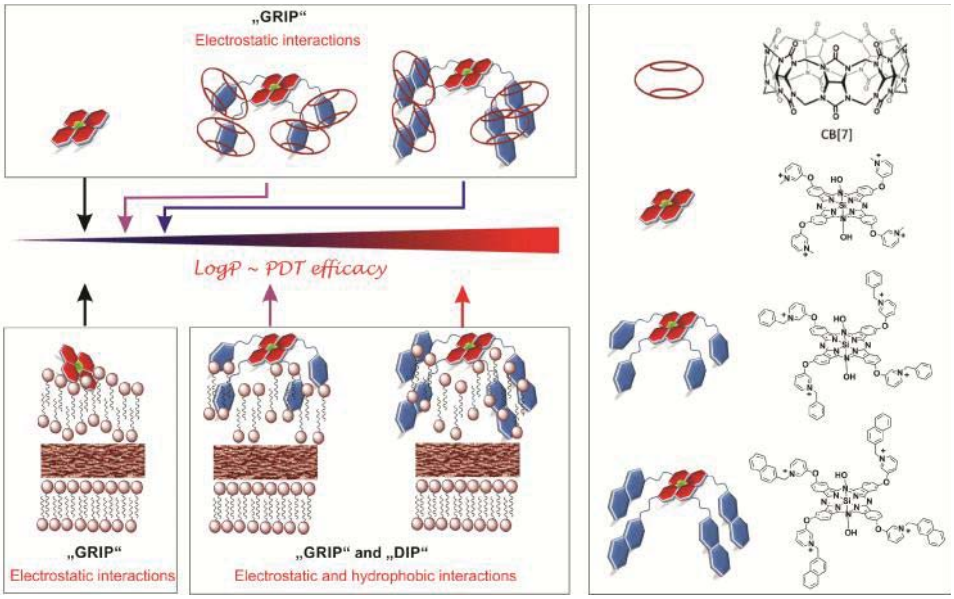

Figure 1. *Schematic representation of probable disposition of the cationic silicon(IV)phthalocyanine molecules with different lipophilicity in the outer membrane of Gram-negative bacteria.*

Control of molecular structure is critical for the development of new, more effective PSs. In our recent study based on zinc(II)phthalocyanine derivatives, we show that PS demonstrates very high photodynamic efficacy when chromophore unit itself can intercalate into densely packed lipid bilayer. In contrast, the interaction of PS decorated with non-flexible ligands with lipid bilayer is hindered and as a result it demonstrates weaker efficacy, despite favorable photophysical characteristics (higher $^1O_2$ quantum yield, near infrared absorption, low tendency to aggregate *etc.*).[3]

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Cooperative binding promotes demand-driven recruitment of AnxA8 to cholesterol-containing membranes

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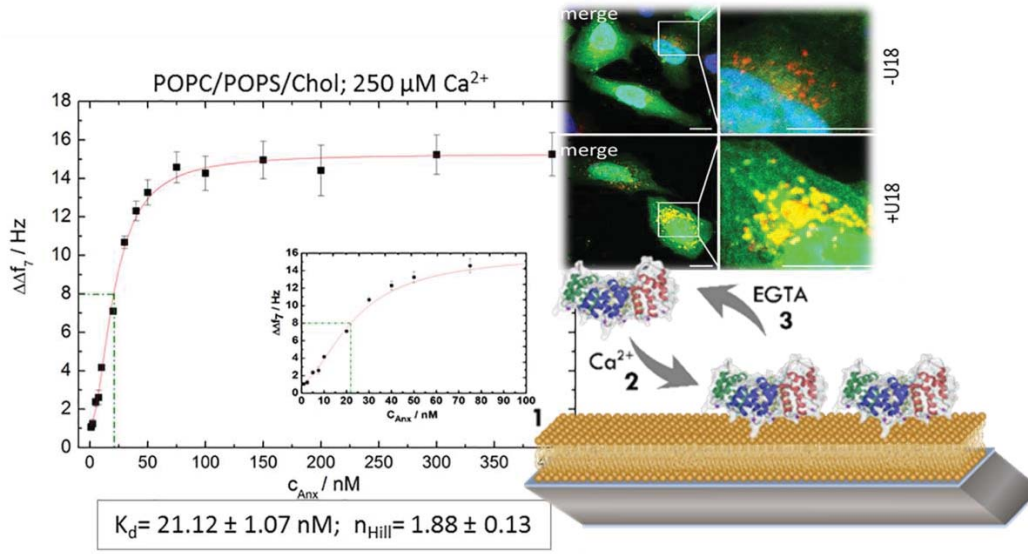
* equal contribution

The lipid composition critically determines the functionality of cellular membranes. Occurrence of enlarged pool of cholesterol in the late endosome/lysosome (LEL) system is commonly linked to endolysosomal dysfunction. Here, we show that Annexin A8 (AnxA8), a member of the annexin family of Ca^{2+} dependent membrane-binding proteins, participates in the endosomal regulation of cholesterol homeostasis. Depletion of AnxA8 caused accumulation of cholesterol in LEL, and pharmacological inhibition of the LEL cholesterol export recruited AnxA8 to the cholesterol-laden LEL. Biophysical analysis revealed that cholesterol enhanced the Ca^{2+}-dependent affinity of AnxA8 to lipid bilayers and induced positive cooperativity of membrane binding. Our findings identify AnxA8 as a potential regulator of LEL cholesterol balance and point to altered cooperativity in membrane binding induced by aberrant lipid composition in the target membrane to control the demand-driven recruitment as a means this cytosolic regulatory protein.



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Cooperative Binding of a Pt(II) Complex to Guanine Quadruplex DNA

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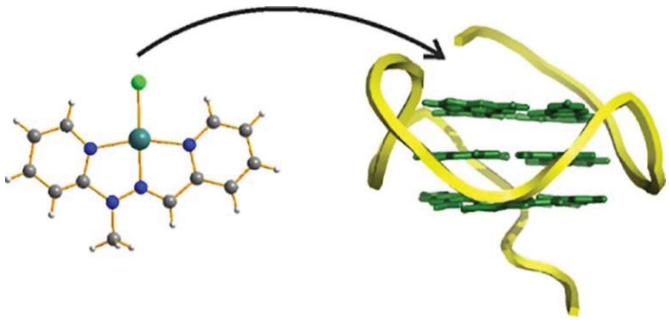
G-quadruplexes represent a polymorph of DNA with a four-stranded helix consisting of two or more stacked G-tetrads. G-tetrads are a planar arrangement of four guanine bases, which are held together by H-bonding interactions *via Watson-Crick* as well as *Hoogsteen* faces and are further stabilized by monovalent cations such as K^+ and Na^+. These higher-order structures are commonly found in the telomeres and in guanine-rich sequences of promoter regions of oncogenes (*c-myc, c-kit*) and thus play a key role in several biological processes.[1] Hence, there is great current interest in developing molecules that stabilize quadruplexes in either the telomeric region or in the promoter regions of oncogenes. Such molecules could provide a basis for the development of novel anticancer drugs.[2]
We studied a series of platinum(II) and palladium(II) complexes with hydrazone-based tridentate ligands using CD, UV and SPR spectroscopy. Two G-quadruplex forming sequences, H-telo and *c-myc* were chosen to study the binding of these complexes. To compare binding selectivity for quadruplex over duplex DNA, a sequence known to form a double strand was chosen, too. All complexes bind more selectively to the quadruplex-forming sequences.[3] By SPR, we found that one of the platinum(II) complexes binds cooperatively to the *c-myc* sequence.



Representation of a platinum(II) complex interacting with G-quadruplex DNA.

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Coiled-coil-based peptide hydrogels as ECM mimics for stem cell differentiation

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Biomaterials have numerous applications in the fields of tissue engineering and regenerative medicine, which rely on the use of stem cells or progenitor cells. Various approaches and applications using peptides as substrates for directing stem cell behavior have been reported. Peptide-based biomaterials have many advantages, as for example

i) biocompatibility and biodegradability,
ii) tunable properties based on the amino acid sequence,
iii) ease of synthesis,
iv) big repertoire of structural motifs and higher-ordered assemblies.

As an example, the coiled-coil structural motif consists of a core of periodical repeats of seven amino acids (heptad) $(a\text{-}b\text{-}c\text{-}d\text{-}e\text{-}f\text{-}g)_n$,[1,2] where especially the a and d positions are occupied with hydrophobic amino acids.[2,3] Coiled-coil motifs have benefits which make them ideal candidates for the design of self-assembling peptide based materials to influence stem cell fate. For example, their straight-forward design based on heptad repeats, facile covalent modification[2,4] and high thermal stability.[4]

Furthermore, coiled-coil based peptides have been increasingly investigated as highly suitable scaffolds for cell culture applications due to their predictable self-assembly properties, which also allow multivalent ligand presentation.[2] Moreover, temperature-responsive hydrogels have been shown to promote growth and differentiation of rat adrenal pheochromocytoma cells.[5] To date, however, very few examples of 2D and 3D coiled-coil based scaffolds that influence stem cell behavior exist.

Our group uses methodology ranging from solid-phase peptide synthesis and reversed-phase high-performance liquid chromatography to circular dichroism spectroscopy and transmission electron microscopy. The goal is to discover the potential of coiled-coil based peptides to directly influence stem cell fate, and to test coiled-coil derived hydrogels that covalently display specific recognition motifs to mimic the extracellular matrix of stem cells.

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Dynamics of a weakly multivalent walker

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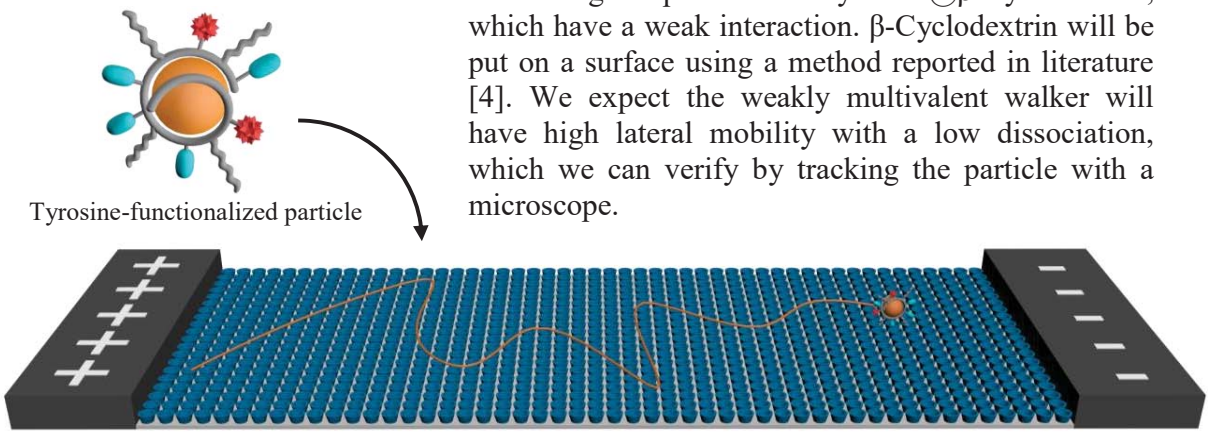
Multivalency is the simultaneous, specific association of multiple, noncovalent interactions, with an affinity surpassing the sum of its parts [1, 2].
In synthetic systems, multivalency is typically used as a tool to increase affinity but tends to kinetically trap a system. Biological systems which employ multivalency, however, are normally dynamic. Viruses for instance use several tens of interactions, but still rapidly move over a cell surface [3].

The overarching goal is learning the design rules behind dynamic multivalent systems. We hypothesize using individually weak interactions in a multivalent fashion will lead to such a dynamic multivalent system. The goal of this project is therefore to make a multivalent walker with individually weak interactions and observe its dynamics.

The core of the walker consists of a negatively charged, fluorescent, polystyrene nanoparticle. The guest, as well as oligo-ethylene-glycol units for antifouling properties, will be attached to the positively charged polymer poly-L-Lysine, which will then wrap itself around the negatively charged core.



The host-guest pair will be Tyrosine@β-Cyclodextrin, which have a weak interaction. β-Cyclodextrin will be put on a surface using a method reported in literature [4]. We expect the weakly multivalent walker will have high lateral mobility with a low dissociation, which we can verify by tracking the particle with a microscope.

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Novel luminophores with aggregation-induced emission properties for protein and amine recognition

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Since the discovery of the fluorescence phenomenon called aggregation-induced emission (AIE)[1], it has become a versatile tool in different disciplines in modern bio-chemistry[2]. The main advantage of AIE luminophores is their ability to light up when their motion is restricted. Only few examples are known from literature using this fluorophore class for the binding to proteins, so that the influence of the binding event is largely unknown. This fluorescence “on“ behaviour enables the direct read-out of binding processes or morphological changes such as gelation, crystallisation, binding or polymerisation, which gives the AIE important applications for bio-chemistry in future. Therefore our aim is the development of novel luminophores with AIE properties as small ligands for the recognition of protein surfaces, binding pockets and specific amines. For this purpose, we use our AIE basic structure functionalised with short amino acid sequences and charged substituents.

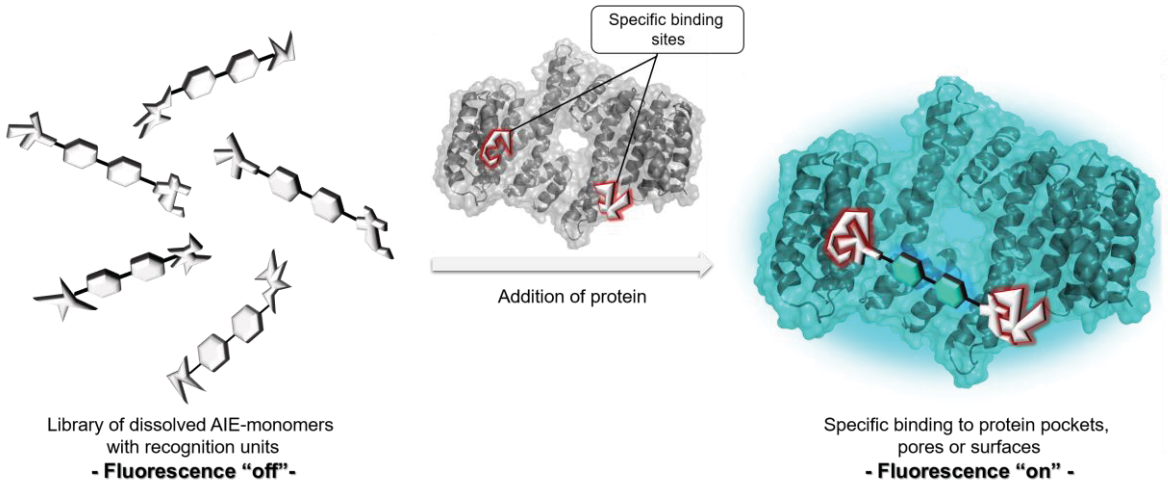

Fig. 1: Schematic presentation of the fluorescence ”on“ behaviour upon protein binding.

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Short and Protecting Group free Total Synthesis of (–)-Δ^8-THC, (–)-Machaeriol B, D and Analogues

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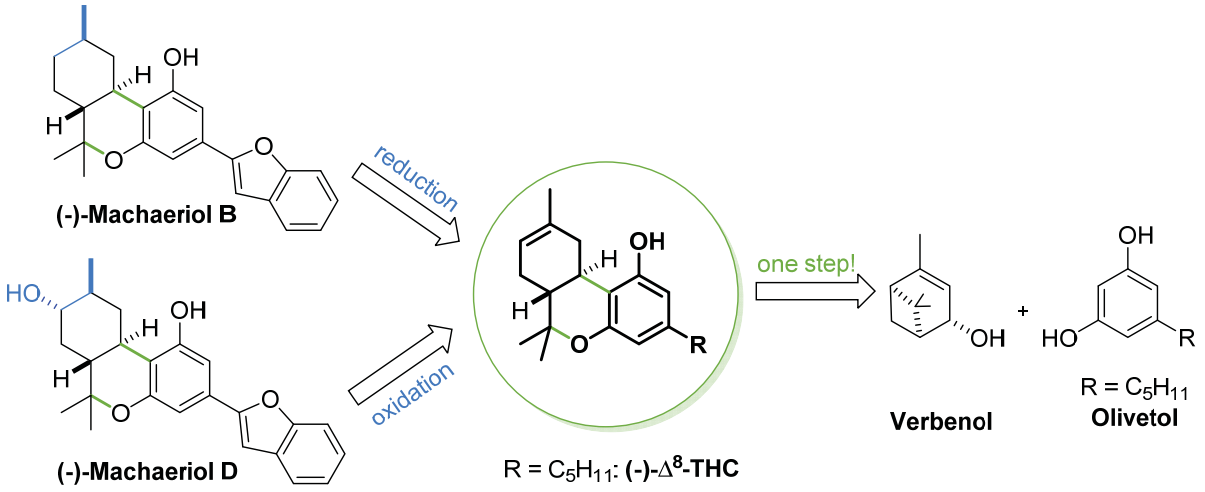
Since the discovery of the biological and medical importance of (–)-Δ^9-Tetrahydrocannabinol and its isomer (–)-Δ^8-THC, the cannabinoid family has gained a lot of research interest of scientists worldwide. Due to their pharmacological potential, some of these natural products have found applications as drugs for example against chronic pain, nausea and spasticity.[1,2]

Machaeriols such as (+)-Machaeriol B and (+)-Machaeriol D are natural products with cannabinoid related structure. First investigations revealed that these compounds have potent *in vitro* antimalarial activity. Despite their important biological activity, only few total syntheses of these compounds have been reported.[3-5]

All these compounds feature a tricyclic dibenzopyran motif as common structural element. In contrast to THC derivatives, machaeriols contain an additional hydroxy-bearing stereogenic center *anti* to the methyl group, rendering their synthesis more challenging.

Herein we present a short and protecting group free total synthesis in which the common structural element is constructed in only one step by a condensation reaction of (*S*)-*cis*-Verbenol with different resorcinol derivatives. A selective hydroboration of the double bond and subsequent reductive or oxidative work-up directly provides the natural products Machaeriol B and Machaeriol D.



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Self-Sorting of Covalent Organic Cage Compounds

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Porous functional materials have recently gained increased interest in material sciences due to potential applications in heterogeneous catalysis, sensing, gas storage and separation or membranes.[1] In particular, discrete molecular structures such as covalent organic cage compounds combine unique properties such as solution processability with intrinsic porosity. Efficient cage synthesis can be achieved through dynamic bond formation via boronate esters or imines.

Here we report on the synthesis of a series of covalent organic cage compounds based on catechol-functionalized tribenzotriquinacene (TBTQ) derivatives and various diboronic acids. Following a *molecular design approach*, geometrical shapes, structures and sizes of these molecular nanoarchitectures can be adjusted by controlling the bite angles of the respective building blocks.[2, 3] Furthermore, multi-component reaction mixtures lead to competitive, narcissistic or social self-sorting processes and cage-to-cage transformations can be performed utilizing relative stabilities for these cages.

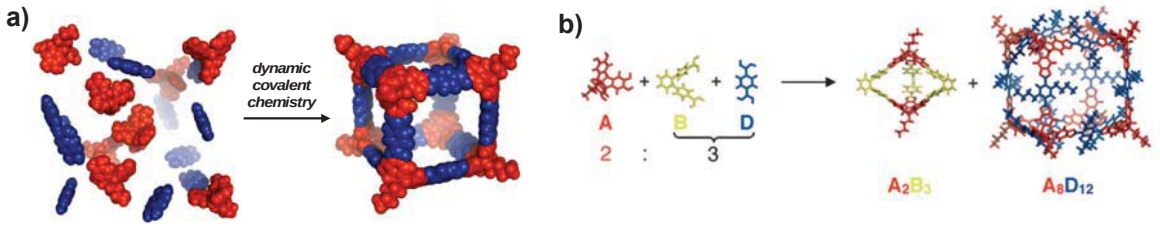

Figure 1. a) Organic covalent cage formation via dynamic covalent chemistry. b) Narcissistic self-sorting.

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Asymmetric organocatalysis with chiral [2]catenanes

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The development of chiral organocatalysts has gained much attention in the last decade.[1] Especially chiral Brønsted acids like 1,1'-binaphthyl phosphoric acids induce high enantioselectivities in a variety of catalytic reactions. Gong *et al.* were able to show that the use of covalently linked bisphosphoric acids can lead to drastically increased enantioselectivities when compared to monophosphoric acids.[2]

Our group has developed a novel approach towards non-covalently linked bisphosphoric acids by incorporating two chiral Brønsted acids into a [2]catenane structure (see figure 1).[3] Due to the mechanical bond, functional groups which are in close proximity can be prevented from dissociation without decreasing the conformational flexibility. The catenane (*S*,*S*)-**1** was applied in the asymmetric transfer hydrogenation of 2-substituted quinolines to give the corresponding tetrahydroquinolines in high enantiomeric excesses.[4] Additionally, we have now investigated catenanes with different ring sizes as this might influence the conformational flexibility. While the enantioselectivities stayed the same for three differently sized catenanes, we could show that the yield in the Calcium-template-directed synthesis of catenanes drastically increases with larger ring sizes.

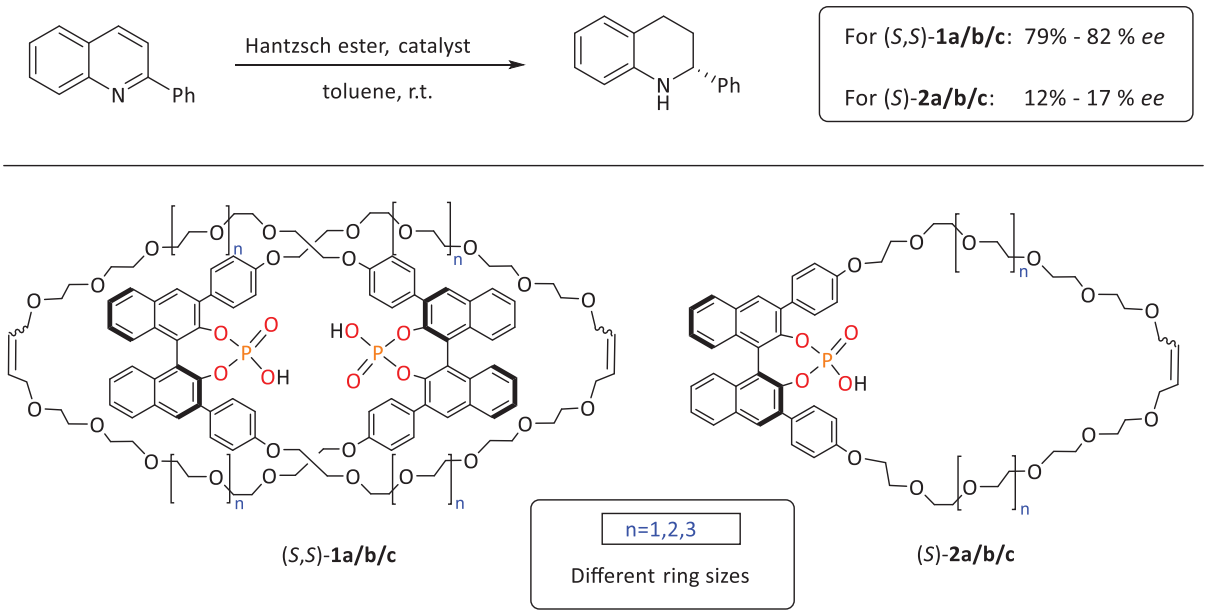

Figure 1: Catenanes and macrocycles that were used in the study.

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1H-Imidazo[4,5-f][1,10]phenanthroline - a versatile nucleobase surrogate in metal-modified nucleic acids

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DNA is a genetic material which encodes genetic information among all living organisms by a synchronous way of replication and transcription, according to the central dogma of molecular biology. In addition, the three-dimensional existence of DNA and its structural features provided a new horizon to supramolecular chemistry for its unique self-assembly and molecular recognition behavior, which can be manipulated in a predetermined fashion for the construction of various supramolecular nanoarchitecture. A way to diversify nucleic acids is the introduction of artificial base pairs. They can either rely on hydrogen bonding or the hydrogen bonds can be replaced by metal-ligand coordinate bonding. Towards the end, several promising applications have already been established in this area, including the construction of nanowires, switchable devices, the specific detection of canonical nucleobases, and an expansion of the genetic four letter code etc.[1]

1,10-Phenanthroline is a very popular ligand in the context of coordination chemistry. The planarity of its imidazole-appended derivative (imphen) makes that ligand preferable as an artificial nucleobase in nucleic acids due to its stabilizing π-stacking interaction with neighbouring bases.

Here we report the versatility of the GNA-functionalized imphen towards the introduction of metal-based functionality within different topologies of nucleic acids (GNA: glycol nucleic acid). The geometrical constraints imposed by imphen were systematically utilized for the unprecedented stabilization of Cu(I) in aqueous medium via metal-mediated base pairing. Based on the observation of imphen-M-pyrimidine hetero base-pair formation, we developed a molecular beacon capable of discriminating the pyrimidine nucleobases.[2] This beacon indeed performed well for the detection of SNP-related diseases like breast cancer and pancreatic cancer.[3] In addition, we devised the first heterometallic assembly by the involvement of only artificial imphen nucleoside analogue. It enabled the synchronous incorporation of two different soft metal ions under precise control over their positions in the nucleic acid scaffold. At the end, the tendency of forming an octahedral metal complex was categorically exploited by generating different metal-containing three-way junctions.

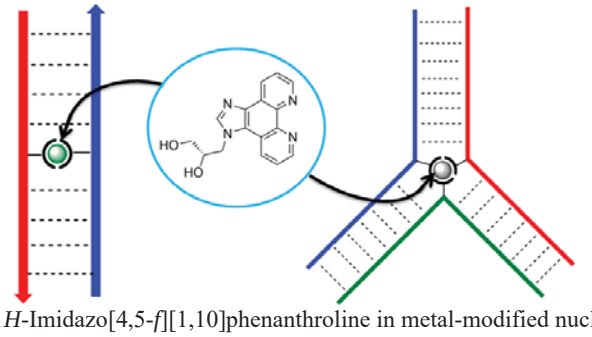

Figure 1. 1*H*-Imidazo[4,5-*f*][1,10]phenanthroline in metal-modified nucleic acids.

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Multivalent Sialylated Polyglycerol Derivatives Inhibit Influenza Virus Propagation

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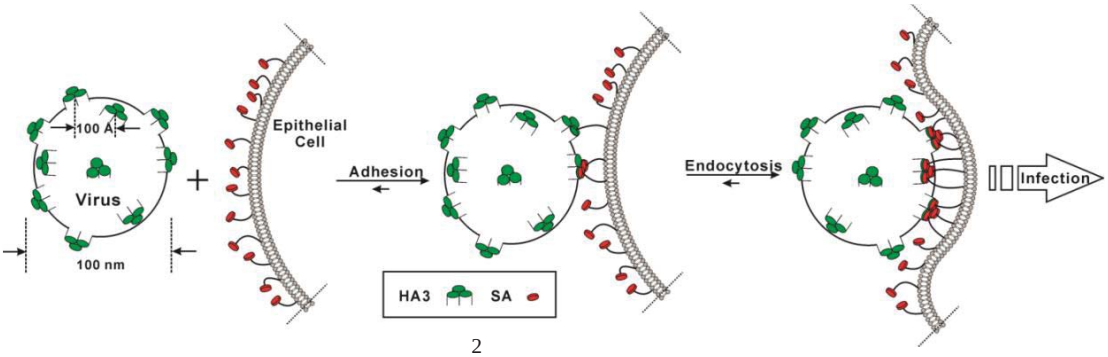
Yearly Influenza Virus vaccination yields dissatisfactory protection and the efficacy of existing drugs is limited due to the development of resistant virus strains. Hence, novel drugs are needed urgently.

Inhibition of influenza A virus (IAV) infection by multivalent sialic acid (SA) inhibitors preventing viral hemagglutinin binding to host cells of the respiratory tract is a promising strategy. However, optimal geometry and optimal ligand presentation on multivalent scaffolds for efficient inhibition both *in vitro* and *in vivo* application are still unclear.

Here, in this work we tried to optimize the geometry and ligand density of the multivalent inhibitor for an efficient infection inhibition *in vitro* and *in vivo*



SA: 50-200 per 100 nm^2 on the surface of the target cell

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Iterative Preparation of Heteroatom-Rich Systems – Towards an Atom for Atom Synthesis of Carbohydrates

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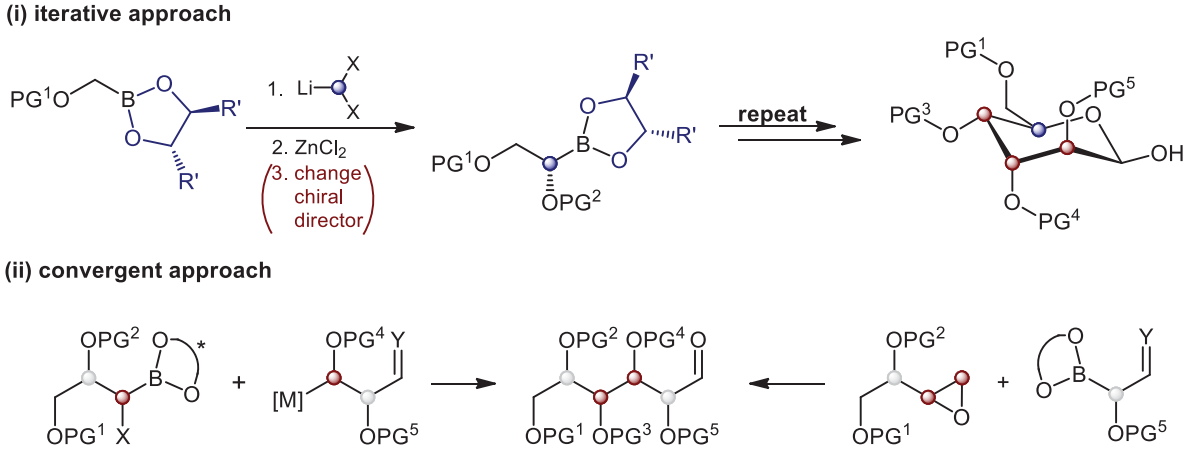
Many biosyntheses of heteroatom-rich natural products, like polyketides and carbohydrates, are based on the iterative assembly of smaller building blocks.[1] In principle the iterative application of Matteson homologation/substitution sequences offers a C_1-based synthetic approach to individually protected derivatives of these structures. Unfortunately, highly heteroatom substituted systems present a serious challenge to this chemistry and no carbohydrates longer then pentoses have been achieved so far.[2] To address this challenge we investigate both (i) iterative and (ii) convergent synthetic strategies for the synthesis of carbohydrates based on carbenoid/boronate chemistry (Scheme 1).



Scheme 1: Iterative and convergent route to diversely protected monosaccharides.

(i) For Matteson homologations a chiral boronic ester is treated with a carbenoid to form an ate complex, followed by $ZnCl_2$ mediated, diastereoselective 1,2-rearrangement. Subsequent addition of a corresponding nucleophile (e.g. alkoxides) allows for introducing diversely protected hydroxy substituents.[3] By using appropriate protecting group patterns we aim to overcome earlier limitations, which could have been caused by coordination of the boronic ester moiety to individual alkoxy groups. (ii) If these limitations remain persistent, convergent assembly of two building blocks present an alternative strategy. To achieve this, we investigate substitution of α-haloboronic esters with chiral carbanions and epoxide insertion into boronic esters in order to form differentially protected 1,2-diols.[4]

From these experiments a new synthesis of the lupine alkaloid cytisine, as well as an iterative, transition metal free synthesis of alkenes emerged, which are also presented.

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Exploring the Scope of Radical-Polar Crossover Reactions of Vinyl Boron Ate Complexes in Three Component Couplings

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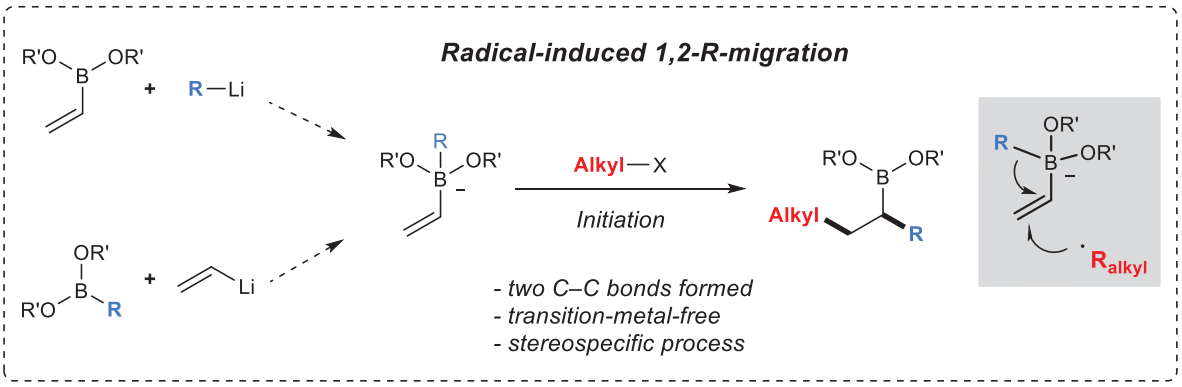
Vinylboronic esters are highly important building blocks for C–C bond formations in the *Suzuki-Miyaura* coupling.[1] Importantly, vinyl boron ate complexes can be also used in three component coupling reactions, in which two new bonds are formed and the valuable boronic ester moiety remains in the product. The general strategy is based on the ability of boronic esters to form vinyl boron ate complexes with carbon nucleophiles, which further can undergo a 1,2-metalate rearrangement induced by different electrophilic trigger mechanisms.[2,3]

Along these lines, we demonstrated that *in situ* prepared vinyl boron ate complexes react efficiently with electrophilic alkyl radicals generated from alkyl iodides. The resulting radical anions undergo a radical-polar crossover reaction and a 1,2-alkyl/aryl shift from boron to the α-carbon sp^2-center provides valuable secondary and tertiary alkyl boronic ersters.[4]



Notably, the cascade proceeds without the help of any transition metal and uses commercial starting materials allowing a readily construction of molecular complexity. The reaction sequence tolerates α- and β-substituted vinyl boronic esters and the scope of the radical precursor includes perfluoralkyl iodides, α-iodo esters, iodoacetonitriles, α-iodo phosphonates and α-iodo sulfonates. Initiation of the chain reaction can be either achieved by catalytic amounts of BEt_3[4], by photo-[5] or photoredox initiation.[6]

Furthermore, we recently demonstrated that vinyl boron ate complexes of enantioenriched secondary alkyl pinacolboronic esters undergo stereospecific radical induced 1,2-migration in radical polar crossover reactions.[6] A subsequent oxidation or protodeborylation leads to valuable α-chiral ketones and chiral alkanes with excellent enantiopurity.

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α-Diazo Ketones in On-Surface Chemistry

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While the on-surface reactivity of many functional groups like organic halides, terminal alkynes or carbonic acids has already been investigated, some groups that have non-interchangeable properties in solution phase chemistry are still unknown in surface assisted polymerization.[1] Carbenes are highly important intermediates in solution phase chemistry, but have so far not been formed, characterized and converted at single crystal surfaces In addition *α*-diazo ketones, being well understood carbene precursors, are so far unknown. Herein we present the on-surface reactivity of *α*-diazo ketones (Figure 1).[2]

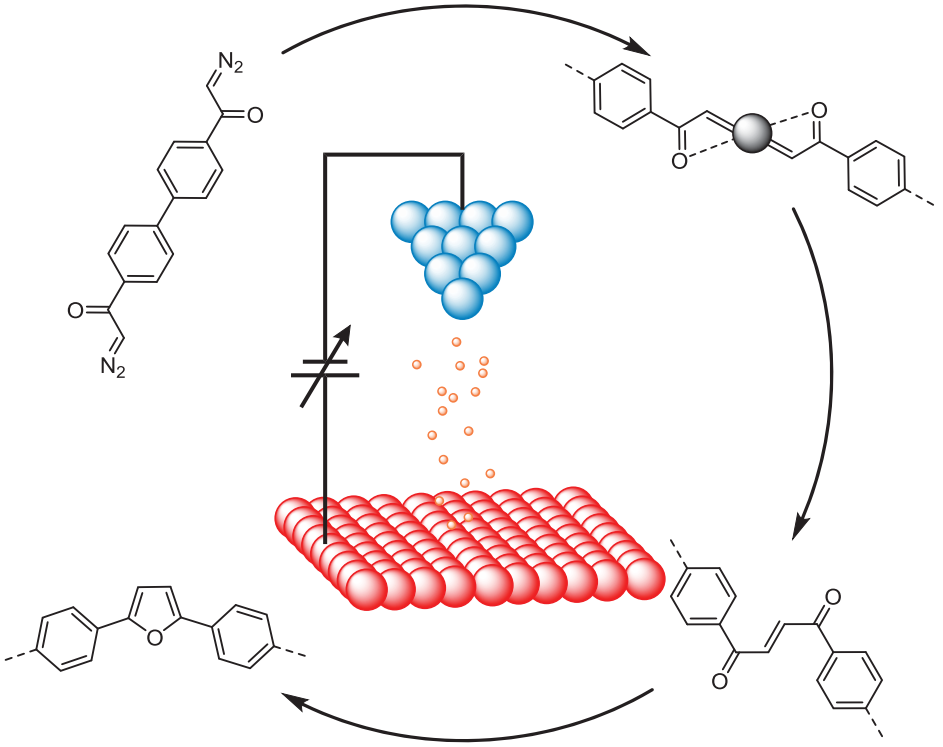

Figure 1. The observed on-surface reactions of biphenyl-4,4'-diyl-bis(2-diazoethan-1-one).

We observed the formation of two different strictly alternating copolymers at elevated temperatures and different reaction behaviours on Au(111) and Cu(111). This is the first example for *α*-diazo ketones and the formation of furans in on-surface chemistry. To elucidate the structures that were formed, we performed STM, nc-AFM, XPS and DFT studies.

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Au(I)-mediated synthesis of hexathymidine-DNA-pyrazol(in)e chimeras, an efficient entry to DNA-encoded libraries inspired by drug structures

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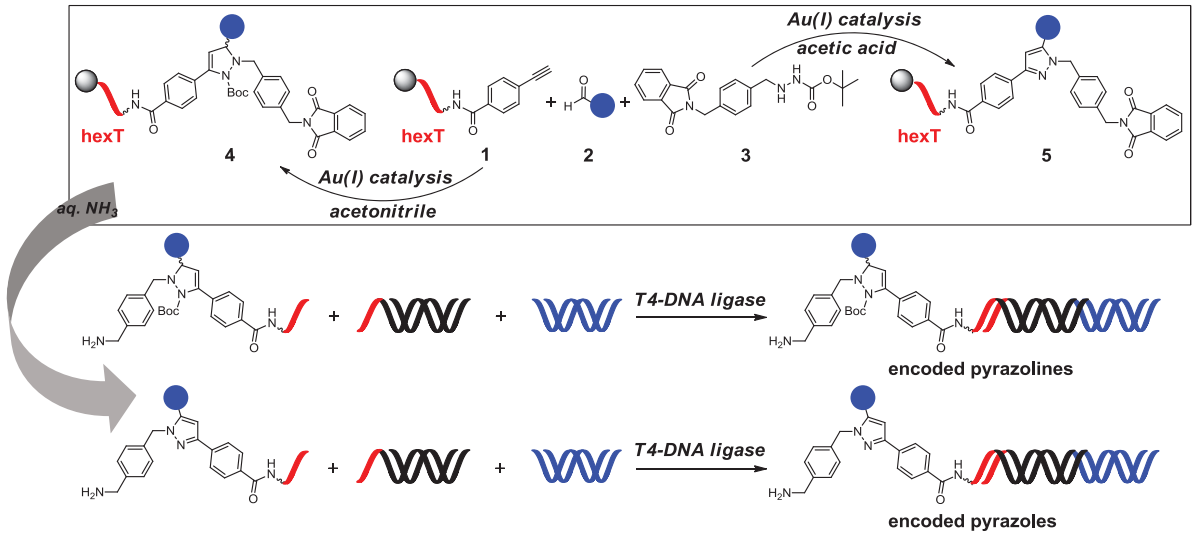
The selection of large, pooled DNA-encoded small molecule libraries (DELs) is a validated technology for the target-based identification of bioactive compounds. DELs are synthesized by alternated organic synthesis and encoding steps in combinatorial manner.[1] Prerequisite for library synthesis are DNA-compatible preparative organic reactions. Au(I) catalysts enable access to drug-like heterocycles from simple educts, yet they are not available for library synthesis as they interact with purine nucleosides, eventually causing depurination. To circumvent depurination, we initiate library synthesis with a hexathymidine DNA sequence called "**hexT**" which allowed us to use a broader spectrum of catalysts in the very first step of DEL synthesis. Accordingly, we call this synthesis strategy "**TiDEC**" (oligo**T**hymidine-**i**nitiated **D**NA-**E**ncoded **C**hemistry).[2] Here, we demonstrate the synthesis of **hexT**-conjugates of highly substituted pyrazolines and pyrazoles from **hexT**-alkynes and readily accessible starting materials: the solid phase-bound **hexT**-alkyne **1** was reacted with aldehydes **2** and hydrazides **3** using a catalytic system consisting of a Au(I)-complex and a Ag(I)-salt in acetonitrile to give rise to **hexT**-pyrazolines **4**, whereas the same reaction performed in glacial acetic acid yielded **hexT**-pyrazoles **5**.[3] The hexT-heterocycle conjugates were cleaved from the solid phase, and ligated to coding sequences to record the heterocycle synthesis.



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Cage-like nanocapsules for molecular recognition and catalysis

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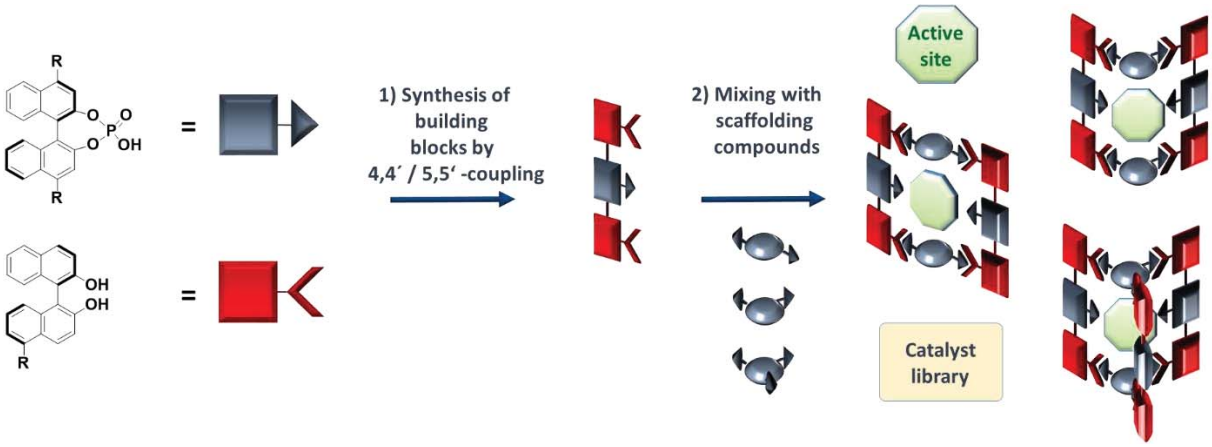
Naturally occurring catalysts such as enzymes are widely known for their excellent catalytic activities and ability to discriminate between different substrates. Their well-defined tertiary structure provides a suitable environment for host-guest chemistry and catalysis. It has been one of the central aims of supramolecular chemistry to mimic enzymatic behaviour for catalytic purposes, for example by providing a confined reaction environment inside a molecular capsule. [1]

This project focuses on the development of supramolecular capsules which are endohedrally functionalised with catalytically active groups. This simulates the active site of an enzyme catalyst by providing a closely confined reaction space, bringing the substrates in close proximity and thereby driving the reaction forward.



Scheme 1. Synthesis and self-assembly of building blocks to form supramolecular cages.

The formation of the supramolecular capsules takes place by self-assembly of linear building blocks derived from BINOL-based phosphoric acids with suitable scaffolding compounds in a 2:2 or 3:2 fashion, e.g. via hydrogen bonding or by dynamic covalent chemistry.

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Enantioselective Synthesis of Chiral Trifluoromethylated Allenes by S_N2'-Reaction

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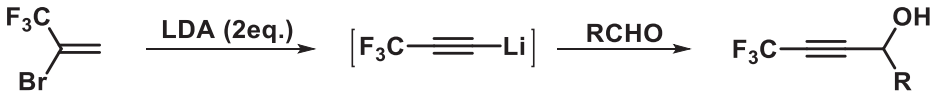
The trifluoromethyl group (CF_3) plays an important role in organic chemistry because of its unique electronic properties. Due to the highly stability of C–F bonds and the increased lipophilicity by incorporation of CF_3-groups, trifluoromethylated compounds play a key role in Chemical Biology and Medicinal Chemistry and are used for a large number of pharmaceuticals and agrochemicals. [1,2]

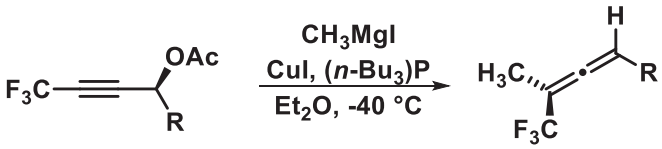
The *anti*-selctive S_N2'-substitution of propargylic electrophiles with organometallic reagents is one of the most efficient methods for the stereoselective synthesis of allenes.[3] Likewise, an *anti*-selective S_N2'-reduction of propargyl oxiranes using an NHC-stabilized copper hydride catalyst has been developed.[4]

The synthesis of enantiomerically enriched or pure CF_3-containing molecules is very challenging. We started from 2-bromo-3,3,3-trifluoropropene, which is treated with 2 eq. of LDA. The acetylide can be added to various aldehyds and ketones to generate a wide range of trifluoromethyled propargyl alcohols (Scheme 1).[5]



Scheme 1: Synthesis of trifluoromethylated Alcohols.

We use enantiomerically enriched trifluoromethylated propargylic acetates for the preparation of chiral allenes. With methyl magnesium cuprate, which is formed *in situ* from a Grignard reagent and copper(I) salt in presence of tributyl phosphite, enantiomerically enriched CF_3-containing allenes are obtained by *anti*-selective S_N2'-substitution (Scheme 2).[6]



Scheme 2: Synthesis of trifluoromethylated allenes by S_N2'-substitution.

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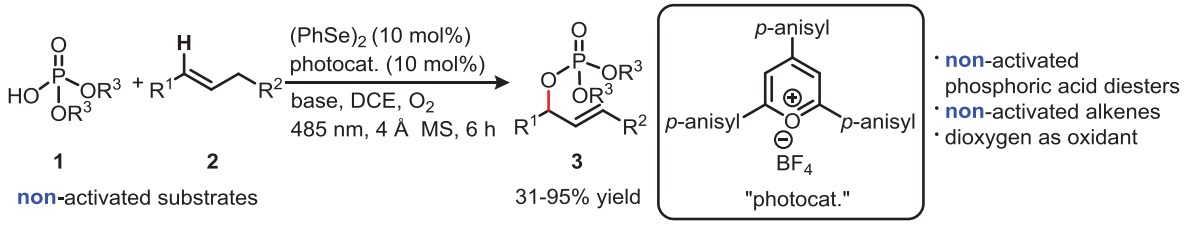
Aerobic Phosphatation of Alkenes *via* Dual Selenium Catalysis

Felix Krätzschmar, Goettingen/D; Christian Depken, Goettingen/D;Rene Rieger, Goettingen/D; Katharina Rode, Goettingen/D; Alexander Breder, Goettingen/D

Phosphoric acid esters are omnipresent structural motifs, which not only fulfill essential functions in living organisms, but are also crucial to the industrial production of functional materials such as flame retardants and plasticizers.[1] Phosphoric acid esters have also important applications as organo-catalysts[2] or electrophilic reagents in transition metal catalysis[3]. Owing to the multifaceted pertinence of organic phosphates in the realm of biology, material sciences and chemistry, there is a strong need for economical strategies to build up these motifs from readily accessible, cheap, and easy to handle starting materials. Traditional methods often involve the stoichometric use of pre-activated phosphorus (V) compounds[4] which are coupled with alcohols under Brønstedt-acidic or Lewis-basic conditions.[5] The toxicity and moisture sensitivity of, for example, common phosphoric acid chlorides are severe disadvantages compared to phosphoric acid itself or organic hydrogen phosphates which would make the direct use of the latter species very attractive. Herein we present a new dual catalytic regime to transform non-activated alkenes and non-activated hydrogen phosphates to phosphoric acid triesters (Scheme 1).[6] The application of a photoredox/selenium-π-acid catalysis manifold enables the use of molecular oxygen as an atom-economical and environmentally benign terminal oxidant trough a proton-coupled electron transfer.



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Stereoselective Synthesis of the Benzodihydropentalene Core of the Fijiolides

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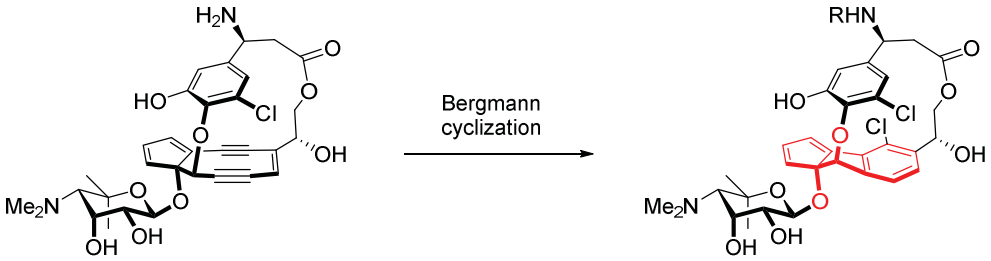
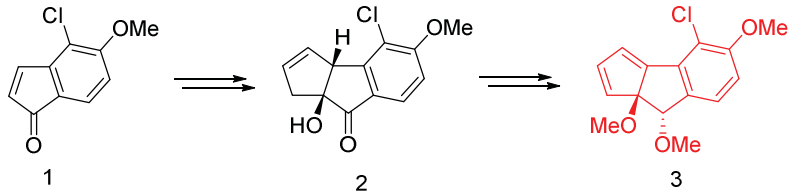
Philipps-Universität Marburg, Fachbereich Chemie, Hans-Meerwein-Straße, 35043 Marburg

Ene-diyne derived natural products and their corresponding Bergmann-cyclization products display an interesting family of secondary metabolides, both in terms of molecular architecture and biological activity. While most of them lose their DNA damaging abilities upon cyclization[1)] the fijiolides A and B, derived from Bergman-cyclization of C-1027, were found to be potent inhibitors of TNF-α-induced NFκB activation with 70.3% for fijiolide A (IC_{50} 0.57 µM) and dose-independent 46.5% for fijiolide B.[2)] Furthermore, fijiolide A was found to induce quinone reductase-1 (QR 1) with a ratio of 3.5 (28.4 µM). In combination with their fascinating geometric structure, which includes a rotational restricted *p*-cyclophane moiety, a sterically hindered glycosylated tertiary alcohol at a cyclopentadienol as part of a 8,9-dihydroxylated benzodihydropentalene substructure, they present a challenging target for natural product synthesis.





Herein, a stereoselective synthesis of the fijiolide`s benzodihydropentalene core is described, starting from indenone **1**. The synthesis includes a rhodium catalyzed asymmetric conjugate addition to **1** for subsequent construction of cyclopentene **2**. Directed reduction of the ketone and regioselective transformations addressing the olefin then allow introduction of the cylopentadiene to give the fijiolide`s core structure **3**.[3)]

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Guest-to-Host Chirality Transfer in Photoswitchable Metallocages

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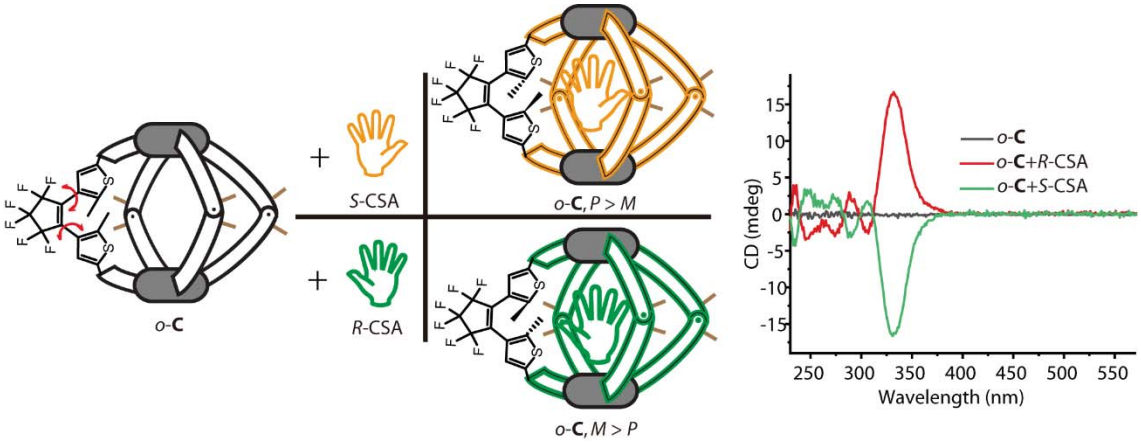
In supramolecular chemistry, the self-assembly of symmetrical banana-shaped bis-monodentate ligands and square-planer Pd^{II} or Pt^{II} cations has proven to be a very effective method to form discrete coordination cages.[1] Previously, our lab has introduced light-switchable function into the coordination cages based on dithienylethene (DTE) ligands. Interconverting between open and closed cage $[Pd_2\mathbf{L}^a_4]$ under different wavelengths of light leads to reversible switching guest uptake and release.[2] With the same DTE backbone, but slight change of ligand design, irradiation converts ligands from their conformationally flexible open form to more rigid ring-closed form. Thereby leading to disassembly and rearrangement between small $[Pd_3\mathbf{L}^b_6]$ triangle and large $[Pd_{24}\mathbf{L}^b_{48}]$ rhombicuboctahedron sphere.[3]



Scheme 1: chiral guest encapsulation by DTE-based coordination cage (left) and CD spectrum of host-guest complex.

Open form DTE is generally achiral due to its structure flexibility and fast rotation around the thiophene-cyclopentene single bonds. While photocyclization to the closed form of DTE produces two enantiomers, which were usually found as a racemic mixture in solution. DTE-based open ligand *o*-**L** assembles with Pd^{II} at 70 °C within 6 hours to form open-cage $[Pd_2(o\text{-}\mathbf{L})_4]$. When adding 1.0 eq. chiral camphoussulfonate guest (*R*/*S*-CSA) to the open cage (Scheme 1, left), it shows strong CD signals of the host-guest complex (Scheme 1, left), indicating the chiral guest induced the chirality of the open cage. Irradiation the host-guest complex [*R*/*S*-CSA@$Pd_2(o\text{-}\mathbf{L})_4$] at 313 nm, it shows enantioselectivities of ring closure of the DTE ligand, which was detected by HPLC. Their enantioselectivity depends on the temperature. As the temperature goes down from room temperature to 77 K during irradiation, the enantiomer excess (ee) value of closed ligand goes up from 6.8% to 27.1%.

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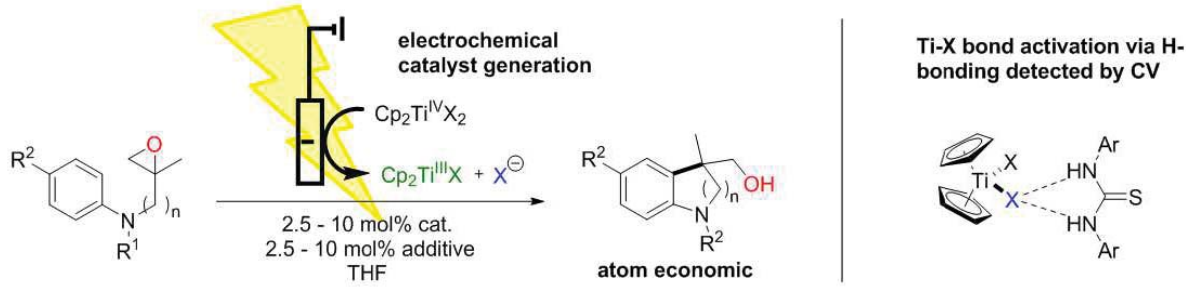
Mechanism-Based Condition-Screening for Sustainable Catalysis in Single Electron Steps by Cyclic Voltammetry

T. Liedtke, P. Spannring, L. Riccardi and Prof. Dr. A. Gansäuer

Catalysis with a thunderbolt through screening with cyclic voltammetry! A cyclic voltammetry based screening method for Cp_2TiX-catalyzed reactions is introduced. Our mechanism-based approach enables the study of the influence of various additives on the electrochemically generated active catalyst Cp_2TiX which is in an equilibrium with catalytically inactive $[Cp_2TiX_2]^-$. Thioureas and ureas are most efficient in the generation of Cp_2TiX in THF. Ti-X bond activation by thioureas enables bulk electrolysis of Cp_2TiX_2 and sustainable catalysis. This key-interaction was identified by a CV-screening method that directly observes mechanistic aspects of the electrolysis and catalysis in single electron steps.[1]



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Reactions of Donor–Acceptor Cyclopropanes with Naphthoquinones: Redox and Lewis Acid Catalysis Working in Concert

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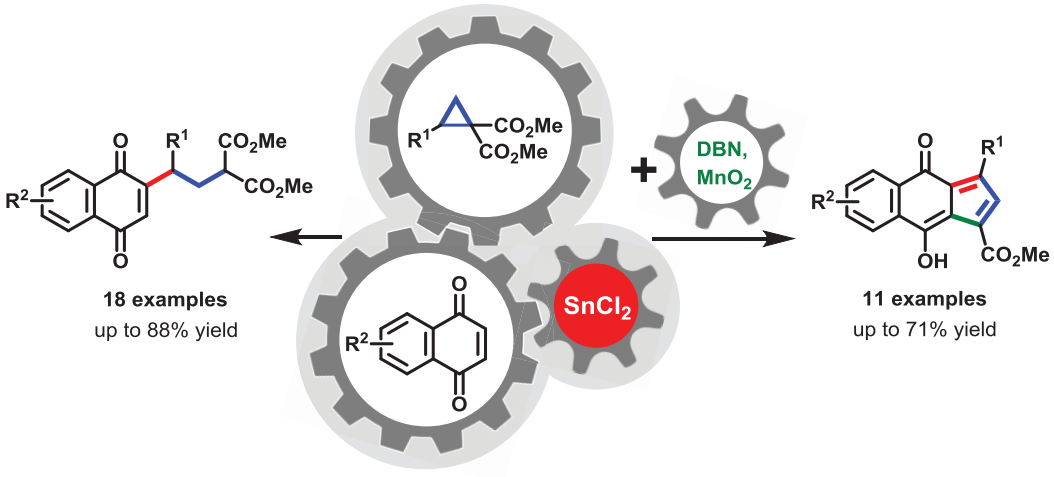
In the past decade, donor-acceptor (D-A) cyclopropanes have become an important three carbon atom building block. The driving force of these reactions is the high ring strain of cyclopropanes (27.5 kcal/mol). Furthermore, one bond is polarized by a donor and an adjacent acceptor moiety. This vicinal substitution pattern stabilizes a 1,3-zwitterion which can undergo cycloaddition reactions, rearrangements or ring-opening reactions.[1,2]



Up to now, D-A cyclopropanes have never been reacted with carbon electrophiles. Herein, we report, that 1,4-naphthoquinone is able to open a D-A cyclopropane by forming a new C-C-bond. The first step is the *in-situ* umpolung of the naphthoquinone to its dianion in the presence of $SnCl_2$. Additionally, a tin cation activates the D-A cyclopropane to trigger the ring-opening. Further investigations have shown that these 2-functionalized naphthoquinones form red dyes under basic and oxidative conditions. The colour can be easily change by substitution of the hydroxygroup.[3]

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DNA-supported bimetallic photoredox catalysis

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In the era of climate change and limited fossil resources, the generation of energy or the synthesis of materials from renewable resources is particularly important. Over the last years, catalytically active bimetallic photoredox-systems have been developed, which allow the use of solar energy for the generation of hydrogen from aqueous solutions or the formation of new C-C bonds.[1,2] However, the rational design of effective photoredox-catalysts is still difficult, which has limited the success in generating highly active and stable systems. For this reason, novel approaches that allow for the fast generation of catalyst libraries are highly sought after, since these might allow the identification of promising new catalyst structures.

We herein present a concept for the generation of novel bimetallic photoredox-catalysts based on DNA-templation. The synthesis of such photoredox catalysts is being accomplished by tethering organometallic complexes (a photosensitizer and a reaction center, see figure 1) to complementary oligonucleotide strands. Coupling worked best via strain-promoted copper-free click reaction. The resulting functionalized DNA-strands can then undergo hybridization to generate the corresponding double-helical structures, thereby bringing the respective metal-complexes into close proximity and giving the desired bimetallic catalysts. Combination of differently functionalized strands thus allows the easy generation of a library with a plethora of photoredox catalysts.

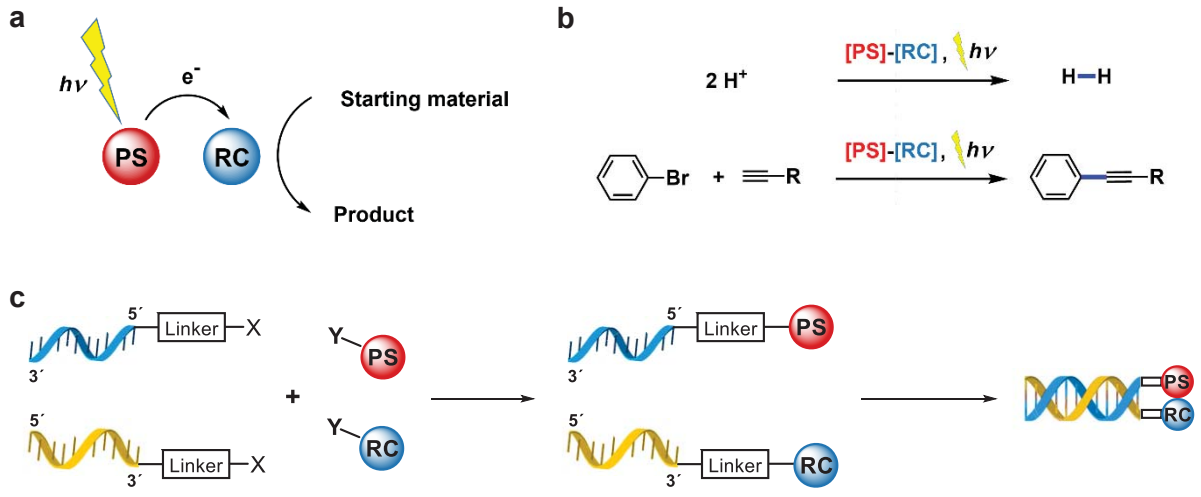

Figure 1: a) Concept of photoredox-catalysis via photosensitizer and reaction center, **b)** Possible reactions via photoredox-catalysis, **c)** Generating a bimetallic catalyst-library by hybridization of differently functionalized oligonucleotides.

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The Efficient Allylation of Ketones– Bench-Stable Reagents for the Highly Enantioselective Generation of all Stereoisomeres of Tertiary Homoallylic Alcohols

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[b]*Department für Chemie, Universität zu Köln, Cologne/Germany*
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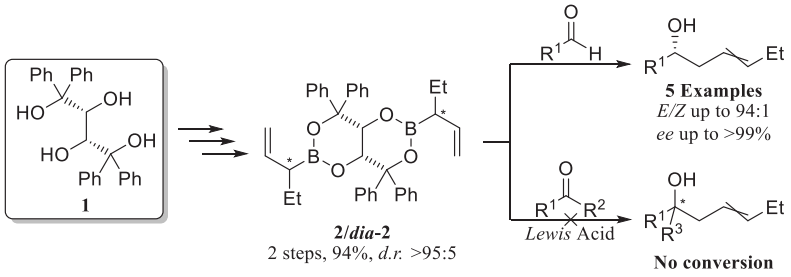
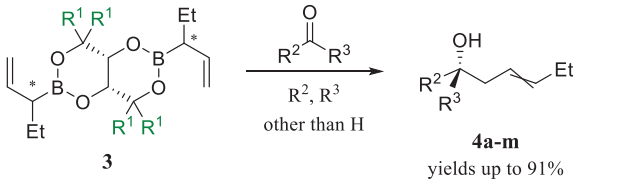


The boron based allylation of carbonyl compounds is an effective and reliable tool for the generation of enantiomerically pure homoallylic compounds, a moiety of widespread presence [1]. As a very potent agent on this behalf, we developed tartrate derived protecting group **1** providing an outstanding reactivity/stability balance. Thus, the convenient and highly selective syntheses of all four stereoisomers of secondary homoallylic alcohols depending on the configuration of the corresponding allylboronate **2/*dia*-2** could be demonstrated. However, due to their inherently lower reactivity, ketones remained inert to the systems established [2].



In order to overcome this problem, rational reagent design was employed 'tuning' the reagents' reactivity suitably. Herein we present new allylation reagents **3** enabling the very convenient and highly selective generation of all stereoisomers of tertiary homoallylic alcohols **4a-m**. Not only can the 2nd generation compounds be utilized without requiring inert conditions, but moreover highly selective access to *E*- and *Z*- configured tertiary homoallylic alcohols was given for the first time. Conclusively, all synthetic approaches and findings were investigated by DFT-calculations, revealing further mechanistic insight and rationalizing the presented methodology thoroughly [3].

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Supramolecular Polymerization of Pd(II) and Pt(II) BODIPY-based Structures

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BODIPY dyes have attracted considerable attention in the past decades due to their excellent optical, photochemical and electronic properties as well as physiological stability, which have enabled their application in fields as diverse as optoelectronics and biomedicine.[1] Some of these applications require an organized dye arrangement into well-defined aggregates, which can be achieved by molecular design.[2] In addition, BODIPY-dyes have the ability to self-assemble in an H- or J- type fashion, because of the presence of π-π interactions and the small size and planarity of the BODIPY core.

Herein, we synthetized an asymmetric BODIPY dye endowed with a pyridine functional group which can react with Pd(II) or Pt(II) in order to form the corresponding metal complexes. Also, these structures are soluble in apolar solvents due to the presence of long aliphatic side chains. These characteristics allow us to investigate the supramolecular self-assembly in solution for the ligand and the metal complexes.

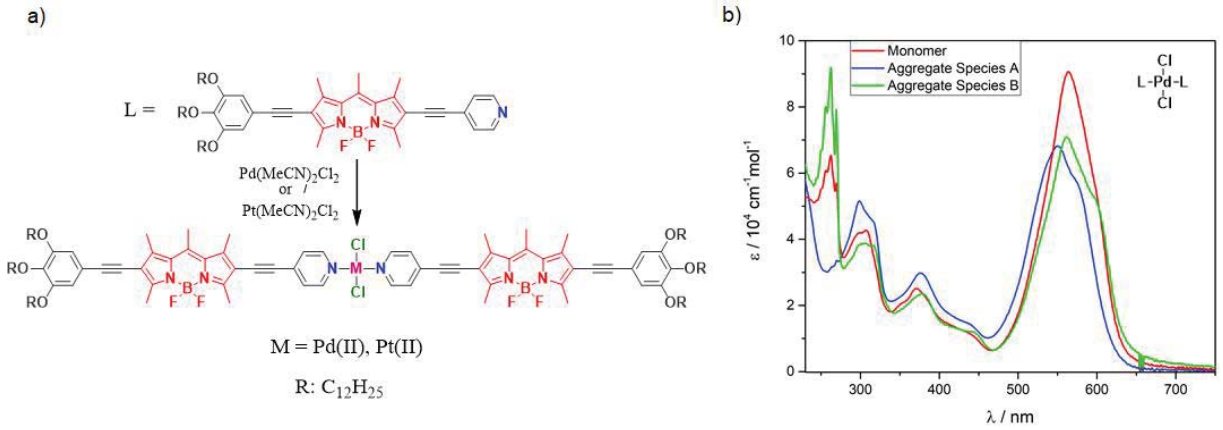

Figure 1. a) Synthetic pathway of Pd(II)- and Pt(II)-BODIPY complexes. b) UV/Vis spectra of Pd(II)-BODIPY complex at 90ºC and 10ºC (MCH, 1 x 10^{-5} M).

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Positive Cooperativity and Substrate Specificity of Peptide-Nanoparticle Conjugates

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SUMMARY

The self-assembly of cysteine-containing peptides onto the surface of gold nanoparticles (Pep-Au-NPs) creates a promising way towards artificial enzyme-mimics. The high peptide density surrounding the nanoparticle generates new microenvironments, which are able to establish new hydrogen bond and charge-relay networks leading to cooperative effects and, thus, generate catalytic properties that are absent when the peptides are free in solution.[1–3] To provide further insight into the properties of these systems we studied the effect the location of the catalytic unit within the peptide-monolayers relative to the nanoparticle surface has on the catalytic efficiency and substrate specificity. Therefore, kinetic studies were performed using three esterolytically active Pep-Au-NPs, which differ in the location of the catalytic center. The catalytic unit was placed either near the solvent exposed position of the peptide-monolayer, in the middle of the peptide sequence close to the nanoparticle surface. Hill-kinetics using model substrate *p*-nitrophenylacetate (*p*NPA) revealed *p*NPA to be cleaved most efficiently in the middle of the peptide-monolayer. Additionally, positive cooperative substrate binding was observed for all three Pep-Au-NPs. This effect increased, the closer the catalytic unit was located to the nanoparticle surface. Besides, substrate specificity was studied applying pseudo-first-order kinetics using carboxybenzyl-protected nitrophenyl esters of amino acids of increasing hydrophobicity Z-L-Gln-ONp, Z-L-Ala-ONp, Z-L-Phe-ONp and Z-L-Leu-ONp. Highly hydrophobic substrates Z-L-Phe-ONp and Z-L-Leu-ONp were cleaved most rapidly at the catalytic center, least solvated, near the nanoparticle surface. Z-L-Gln-ONp and Z-L-Ala-ONp were cleaved, like *p*NPA, most efficiently in the middle of the peptide-monolayer. These results give insight into the importance of the position of the catalytic center on the catalytic properties of peptide-nanoparticle conjugates.

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Coiled-Coil Induced Assembly of Inactive hPin1 WW-Domain Fragments to Functional Protein Modules

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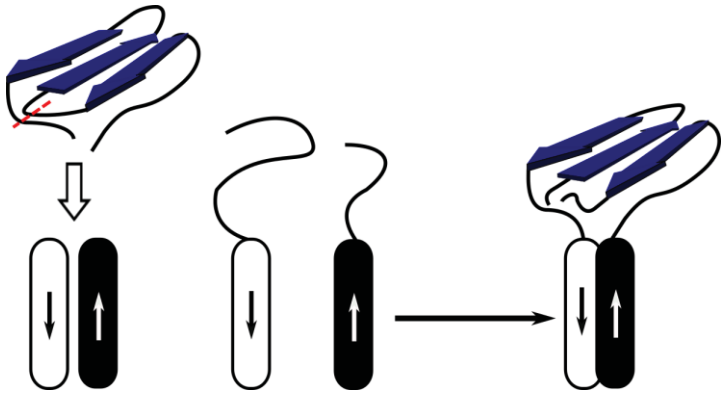
Abstract

WW domains are well-characterized β-sheet protein domains, which bind to proline-rich protein regions. One of the best studied representatives is the human Pin1 (hPin1) WW domain. hPin1 induces conformational changes in proteins by isomerization of phosphorylated Ser/Thr-Pro bonds. In this way it acts as a key player in various cellular processes [1]. The WW domain of hPin1 folds rapidly, is thermodynamically stable, and retains its ligand-binding function upon separation from the hPin1 protein. This makes it an excellent model to study sequence-to-structure-to-function relationships in β-sheet peptides [2, 3].

Aggregation and solubility issues often hamper the chemical synthesis of WW domains or β-sheet peptides. In order to study WW domains in a high throughput, we envisage a combinatorial method to facilitate the synthetic access. The concept includes coupling of WW-domain fragments onto an antiparallel heterodimeric coiled coil. Coiled coils interact quickly, specifically and with high affinity. Therefore, we hypothesize reconstitution of the WW-domain fold through a cooperative effect induced by coiled-coil association. As a model system, we chose the WW domain of hPin1, which is split at the *N*-terminal loop. CD and NMR spectroscopy indicate the formation of the hPin1 WW domain upon coiled-coil interaction. CD-thermal denaturation profiles reveal a higher thermodynamic stability compared to the unmodified coiled coil and led us to conclude that reconstitution of the WW domain in a split-WW-domain-coiled-coil construct is indeed successful.

We aim to use this combinatorial tool to modulate the binding specificity of hPin1 and, hence, to create WW domains with new properties and functions including expanded substrate recognition or catalytic activity.



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C8 Metalation of Adenine. Synthesis of Rh^{III} and Ir^{III} Complexes featuring bidentate di-NHC ligands.

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Since the first C8 metalation of adenine by Houlton[1] only few examples of adenine-based organometallic complexes have been reported in the literature, since the formation of Werner type bonds is favored with the unsubstituted N atoms of the adenine skeleton. However, after the first regioselective C8 metalation of adenine *via* oxidative addition[2], highlighting its potential as a N-heterocyclic carbene (NHC), we became interested to the C8 metalation of adenine bearing σ-donor groups[3]. Herein we present the selective metalation of adenine bearing unsymmetrical bis-NHC ligands, an unexplored alternative for the directed metalation of purine nucleobases. The bidentate ligand **1** (Figure 1) reacts with $[M^{III}Cl_2Cp^*]_2$ (Cp^* = pentamethylcyclopentadienyl, M = Rh, Ir) in the presence of NaOAc and Cs_2CO_3 to yield complexes type **2** and **3**.

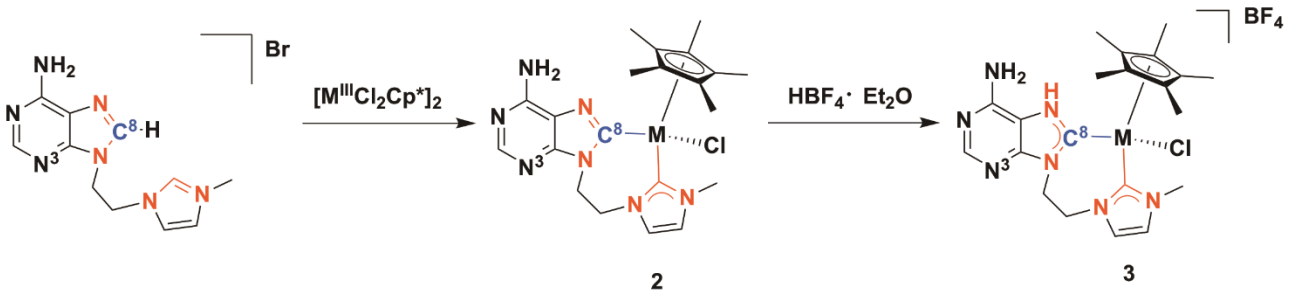

Figure 1 Synthesis of adenine-based complexes 2 and 3.

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Fe(II) SCO Complexes:

Cooperativity in the Bulk and in Vacuum Deposited Films

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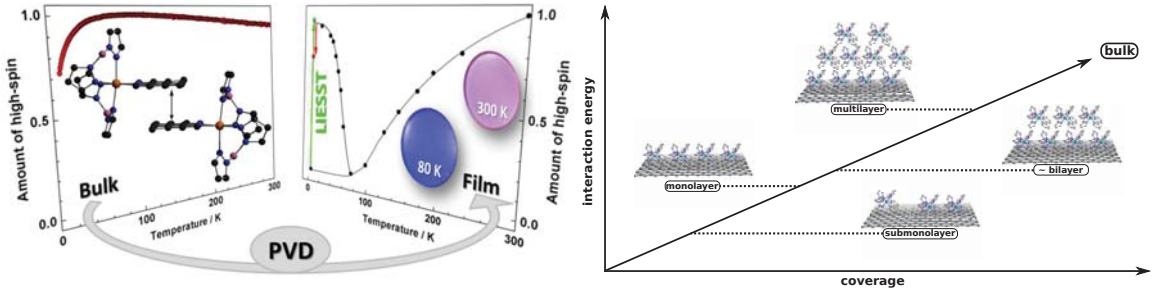

Spin crossover (SCO) transition-metal complexes continue to be a fascinating class of functional materials in the field of coordination chemistry and have the potential to play a significant role in spintronics. Transitions between the diamagnetic low-spin (LS, S=0) and the paramagnetic high-spin (HS, S=2) state of these complexes can be induced by stimuli like temperature and light (LIESST/reverse-LIESST). We synthesized a number of octahedral iron(II) spin crossover (SCO) complexes $[Fe(H_2B(pz)_2)_2(L)]$ (with pz = pyrazole and L = coligand, e.g. 2,2-bypridine and 1,10 phenanthroline) which successfully were vacuum-deposited and characterized on various surfaces (quartz, Au(111), Bi(111) and HOPG).[1]

Both in the bulk and on surfaces we found in evidence of cooperative effects which influence the spin transitions of our complexes: For a few complexes the SCO is observed only in vacuum-deposited films and not in bulk material.[2] Moreover we found in vacuum deposited films on HOPG ranging from submonolayer to multilayer a buildup of cooperative effects.[3]

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[3] Kipgen *et al.*, *submitted.*

Surface gradients in lipid bilayers to study multivalent binding of influenza

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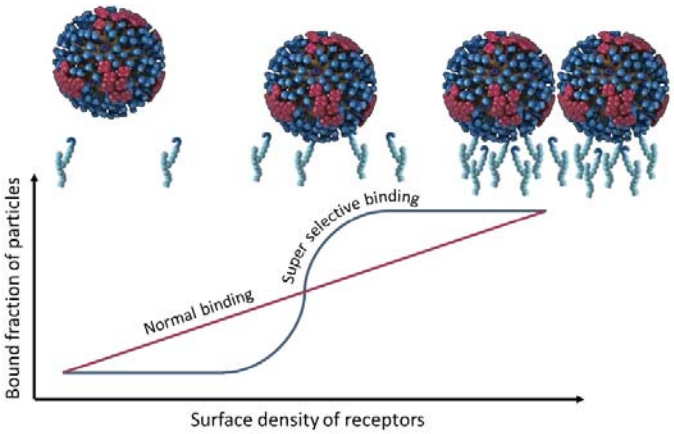
When influenza virus infects a cell, it binds to a cell membrane using weak interactions between hemagglutinin on the virus and sialic acid-terminated glycans on the cell membrane. The infectivity and the fast adaptation of the virus to immunity are suspected to rely on the multivalent character of this binding. The multivalent binding strength depends nonlinearly on the number of interactions that are involved, which gives rise to super selectivity towards high glycan coverage. We aim to develop an easy method that can give a quantitative assessment of the multivalent binding of a virus.



We developed a method to form functional surface gradients in supported lipid bilayers (SLBs)[1,2]. An SLB is formed in a microfluidic device. When a potential is applied over the SLB, charged lipids move to one side. With saturated lipids, a gradient can be formed at elevated temperature, which is frozen upon cooling the device. This gradient can be modified with streptavidin, on which biotinylated glycans are assembled. The virus is expected to adhere where the surface coverage is high enough to bind sufficient glycans. Fluorescence microscopy is used to assess where the virus binds strongly and where not.

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Heterobifunctional [2]rotaxanes based on phosphate-ammonium interactions

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The particular nature of mechanically interlocked molecules makes them suitable as artificial receptors or sophisticated chemical catalysts. For example catenanes (composed of interlocked macrocycles like the chain of a necklace) can afford a three dimensional central cavity for specific binding of guest molecules. Recently, a bifunctional chiral homo-[2]catenane based on 1,1'-binaphtyl-phosphoric acids has been synthetized in our lab.[1] It has been used as receptor for dicationic molecules and as asymmetric organocatalyst for the stereoselective transfer hydrogenation of quinolines by Hantzsch-esters.[2]

Here, we present the preliminary steps for the extension of this project towards the study of [2]rotaxane **3** (one macrocycle trapped around a linear unit with stoppers at both ends) through the development of the bifunctional pseudo[2]rotaxane **1** (see Fig. 1). The stability of this architecture is insured by the ion pairing of an axially chiral phosphate-macrocycle and a symmetrical secondary ammonium thread. Addition of bulky azide **2** leads to the rotaxane **3** by the *capping method* and the *copper(I)-catalyzed alkyne-azide cycloaddition*. This heterobifunctional interlocked molecule will be tested as a new synthetic receptor for zwitterionic species such as amino-acids. We will also investigate the use of **3** for asymmetric counteranion-directed catalysis.[3]

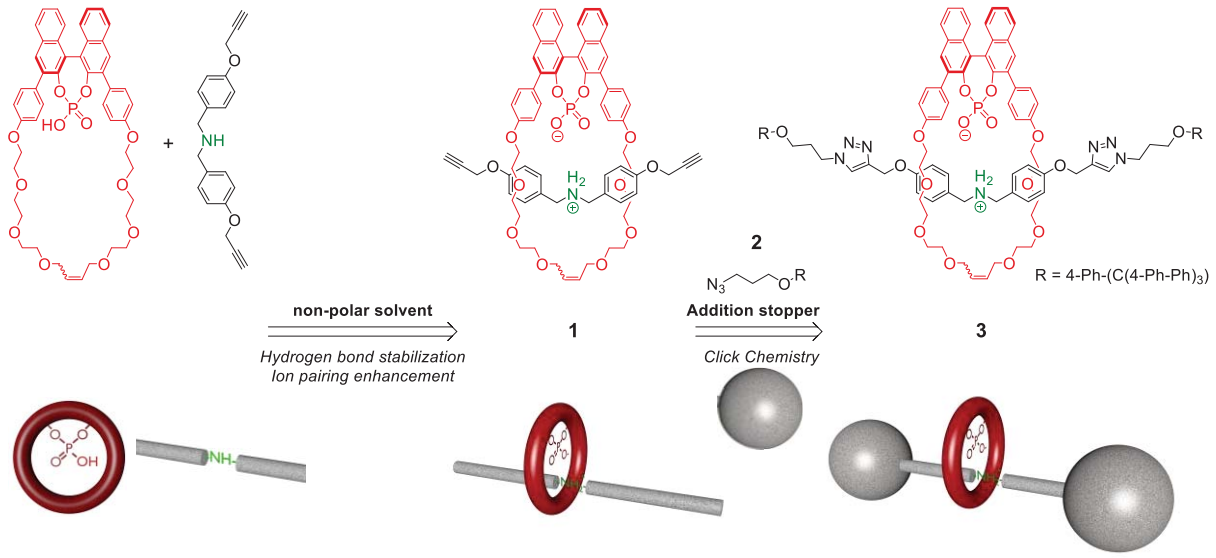

Figure 1: *Retrosynthesis - Chemical structure of [2]rotaxane **3***

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Catalytic Three-Component Machinery: Control of Catalytic Activity by Machine Speed

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Three supramolecular slider-on-deck systems **DS1-DS3** were created as two-component aggregates from the sliders **S1-S3** and deck **D** with its three zinc porphyrin (ZnPor) binding sites. The binding of the two-footed slider to the deck varies with the donor qualities of and steric hindrance at the pyridine/pyrimidine (pyr) feet and was effected by two $N_{pyr} \rightarrow$ ZnPor interactions. Accordingly, the sliders move at different speed over the three zinc porphyrins in the deck: with 32.2, 220 and 440 kHz at room temperature. Addition of N-methylpyrrolidine as organocatalyst to **DS1-DS3** generates catalytic three-component machinery. Using a conjugate addition as a probe reaction, we observe a correlation between the operating speed of the slider-on-deck (**DS**) systems and the yields of the catalytic reaction. With decreasing thermodynamic binding of the slider, both the frequency of the sliding motion and yield of the catalytic reaction increase. The results show clearly the prevalence of kinetic over thermodynamic factors in the liberation of catalyst into solution and highlight the usefulness of dynamic multicomponent machinery.

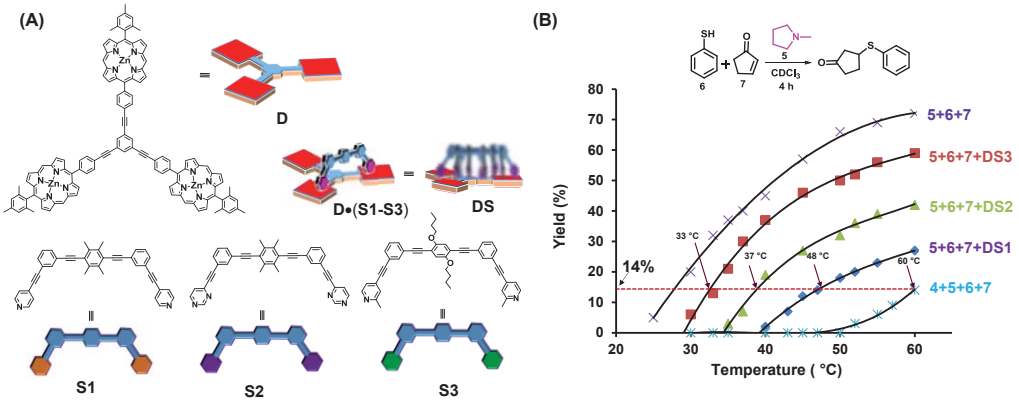
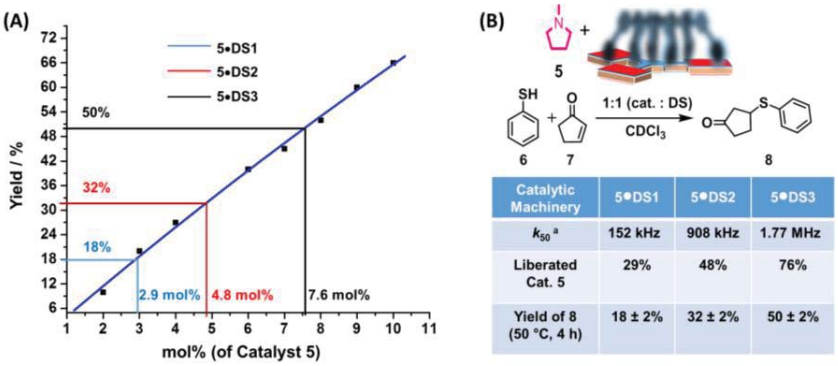


Figure 1. (A) Molecular structures and cartoon representations of deck **D**, sliders **S1-S3** and aggregates **DS1-DS3. (B)** Yields of the conjugate addition between **6** and **7** with catalyst **5** in presence of **4** or **DS1-DS3**.



Catalytic Machinery	5•DS1	5•DS2	5•DS3
k_{50} [a]	152 kHz	908 kHz	1.77 MHz
Liberated Cat. 5	29%	48%	76%
Yield of 8 (50 °C, 4 h)	18 ± 2%	32 ± 2%	50 ± 2%

Figure 2. Yields of the model reaction between **6** and **7** at 50 °C (4 h) using variable amounts of **5**. The yields (18%, 32%, and 50%) are those of the corresponding reactions with the catalytic machineries **5•(DS1-DS3)**. (B) Data for the catalytic machineries.

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Exploring Acenaphth(yl)ene Chemistry

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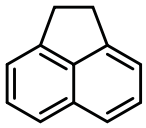
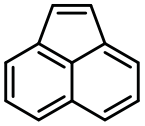
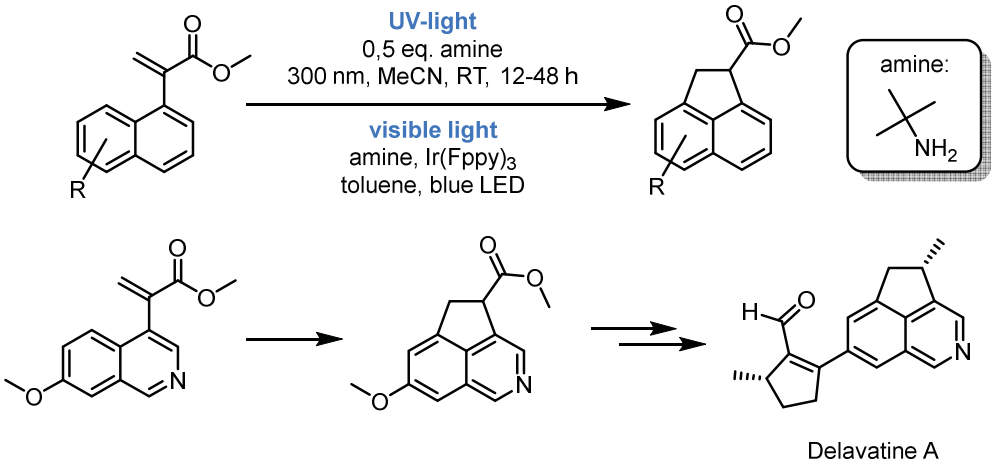


Acenaphthene



Acenaphthylene

Acenaphthenes and acenaphthylenes are an interesting compound class which is prevalent throughout various disciplines of chemistry and is present in natural products[1]. Despite the large interest in these compounds, a functional group tolerant ring closure of the five-membered ring still remains elusive. Due to the high ring strain the most widely used methods are harsh, involving FVP[2], WURTZ coupling[3] or FRIEDEL-CRAFTS reactions[4]. Since application of these conditions is restricted to very simply functionalized systems, the synthesis of specifically designed acenaphth(yl)enes remains a great challenge, leaving their chemistry largely unexplored. In order to explore this chemistry, we have developed a photochemical, base catalyzed ring closure reaction[5] functional group tolerant enough to be applied to the enantioselective synthesis of Delavatine A, a natural product from *Incarvillea delavayi*[1].



Delavatine A

After application to the synthesis of Delavatine A, the reaction was studied in depth and reaction conditions discovered which allow the use of visible light instead of UV-light to facilitate the transformation. The mechanism of the reaction was elucidated by DFT-calculations, revealing an interesting intramolecular proton transfer mediated by the primary amine base.

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Collaborative mechanism of catalysis and localization of the Rab7/Ypt7 GEF (guanine nucleotide exchange factor) Mon1-Ccz1

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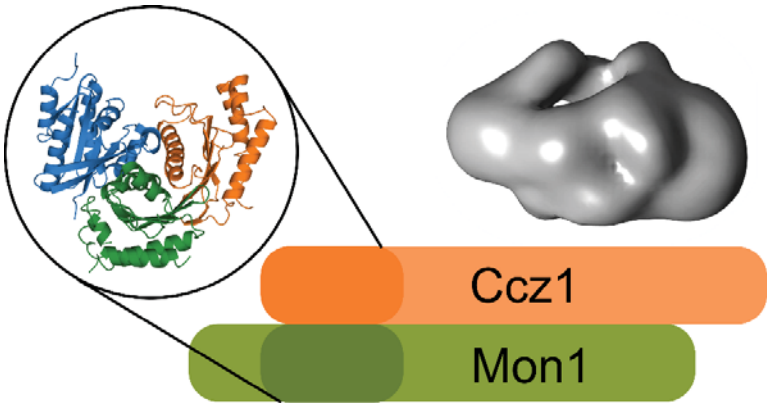
The GTPase Rab7 is a crucial regulator of intracellular trafficking and controls membrane fusion at lysosomes during endosomal maturation and autophagy[1]. Its activation by the guanine nucleotide exchange factor (GEF) complex Mon1-Ccz1 (MC1) is thus essential for cellular homeostasis[2,3]. Our structural and biochemical work reveals that both complex subunits jointly are required for function of MC1[4].
The crystal structure of a catalytic MC1 core complex bound to Ypt7 shows how Mon1 and Ccz1 constitute a combined interface for Ypt7. Binding of Ypt7 leads to a conformational changes in the GTPase substrate binding site, which facilitates nucleotide exchange. We also elucidate a novel mechanism of catalytic activity involving the remodeling of a conserved lysine residue in Ypt7 to interfere with nucleotide binding and thus promoting exchange.
The structure of the full-length MC1 complex by electron microscopy (EM) shows extensive interactions between Mon1 and Ccz1 also beyond the catalytic core domains. We identify two localization domains that recognize lysosomal phosphatidyl-inositol-phosphate marker lipids and lipid packing defects, respectively. Localization studies show that both domains are required for proper organelle recruitment *in vivo*. MC1 contains multiple interaction sites, also including recruitment cues mediated by protein-protein interactions, that are collectively required for membrane association, supporting a model where MC1 integrates different inputs for proper spatiotemporal initiation of Rab7-mediated membrane fusion.



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Novel addressable cholesterol analogs for live imaging of cellular membranes

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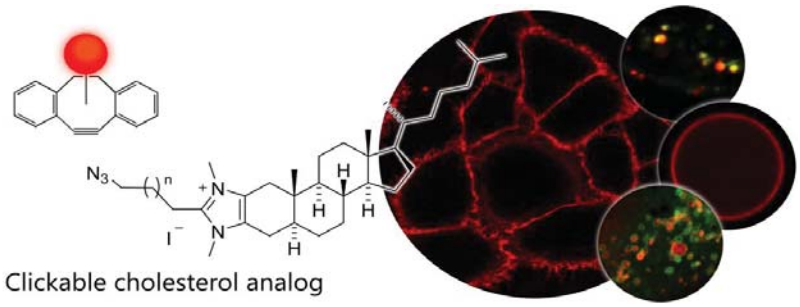
Cholesterol is an essential component of most biological membranes and serves important functions in controlling membrane integrity, organization and signalling.[1] However, probes to follow the dynamic distribution of cholesterol in live cells are scarce and so far show only limited applicability.[2] Herein, we addressed this problem by synthesizing and characterizing a novel class of versatile and clickable cholesterol-based imidazolium salts. We show that these cholesterol analogues faithfully mimic the biophysical properties of natural cholesterol in phospholipid mono- and bilayers and that they integrate into the plasma membrane of cultured and primary human cells. The membrane-incorporated cholesterol analogues can be specifically labelled by click chemistry and visualized in live cell imaging experiments that show a distribution and behaviour comparable to that of endogenous membrane cholesterol. These results indicate that the novel cholesterol analogues can be used to reveal the dynamic distribution of cholesterol in live cells.



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Synthesis of Trifluormethylated Pyridines

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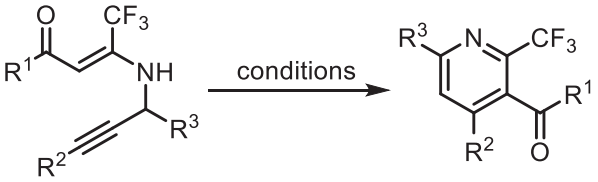
The pyridine scaffold is a very common structural motif among a variety of bioactive natural products and one of the most important heterocycles in modern drug discovery.[1] Because of this the investigation of new and alternative synthetic protocols towards highly functionalized pyridines is an ongoing field of interest in modern organic chemistry.[2]

Over the last decades the number of fluorine containing drug molecules is rapidly increasing. Nowadays 30% of all new approved drugs contain at least one fluorine atom.[3] Because of its unique properties this element is of great interest and value for the design and development of new drugs, making it highly desirable to develop new ways towards fluorinated target molecules.[4]

Herein we present the synthesis of multisubstituted trifluormethylated pyridines via transition metal catalysis, starting from commercially available fluorine containing starting materials. Furthermore, we contribute to Green Chemistry by establishing the reaction in a water-based micellular catalysis system.



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A new tool for sequence-specific manipulation of N^6-methyladenosine

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Epitranscriptomics is an emerging research field focusing on RNA modifications and their cellular functions. Until now, over 150 reversible and irreversible RNA modifications are known, but their biological roles are mainly unknown. The most abundant internal mRNA modification is N^6-methyladenosine (m^6A) [1]. The methylation is realized by a methyltransferase complex [2] and can be recognized by various reader proteins in the nucleus and cytoplasm [3]. The "demethylases" FTO and AlkBH5 remove the methyl group [4, 5], resulting in a dynamically regulated modification in RNA. Current research elucidates several cellular roles of m^6A on splicing, translation and mRNA decay with impacts on stem cell development and cancer [6, 7]. Until now, the specific role of each m^6A site remains unknown, which could be identified by sequence-specific demethylation of m^6A. To reach this specificity, the RNA-binding protein RCas9 is fused to FTO, respectively. RCas9 is a nuclease-deficient RNA-binding variant of Cas9 [8], which will guide FTO to specific m^6A positions by corresponding single-guide RNAs (sgRNAs) and PAMmers. This concept should be realized *in vitro* and in human cancer cells. The successful sequence-specific demethylation will be measured by a so-called SCARLET (site-specific cleavage and radioactive-labeling followed by ligation-assisted extraction and thin-layer chromatography) assay [9]. After succeeding sequence-specific demethylation, the impact of various m^6A modification sites can be studied.

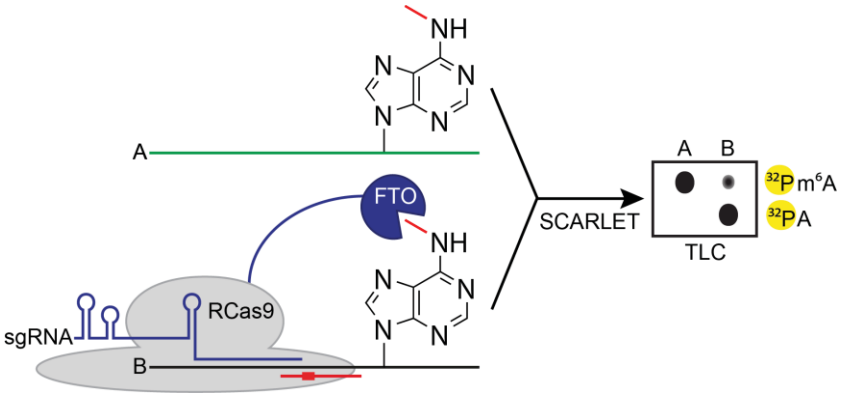

Figure 1: Concept of sequence-specific RNA demethylation. A mixture of different m^6A-RNAs (A and B) is present. RCas9 (grey) is fused with a linker to FTO (blue) and guides it to a specific m^6A-RNA (B) using the sgRNA (blue) and PAMmer (red). The degree of demethylation is analyzed by TLC as a result of SCARLET.

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Development of light-responsive MRI contrast agents for imaging and theranostics

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MRI is an outstanding anatomical imaging technique, due to its excellent resolution. However, the limited functional information obtained by MRI is a major drawback. Thus, contrast agents are needed that respond to the local changes in biochemical processes.[1-2] To boost the sensitivity of MRI, we aim to develop new MRI contrast agents responsive to light, envisioning the use of light-emitting targeting moieties accumulating in the disease tissue. This strategy would lead to significant signal amplification.

We developed a T1 contrast agent, which - in intact form - can be incorporated into liposomes. Photocleavage leads to the conversion of a macromolecular to a small, quickly tumbling contrast agent, causing a change in relaxivity (Figure 1a).[3-5] The Passerini multicomponent reaction (MCR) was used in the synthesis, employing a precursor for the photoresponsive moiety as one of the reactants (Figure 1b).[6] CryoTEM and an FFC relaxometry were used for the visualization of liposomes and acquisition of NMRD profiles.

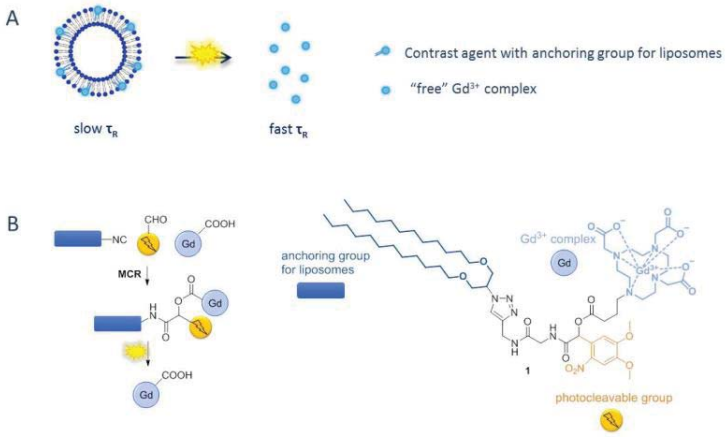

Figure 1

The target compound was successfully synthesized and incorporated into liposomes with DOPC, as confirmed by cryoTEM. The complexation of Gd^{3+} was confirmed by EDX analysis. NMRD profiles (Figure 2b) showed a substantial decrease in relaxivity upon irradiation with light (λ = 400 nm) and indicated a conversion from a macromolecular system to a small molecule following the same kinetics as the photocleavage monitored with UV-Vis analysis. A permeation assay using Calcein indicates the disintegration of liposomes upon irradiation.[7] The permeability of the liposomes upon irradiation gives rise to the possibility of using the system for theranostics.[8-9] The next step is to design red light-responsive molecules showing faster photocleavage, thus improving their suitability for *in vivo* applications.

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Self-assembled $[(Pd/Pt)_2L_4]$ coordination cages based on well-known organic dyes

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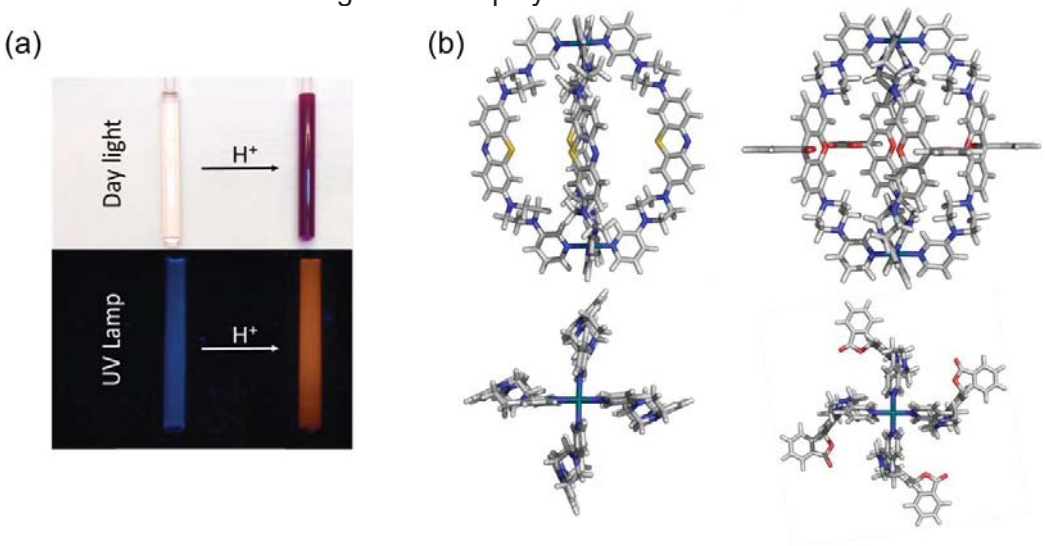
In supramolecular chemistry, the self-assembly of banana shaped *bis*-monodentate pyridyl ligands with square planar palladium(II) and platinum(II) metal ions has proven to be a very reliable recipe for the realization of new functional coordination cages [1,2]. Complementary to the previously reported light-switchable receptors and photo-excitable redox-cages prepared in our lab [3,4], we here present an expansion of the family of cages that interact with visible light by implementing well-known organic dyes as ligand backbones. While the parental dyes are produced on a multimillion ton scale and are broadly use in industry, medicine and research, their implementation into self-assembled supramolecular systems is rather rarely found. We particularly focus on rhodamine which exists in an equilibrium between the colourless lactone form and highly colored fluorescent zwitterionic form, and methylene blue. The latter dye has many uses, e.g. as photosensitizer and as redox indicator that can be cycled between its oxidized (blue) and reduced (colorless) state. The ligands have been successfully synthetized and the optical properties of the parental dyes have been proven to be maintained (Figure a). The correspondent $[M_2L_4]$ (M=Pd, Pt) cage formation has been confirmed with NMR techniques, mass spectrometry (ESI-MS), UV-Vis and fluorescence spectroscopy. Figure b shows the preliminary PM6 models of the methylene blue cage (left) and lactone-form rhodamine cage (right). We are currently studying the uptake of guest molecules as well as the interaction of the coloured cages with biopolymers such as DNA.



(a) Closed-ring lactone form of rhodamine ligand (left) and after protonation (right) under day light and under UV lamp. (b) PM6 models of the cages with ligands based on methylene blue (left) and rhodamine (right), side view (top) and top view (bottom).

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Fluorine-Directed Glycosylation Enables the Stereocontrolled Synthesis of Selective SGLT2 Inhibitors for Type II Diabetes

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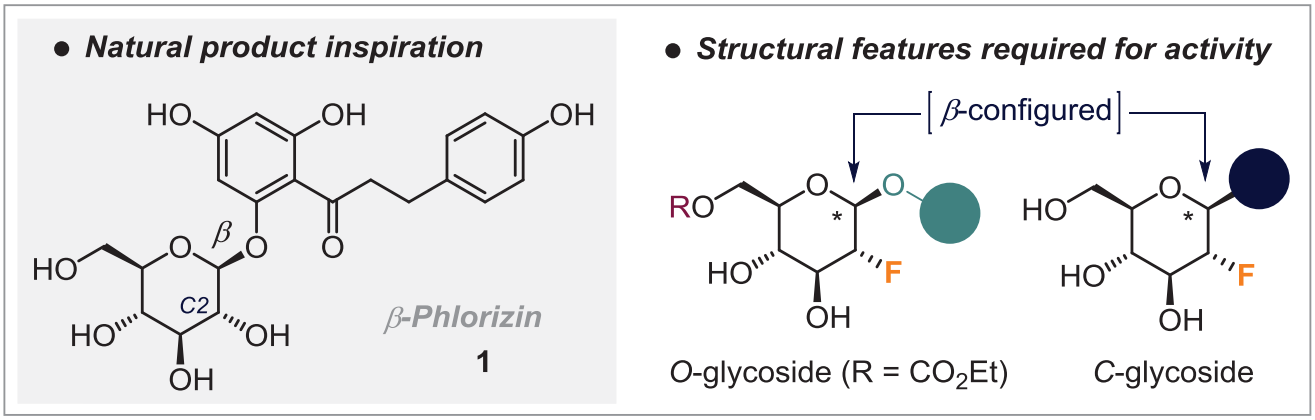
A report from the World Health Organization (WHO) estimated that 422 million people suffer from diabetes mellitus (Type II diabetes). Contemporary strategies for the design of small molecule for the treatment of Type II diabetes, have focused on the selective inhibition of the Type II sodium-glucose co-transporter (SGLT2), a transmembrane protein located in the proximal tubule responsible for the reabsorption of 90% of the glucose that would be otherwise eliminated in the urine. Orally available small molecule drugs based on the D-glucose core of the natural product *Phlorizin* (Gliflozin family) have been proven to be clinically effective impeding the glucose reabsorption.

In this work,[1] we studied the influence of molecular editing with fluorine at the *C2* position of the pyranose ring of *Phlorizin* analogues (*O*-glycoside and *C*-glycoside) to jointly direct *β*-selective glycosylation, required for biological efficacy, and enhance physicochemical properties. Our results showed an increase of the *β*-selectivity of the glycosylation reaction compared to the parental sugars with OH in C2 and 2-deoxy sugars. For the first time this strategy has been exploited for the generation of *C*-glycosides, with the expected 1,2-trans stereochemistry predominating. A single site [OH→F] substitution at C2 in a *Dapagliflozin* model compound (*C*-glycoside) has been shown to preserve the selective inhibition of human/mouse SGLT2 over human/mouse SGLT1. Whilst this target selectivity is accompanied by a loss in efficacy, it should be noted that the drug scaffolds are structurally unoptimised.

Given the abundance of glycosylated pharmaceuticals in diabetes therapy that contain a *β*-configured D-glucose nucleus, it is envisaged that this strategy may prove to be expansive.



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Microtubular Self-Assembly of Covalent Organic Frameworks

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The performance of organic electronics devices such as organic field-effect transistors (OFETs), organic light-emitting diodes (OLEDs) or organic solar cells is strongly influenced by the molecular arrangement of the active components, *e.g.*, solid state packing or crystallinity. Due to the long-range order and high charge charrier mobilities through a widely delocalized π-system, donor-acceptor conjugated covalent organic frameworks (COFs) are promising candidates for electroactive materials in organic electronics.[1]

In search of novel porous materials, a dye-containing framework **DPP-TAPP-COF** was synthesized via dynamic covalent chemistry. The reversible imine condensation of diketopyrrolopyrrole dialdehyde **DPP-1** and 5,10,15,20-tetraaminophenylporphyrin (**TAPP**) resulted in the formation of an acceptor-donor conjugated two-dimensional polymer that shows enhanced light harvesting in the visible region and spontaneously self-assembles into tubular arrangements, thus facilitating the emergent bottom-up construction of well-defined hollow microtube structures.[2]

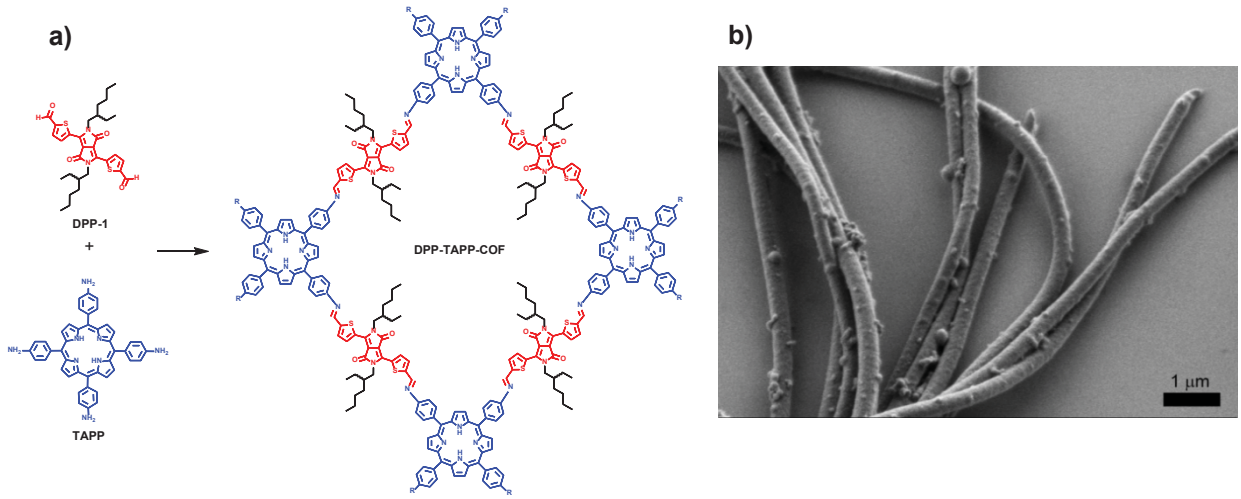

Figure 1. a) Synthesis and b) SEM image of **DPP-TAPP-COF** microtubes.

References:

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A Gold-catalyzed Three-component Spirocyclization to Highly Functionalized [N,N]-Spiroacetals

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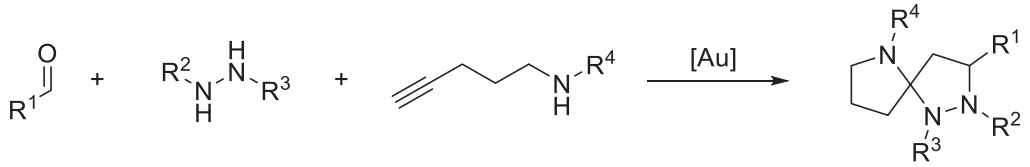
In medicinal chemistry natural products continue to be an inspiration for the design of new drugs. In this context spiroacetals have been found as a key structural unit in many biologically active and structurally diverse natural products.[1] Especially nitrogen-containing spiroacetals represent a very important class of building blocks as the scaffold exists in many natural products and pharmaceuticals.[2] Nevertheless, synthetic approaches to [N,N]-spiroacetals are not well explored.

Previously, we have developed a gold-catalyzed three-component synthesis of functionalized [N,O]-spiroacetals with yields of up to 97%.[3] Based on this method, we now report a one-pot approach to functionalized [N,N]-spiroacetals. In this reaction different kinds of aldehydes, hydrazines and aminopentynes undergo a gold-catalyzed three-component spirocyclization to the corresponding pyrazolidines in good yield (Scheme 1).



Scheme 1: Gold-catalyzed three-component spirocyclization to [N,N]-spiroacetals.

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Chiral N-Heterocyclic Carbenes as Molecular Ratchets

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N-Heterocyclic carbenes (NHCs) have gained large attention for their many uses, including the modification and stabilization of surfaces and nanoparticles [1, 2]. In particular, their strong binding to gold surfaces has been shown to be tunable by the choice of N-substituents [3].

In here, a Molecular Dynamics framework is utilized to investigate the rotation of NHCs on a gold (111)-surface. The reactive force field ReaxFF [4] is employed to adequately describe not only molecules but also metallic surfaces and their interactions, allowing for bond breaking, which is necessary for adatom formation.

Depending on the N-substituents, several NHCs are tested and found to either pull an adatom from the surface and subsequently rotate freely or to strongly bind to the surface and jump between potential minima dictated by the surface symmetry. STM images calculated by Density Functional Theory agree with experimental measurements, confirming the nature of the observed angular distribution. In a quest to design a molecular ratchet, chiral ligands are used to break rotational symmetry and eventually control the direction of the rotation.

This computational approach is shown to be an effective means to examine the interactions of NHCs with metal surfaces. While chiral ligands can achieve step-like rotations, thermal movement alone is found to be insufficient for the motion to be truly unidirectional.

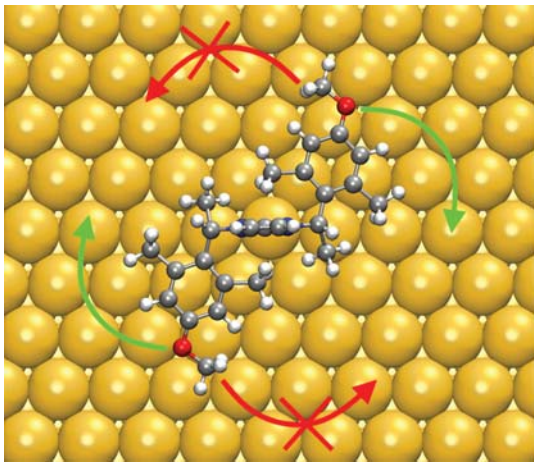

Figure 1: Schematic description of the unidirectional rotation of a chiral NHC on a gold(111) surface.

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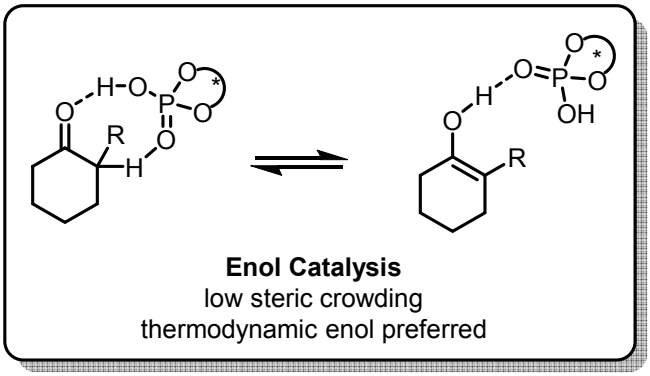
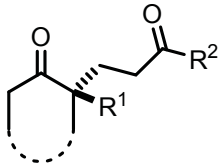
Enol Catalysis – Enantioselective Transformations via Bifunctional Brønsted Acid Promoted Enolization

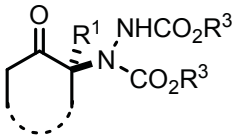
Grigory A. Shevchenko, Gabriele Pupo, Roberta Properzi, Desislava Petkova, Giovanni Bistoni, Frank Neese, Philip Kraft and Benjamin List*

Enantiopure carbonyl compounds bearing tetrasubstituted α-stereogenic centers are versatile building blocks for pharmaceuticals, scents, and natural products. Despite their importance, the synthesis of these compounds via α-alkylation still represents a major challenge both in metal- and organocatalysis since it requires the exclusive formation of the thermodynamic enolate. To tackle this challenge, we developed *Enol Catalysis*. By exploring this novel activation mode, we previously disclosed an asymmetric Michael reaction with enones, an asymmetric α-amination reaction, and the direct asymmetric α-allylation of branched ketones.[1] Recently, we further extended this methodology to asymmetric C–O bond forming reactions as in the direct α-hydroxylation[2].

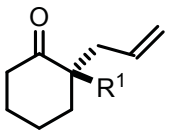




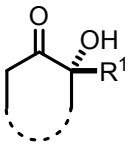
Michael addition[1a]
up to 95% yield
up to 97.5:2.5 er



α-amination[1b,c]
up to 99% yield
up to 98:2 er



α-allylation[1c]
up to 93% yield
up to 98:2 er



α-hydroxylation[2]
up to 58% yield
up to 98.5:1.5 er

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Subphthalocyanines as Model System for Supramolecular Photosensitizers in Biomedical Applications

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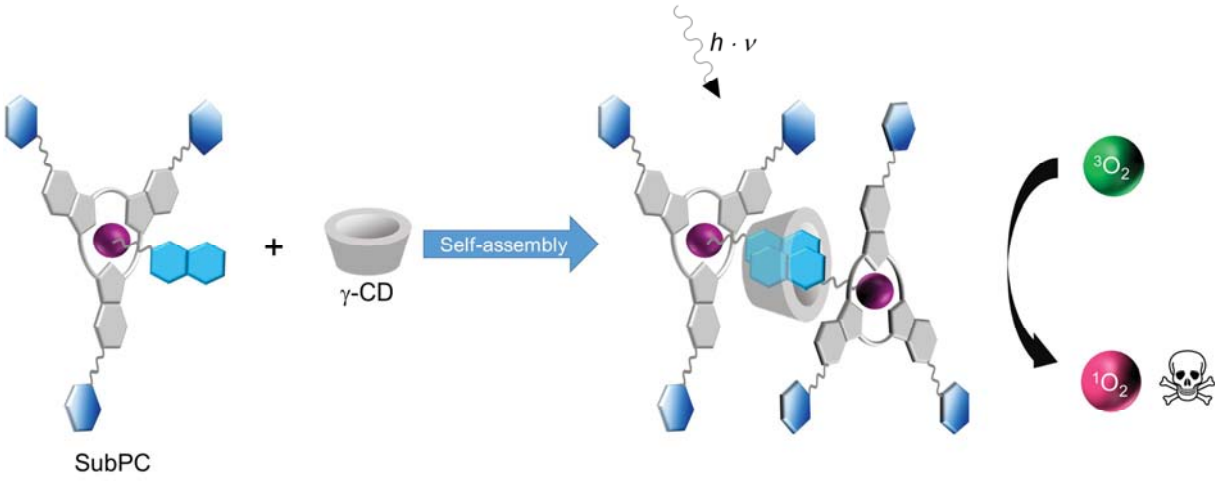
The photodynamic therapy is an important tool in the fight against cancer or pathogens.[1] Furthermore, light-induced activation reduces unwanted side effects of drugs.[2] Common photosensitizers are phthalocyanines (PCs) or porphyrins (PORs). They convert triplet oxygen ($^3O_2$) into cell toxic singlet oxygen ($^1O_2$) when excited with light of long wavelength.[3] Even subphthalocyanines (SubPCs) show this conversion.[4] The major challenge is to prevent *π-π* stacking of the photosensitizers in water which leads to a significant decrease in the fluorescence and hence $^1O_2$ production.[5]

We have already shown that the generation of $^1O_2$ can be increased up to 300 % by immobilization of unsymmetrical PCs on a supramolecular substrate.[6] In this project we present a boron SubPC which is axially functionalized with umbelliferon (**Scheme 1**). The latter is known to form 2:1-complexes with γ-cyclodextrin (γ-CD). This host-guest complex should serve as a spacer between the SubPCs. The spacer should allow high local SubPC concentration without *π-π* stacking and enable the production of $^1O_2$.



Scheme 1: Self-assembly of SubPCs with γ-CD to supramolecular dimers to convert $^3O_2$ into cell toxic $^1O_2$.

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Synergy in and Biosynthesis of Natural Products from Pseudomonads

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Interacting microbial communities are a very rich source of structurally diverse natural products. Soil-dwelling bacteria, for instance, are constantly exposed to a multitude of threats: bacteriophages can infect and kill bacteria; bacterial competitors fight for the same resources; amoebae and nematodes are voracious predators. These evolutionary pressures have shaped intricate bacterial defense strategies. Here, we describe two bacterial strains of the genus *Pseudomonas*, which produce a diverse set of natural products (**Fig. 1**). These non-ribosomal peptides are a) involved in defense against amoebal predation[1,2] and b) display synergistic activity against the human pathogen methicillin-resistant *Staphylococcus aureus* (MRSA).[3] We present their detailed structure elucidation, as well as their biosynthesis and bioactivity.

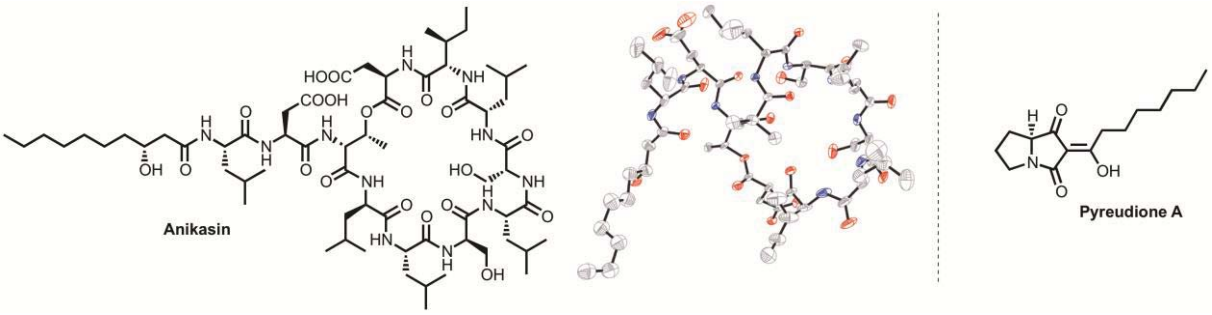

Figure 1. Structures of anikasin[1] (with X-ray crystal structure) and pyreudione A.[2]

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Programmable Ligand Environments for Transition Metal Ion Binding in DNA G-quadruplex Structures

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G-quadruplexes are classic DNA secondary structures formed by Hoogsteen base pairing in guanine-rich oligonucleotides resulting in stacked guanine tetrads. They have been found to regulate the expression of oncogenes and human telomeric properties *in vivo*.[1] Recently in our group, the concept of metal-mediated base pairing, where exchange of the canonical nucleobases by ligands allows for the incorporation of transition metals inside DNA duplexes, thereby imparting a higher stability and conferring unique metal-based properties like magnetism, charge transfer, catalysis, sensing etc. to it,[2] has been successfully extended for G-quadruplexes.
The folding of oligonucleotide sequences containing covalentely incorporated pyridine donors into defined G-quadruplex structures, leads to a pre-arranged ligand environment suitable for binding transition metal ions like Cu^{II} or Ni^{II}. A substantial thermal stabilization of the metal ion-bound secondary structure has been observed, which has been probed by UV/Vis and CD spectroscopy.[3] In a recent study, we demonstrated that the system undergoes a metal-induced control in its folding topology and protein binding.[4]
The concept has further been extended to a selection of bioinspired ligands such as imidazole, carboxylate and sulfur containing donors which are diversely observed in active-sites of metalloenzymes. Incorporation of these different ligands in G-quadruplex structures is expected to result in programmable ligand environments for the formation of heteroleptic transition metal complexes (Figure 1) allowing the exploration of metalated G-quadruplexes as potential enzyme mimics.

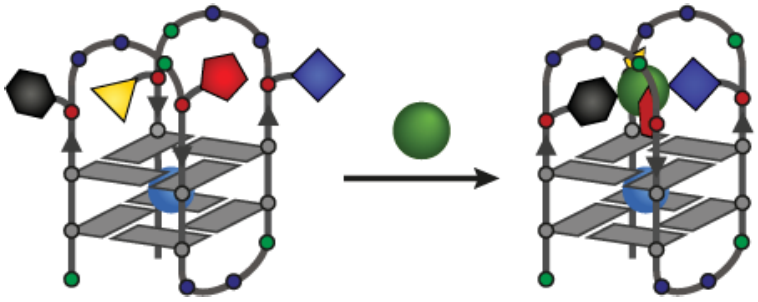

Figure 1: Schematic illustration of a G-quadruplex structure with a designed heteroleptic ligand environment for a transition metal ion.

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Guided Serendipity – A Two-Dimensional Approach Towards Novel Transformations and Mechanisms in Photocatalysis

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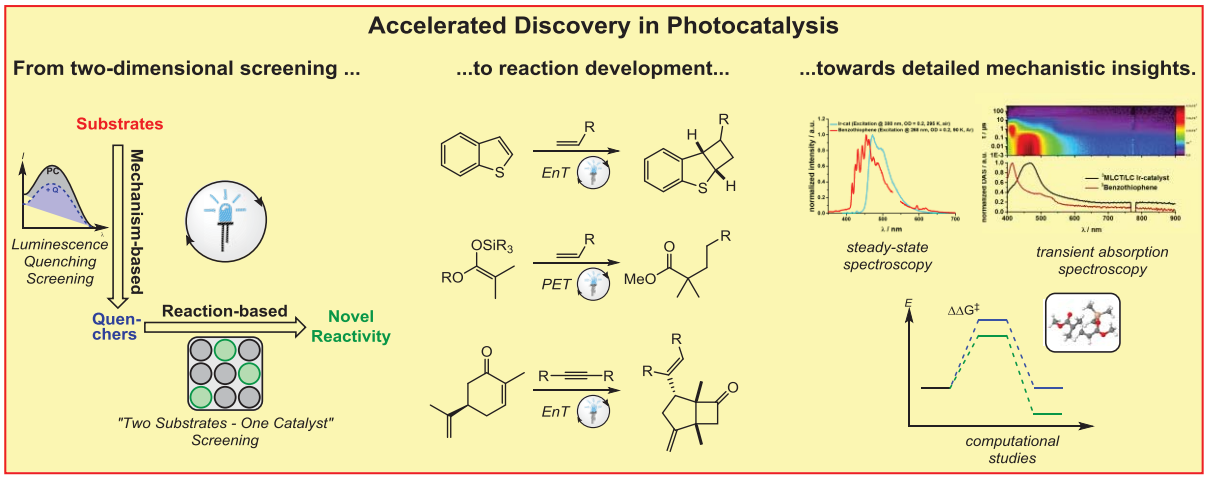
The discovery of novel reactivity patterns, along with their synthetic applications, is a key challenge for organic chemists. Mild, selective and efficient synthetic protocols are required for the precise construction of highly complex molecules. While novel transformations can, to some extent, be rationally designed building on inherent reactivity properties, many ground-breaking discoveries, however, were the result of experimental serendipity. For this reason, serendipity-based screening protocols have emerged as a powerful, complementary approach towards the discovery of novel reactivity within the last 20 years.[1]

Herein, a conceptually unprecedented "guided serendipity" screening approach is reported. This highly efficient two-dimensional symbiotic combination of mechanism-based [2] and reaction-based [3] screening allowed for rapid access to various photocatalytic transformations, including energy-transfer- (EnT) and photoinduced-electron-transfer-mediated processes.



Combining this reaction discovery approach with detailed mechanistic investigation enables further insights into unexpected or unprecedented molecular processes: Advanced spectroscopic experiments (transient absorption spectroscopy), along with computational studies, revealed two unpredicted energy transfer events, as well as a surprising triplet rearrangement cascade – eventually generating the framework for rational reaction design.

Thus, "Guided Serendipity" approaches offer the potential to serve as a versatile, efficient strategy for the discovery of unpredicted reactivity modes in photocatalysis – and beyond.

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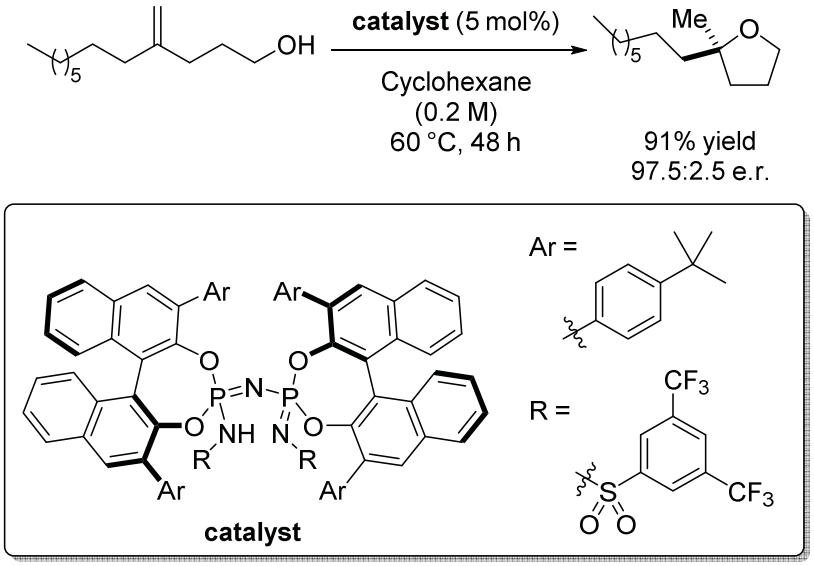
Activation of Olefins via Asymmetric Brønsted Acid Catalysis

Nobuya Tsuji, Jennifer L. Kennemur , Thomas Buyck, Sunggi Lee, Sébastien Prévost, Philip S. J. Kaib, Dmytro Bykov, Christophe Farès and Benjamin List*

The activation of olefins for asymmetric chemical synthesis traditionally relies on transition metal catalysts. In contrast, biological enzymes use Brønsted acidic sites of appropriate strength, which can protonate olefins and thereby generate carbocations that ultimately react to form natural products. Although chemists have recently designed chiral Brønsted acid catalysts to activate imines and carbonyl compounds, mimicking these enzymes to protonate simple olefins that then engage in an asymmetric catalytic reaction has remained a significant synthetic challenge.[1] Here we show that a new class of confined and strong chiral Brønsted acids[2] enables the catalytic asymmetric intramolecular hydroalkoxylation of unbiased olefins.[3] The methodology enables rapid access to biologically active 1,1-disubstituted tetrahydrofurans.



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Hierarchical Helicates – More Than Just Models

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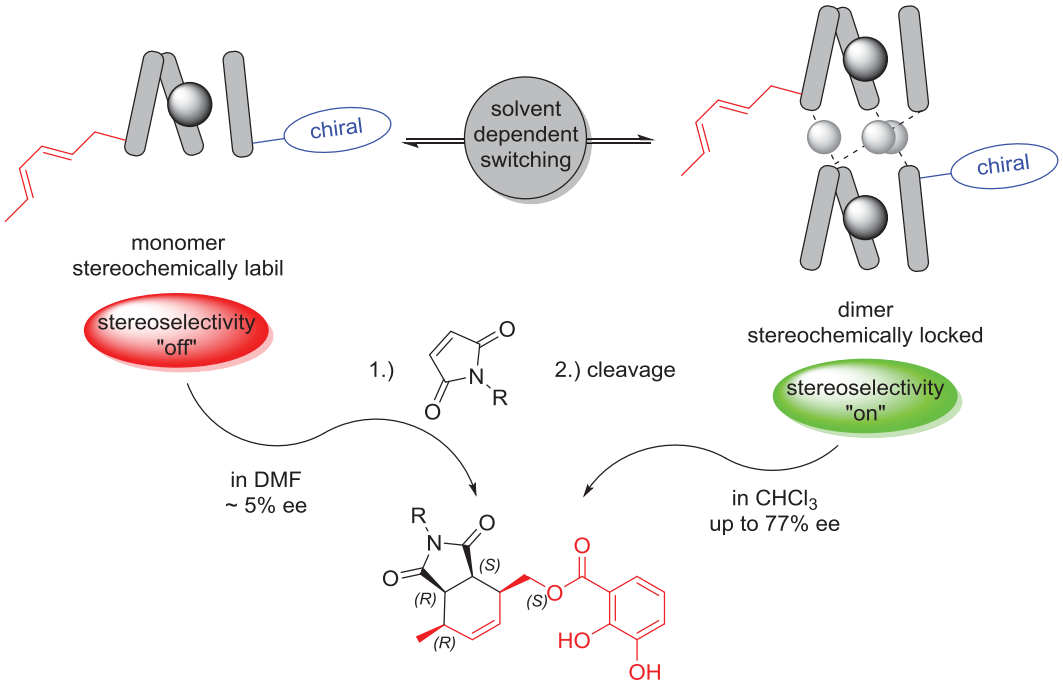
Since the beginning of life, helical structures such as DNA play a fundamental role in the chemistry of nature. On a macroscopic level this structural motif is found in springs, screws and even winding stairs to benefit from its unique properties. J.-M. Lehn defined the term “helicate” in 1987 and introduced this longstanding motif in chemistry.[1]

Hierarchically assembled lithium-bridged titanium helicates were developed by our group two decades later using catechols with keto or ester functionalities in the 3 position.[2] Since then a great variety of ligands were used to observe the equilibrium between a “Werner”-type triscatecholate complex and the corresponding dimer bridged by lithium cations. Bulky chiral ligands with an α-stereogenic center lead to stereochemically locked helicates (dimers) while the monomers are stereochemically labil due to Bailar twist or Ray-Dutt twist rearrangements.[3]

Utilizing helicates consisting of those chiral ligands and a diene ligand allows us to perform stereoselective Diels-Alder reactions in a post-functionalization process. The monomer-dimer equilibrium enables an on/off-switching of the stereoselectivity via the choice of solvent.[4]



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Stimulus-Responsive Degradable Nanocontainers for the Intracellular Release of Lipids

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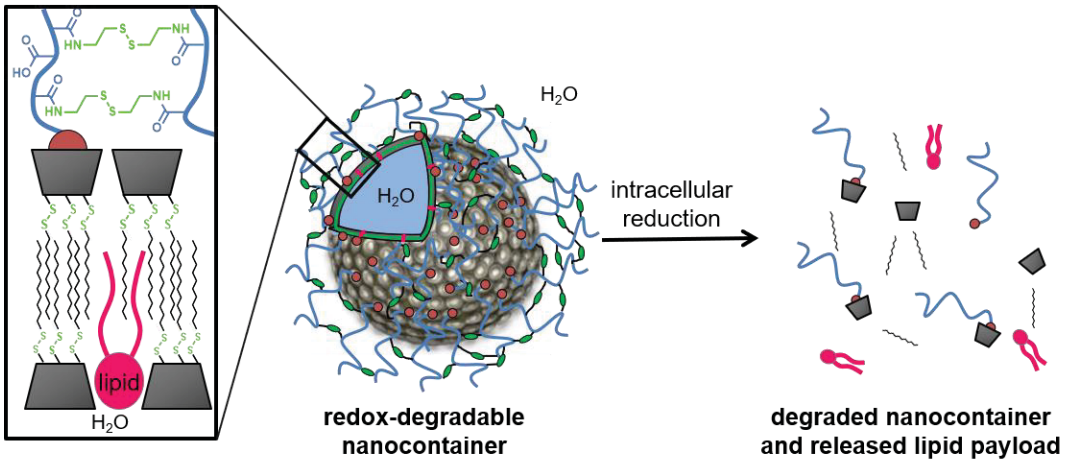
The supramolecular assembly of responsive materials enables the development of versatile nanocontainers with great potential as vehicles for drug delivery, nanoreactors or as protective shells for biomolecules.[1,2] In our previous work, we established redox-responsive polymer nanocontainers comprising a self-assembled cyclodextrin vesicle core and a supramolecular anchored, redox responsive polymer shell for the delivery of hydrophilic cargo into cells and a subsequent efficient intracellular release.[3,4]
In this contribution, we refine this platform into a fully-degradable nanocontainer by synthesizing and incorporating degradable cyclodextrin amphiphiles into the vesicle core for the specific delivery of fluorescently labelled lipids into intracellular compartments. Redox-responsive units are incorporated in the polymer shell (cleavable cystamine crosslinkers) as well as in the vesicle core (degradable cyclodextrin amphiphiles) to guarantee an efficient release of a lipid cargo, which can be loaded readily into the vesicle template. The reductive degradation based on a cooperative response of both responsive units is demonstrated by light-scattering and TEM-experiments and the lipid release is followed by using a FRET-pair of labelled lipids as cargo. Live cell imaging experiments are conducted to follow cellular uptake and as a proof-of-concept these nanocontainers were successfully applied to deliver and release fluorescently labelled lipids into cultured living cells. In future experiments we will expand this concept to assemble dual-responsive (pH and redox) nanocontainers and apply them to visualize the dynamic processes of lipid distribution like microdomain formation inside live cells.



Keywords: Self-assembly, nanocontainer, stimulus-responsive, lipids, vesicles

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Dual Ligand-Enabled Nondirected C–H Olefination of Arenes

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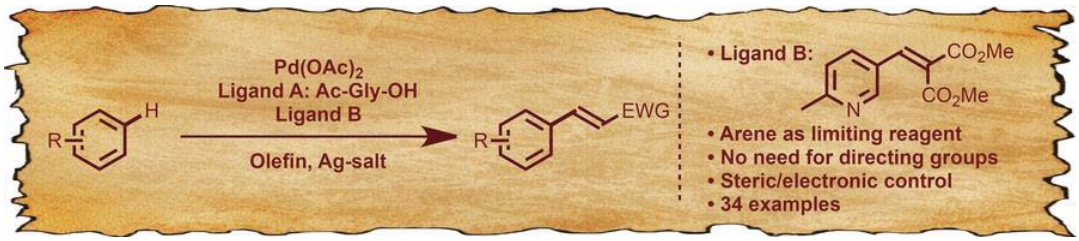
In recent years metal-catalyzed C–H bond functionalizations have become one of the fastest growing fields of synthetic organic chemistry and have enabled the development of highly step and atom economical processes as well as new methods for late-stage functionalization.[1] While the use of directing groups to achieve selectivity and increase reactivity is an established approach, the direct activation of simple substrates without directing groups remains challenging.[1]

Nondirected methods are an attractive target for method development because they inherently offer a complementary regioselectivity and are applicable to a wider range of substrates.[2] The Fujiwara-Moritani reaction, a Pd-catalyzed oxidative C–H olefination of arenes, has been intensively studied since its introduction in 1969 but the nondirected variant has so far remained limited by the need to use the arene in excess.[3]



Scheme 1. The dual ligand-enabled nondirected C–H olefination of arenes.[4a]

We developed a catalytic system that, through the combined action of two complementary ligands, enables the use of directing group-free arenes as limiting reagents in Fujiwara-Moritani reactions. Our protocol thus enables the application of the Fujiwara-Moritani reaction to valuable arenes, which cannot be utilized in excess. The regioselectivity is controlled by a combination of both steric and electronic effects of the arene.[4a,b]

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Mixed Metal Nanoparticles as Highly Active Catalysts for Alkyne *cis*-Semihydrogenation

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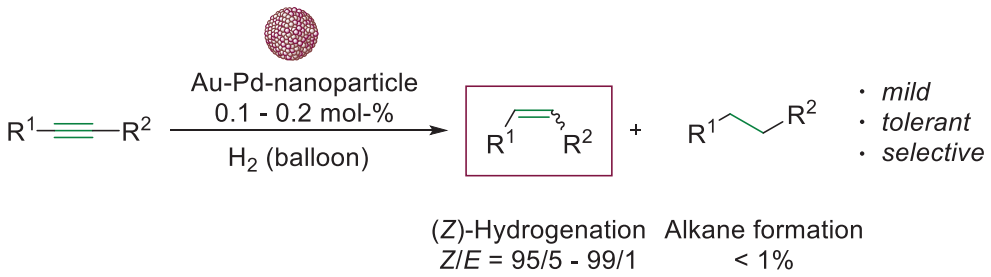
The synthesis of (*Z*)-alkenes by chemo- and stereoselective hydrogenation of alkynes is a key step in the synthesis of vitamins and natural products and is also a relevant reaction in polymer industry.[1-2] The "benchmark" Lindlar catalyst is generally used for these transformations.[3] However, it suffers from major drawbacks in terms of process economy and environmental impact. Lately, different metal nanoparticles - mostly consisting of palladium - have been developed as more efficient catalysts for this reaction. In these systems the reactivity of palladium often has to be adjusted by poisoning with sulfur or phosphorous containing additives to avoid over-hydrogenation and isomerization.[4] However, this catalyst poisoning often also leads to a loss of activity.

Our approach lies in the use of mixed Au-Pd-nanoparticles. In these systems the composition of the catalyst offers the possibility to tune the selectivity while the incorporation of gold into the palladium particles increases the activity. With this strategy the amount of catalyst can be reduced by 95 % compared to corresponding Pd-nanoparticles. Moreover, the catalyst performs well under mild conditions, tolerates many functional groups and can be recycled at least 4 times.



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Salen Complex-based Multicomponent Self-Assembled Cages

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The chemistry of self-assembled coordination compounds has become a very popular research field in the last decades.[1][2] One of the research interests in the Clever Lab is the development of self-assembled (multi)functional coordination cages. A heteroleptic coordination cage, which contains two different ligands, was recently realized by using geometric complementarity between the ligands.[3] However, the rational design and formation of multicomponent assemblies is still challenging. Here we present a series of novel multicomponent self-assembled cage, which was formed by coordination of a salen complex-based binuclear macrocycle with carefully designed banana-shaped ligand on the axial position using Co(III) as rigid nodes (Fig. 1).

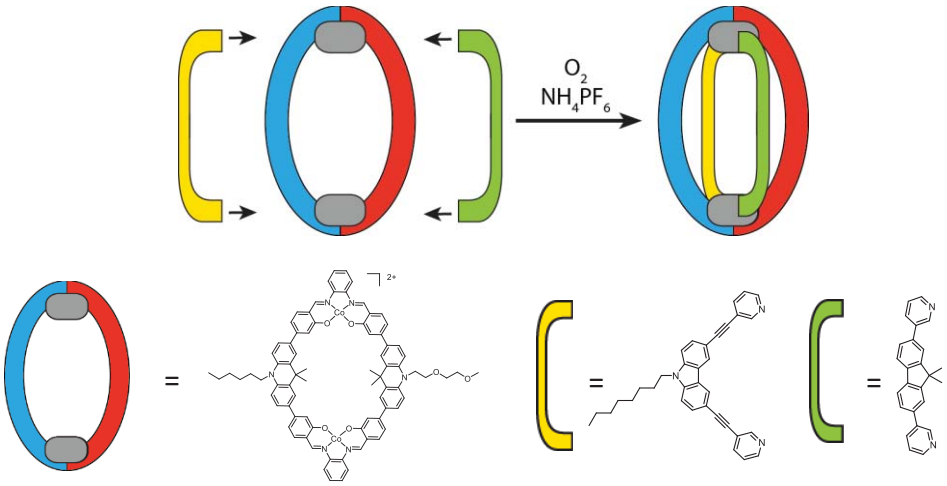

Figure 1: Self assembly of salen complex-based coordination cage.

The macrocycle was synthesized using a condensation reaction, combining with geometric complementarity of banana-shaped ligand, the complex can be formed with up to four different ligands. The complexes were characterized with high resolution mass spectrometry (ESI-MS), NMR spectroscopy and X-ray structure.

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Total Synthesis of the Natural Product (+)-3-*O*-Feruloylcassine

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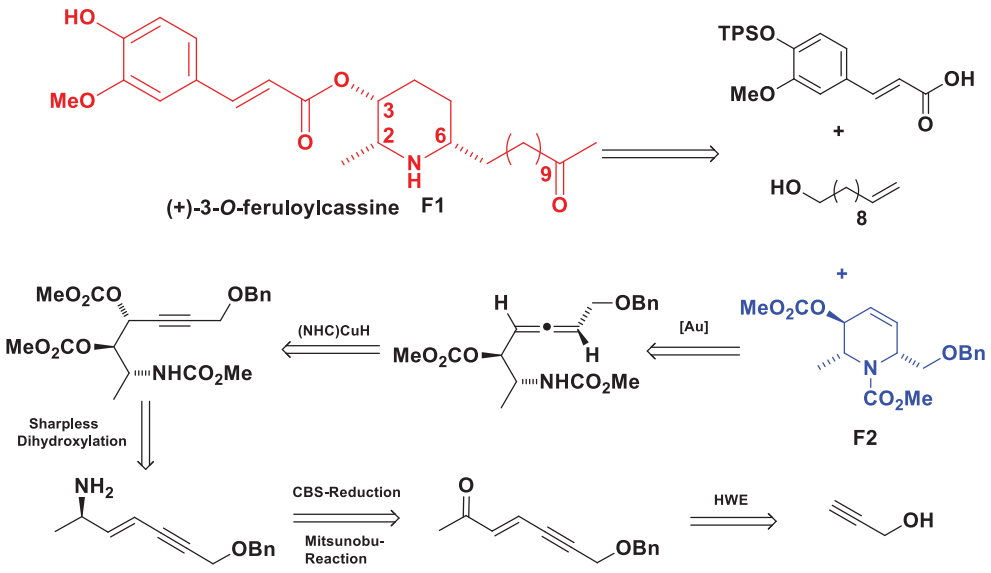
In 2007, (+)-3-*O*-feruloylcassine was first isolated by *Nair et al.* from *Senna spectabilis* green fruits. It is a 2,3,6-trisubstituted piperidine alkaloid, which has interesting biological and pharmacological properties.[1]

To the best of our knowledge, the total synthesis and absolute configuration of this compound has not been reported. We have chosen (+)-3-*O*-feruloylcassine **F1** with the absolute configuration (2*R*,3*R*,6*S*) as the target for our total synthesis. As shown in Scheme 1, the synthesis of piperidine **F2** is the most important step for obtaining the target molecule. Methods developed by our group, *i.e.* the gold-catalyzed cycloisomerization of aminoallenes,[2] as well as, the CuH-catalyzed S_N2'- reduction[3,4], ure used to synthesize this key intermediate.



Scheme 1: Retrosynthetic analysis of (2*R*,3*R*,6*S*)-3-*O*-feruloylcassine.

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