Westfälische
Wilhelms-Universität
Münster

7th MÜNSTER SYMPOSIUM ON COOPERATIVE EFFECTS IN CHEMISTRY

2016
April 22nd

Münster,
Germany

Book of Abstracts

SFB 858

Symposium Schedule

Friday, April 22nd 2016, Aula, Schloss of the WWU Münster

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

10.00 am **Dirk Trauner** — *Chair: Ulrich Hennecke*
Ludwig-Maximilians Universität München, GER
Stringing "Known" Reactions

11.00 am **Donald Hilvert** — *Chair: Mark P. Waller*
Eidgenössische Technische Hochschule Zürich, SUI
De Novo Enzymes by Design and Evolution

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

2.15 pm **MS_CEC Young Researcher Awards 2016** — *Chair: Frank Glorius*
Susanne Löffler, MSc Chemistry,
Technische Universität Dortmund, GER
Dr. Bill Morandi,
Max-Planck Institut für Kohlenforschung, Mülheim an der Ruhr, GER

3.00 pm **Stefan Grimme** — *Chair: Christian Mück-Lichtenfeld*
Rheinische Friedrich-Wilhelms-Universität Bonn, GER
Low-cost Quantum Chemistry for Complex Chemical Systems

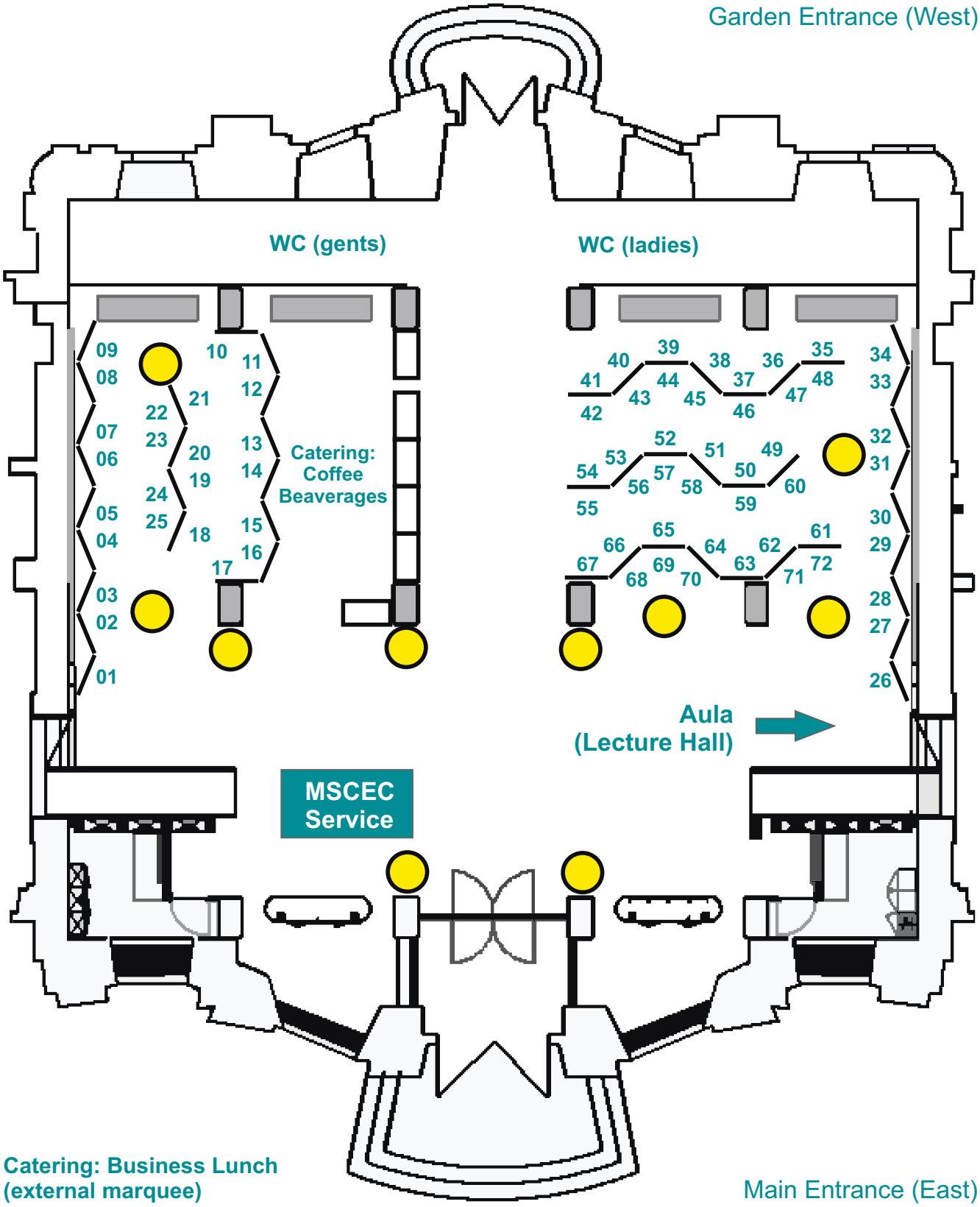
4.00 pm **Kenichiro Itami** — *Chair: Fabian Dielmann*
Nagoya University, JPN
C-H Activation exploring Nanocarbon Materials and Plant Biology

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

SFB 858

7th MÜNSTER SYMPOSIUM ON COOPERATIVE EFFECTS IN CHEMISTRY

Poster Forum



Poster Contributions

in alphabetical order (presenting author's surname)

Nr.	Authors	Institution	Title
01.	D. G. Abradelo, Y. Rey, N. Santschi, R. Gilmour*, and C. A. Strassert*	WWU Münster	Heavy atom effect in homobihalogenated BODIPY molecules
02.	L. K. S. von Krbek, A. J. Achazi, M. Solleder, M. Weber, B. Paulus*, and C. A. Schalley*	Freie Universität Berlin	Cooperativity effects in multivalent systems − A case study
03.	J. Axthelm and A. Schiller*	Friedrich Schiller Universität Jena	Fluorinated Boronic acid-appended Pyridinium Salts for Diol Recognition & Discrimination in Water using ^{19}F NMR Barcodes
04.	V. A. Azov*, J. Warneke, and M. Plaumann	Universität Bremen	Gas-phase binding study of dodecaborate dianions and receptors with hydrophobic binding pockets
05.	J. S. Bruchhage, K. Martinewski, M. Willeke, and W. Uhl*	WWU Münster / SFB 858	Unique Insertion- and Oligomerisation Reactions of Aluminium-Nitrogen Based LEWIS Pairs
06.	T. Buscher, Á. Barroso, C. Denz*, and A. Studer*	WWU Münster	Light as a Multi-Tool for Zeolite L Modification and Assembly
07.	R. Caporaso, S. Manna, and A. P. Antonchick*	Max-Planck-Institut für Molekulare Physiologie / TU Dortmund	Radical Reactions in the Synthesis of Trideuteromethylated Compounds
08.	G. Cheng, A. M. Escorcia, J. P. M. van Rijn, and W. Thiel*	Max-Planck-Institut für Kohlenforschung Mülheim	Computational Study of the Effect of the Acyl Moiety on the Enantioselectivity of *Candida antarctica* Lipase B (CalB) catalyzing Hydrolysis of (*R*,*S*)-Propranolol Esters
09.	W. de Vries, M. Tesch, D. Grill, V. Gerke*, A. Studer*, and B. J. Ravoo*	WWU Münster / SFB 858	Redox-Responsive Polymer Nanocontainers with Tunable Surface Functionalization
10.	A. Dewanji, C. Mück-Lichtenfeld, K. Bergander, C. Daniliuc, and A. Studer*	WWU Münster	Photoinduced Insertion of Isonitriles into the C-F Bonds of Perfluorinated Arenes

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Nr.	Authors	Institution	Title
11.	T. Dresselhaus, S. Eusterwiemann, A. Studer, and J. Neugebauer*	WWU Münster / SFB 858	Black Box *ab initio* Prediction of the Magnetism of Verdazyl Radical Crystals
12.	N. Drosos and B. Morandi*	Max-Planck-Institut für Kohlenforschung Mülheim	Boron-Catalyzed Regioselective Deoxygenation of Terminal 1,2-Diols to 2-Alkanols
13.	P. Dudziński, A. V. Matsnev, J. S. Thrasher*, and G. Haufe*	WWU Münster / Clemson University, SC, USA	Synthesis of SF_5CF_2-containing allylic alcohols and investigation of instability of this group in specific chemical environments and reaction conditions
14.	A. B. Dürr, G. Yin, I. Kalvet, F. Napoly, and F. Schoenebeck*	Rheinisch-Westfälische Technische Hochschule Aachen	Nickel-catalyzed Trifluoromethylthiolation of C_{sp^2}–O Bonds: A Case of Computational Assistance of Method Development
15.	M. Düser and N. Krause*	Technische Universität Dortmund	Synthesis of carbamates from carbon dioxide
16.	P. Franzmann, M. Schubert, S. Beil, and S. R. Waldvogel*	Johannes Gutenberg-Universität Mainz	Oxidative Coupling Reactions Using Mo^V Reagents
17.	S. Gaikwad, A. Goswami, S. De, and M. Schmittel*	Universität Siegen	Four-State Nanomechanical Switch Controlled Sequential Reaction in an ON/OFF Manner
18.	T. Gatzenmeier, M. van Gemmeren, Y. Xie, D. Höfler, M. Leutzsch, and B. List*	Max-Planck-Institut für Kohlenforschung Mülheim	Asymmetric Lewis acid organocatalysis of the Diels–Alder reaction by a silylated C– H acid
19.	C. Gisbert and J. Jose*	WWU Münster	Glowing Chemistry: Fluorescent Labeling of *E. coli* and Surface Exposed Proteins
20.	F. Heins, S. Krupski, D. Paul, F. Glorius, and F. E. Hahn*	WWU Münster / SFB 858	Synthesis of amphiphilic tetrylenes

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Nr.	Authors	Institution	Title
21.	P. A. Held, H.-Y. Gao,* L. Liu, C. Mück-Lichtenfeld, A. Timmer, H. Mönig, J. Neugebauer, H. Fuchs,* and A. Studer*	WWU Münster / SFB 858	On-Surface Domino Reactions: Glaser Coupling and Dehydrogenative Coupling of a Biscarboxylic Acid to Form Polymeric Bisacylperoxide
22.	K. J. Hock, L. Mertens, and R. M. Koenigs*	Rheinisch-Westfälische Technische Hochschule Aachen	Fluoroalkyl-substituted Diazoalkanes – Powerful Reagents for the Synthesis of Fluorinated Heterocycles
23.	M. C. Holland, R. Gilmour,* and K. N. Houk*	WWU Münster / University of Santa Barbara; CA, USA	Intermolecular Hydrogen Bonds Control Stereoselectivity in Allene-Enone (3+2) Annulations Catalyzed by a Bifunctional, Amino Acid Derived Phosphine Catalyst
24.	M. N. Hopkinson, A. Gómez-Suárez, M. Teders, B. Sahoo, and F. Glorius*	WWU Münster	Accelerated Discovery in Photocatalysis using a Mechanism-based Screening Method
25.	A. Junker,* R. Balasubramanian, A. Ciancetta, E. Uliassi, E. Kiselev, C. Martiriggiano, K. Trujillo, G. Mtchedlidze, and K. A. Jacobson*	WWU Münster / National Institutes of Health, Bethesda, MD, USA	Structure-Based Design of 3-(4-Aryl-1*H*-1,2,3-Triazol-1-yl)-Biphenyl Derivatives as $P2Y_{14}$ Receptor Antagonists
26.	I. Kalvet and F. Schoenebeck*	Rheinisch-Westfälische Technische Hochschule Aachen	Nickel-Catalyzed Trifluoromethylthiolation of Aryl Chlorides: Fundamental Studies Revealing the Active Catalytic Species and the Key Roles of Ligand and Additive
27.	F. Kampert and F. E. Hahn*	WWU Münster / SFB 858	Selective C6-metalation of purine nucleobases via oxidative addition
28.	S. J. Kellermann and A. Rentmeister*	WWU Münster	Sequence-Specific Detection of RNA in Two Colors Using a Genetically Encodable System
29.	F. Kempe, H. Buchheit, F. Riehle, S. Hameury, R. Matsidik, and M. Sommer*	Albert-Ludwigs-Universität Freiburg	Cooperative Ligand Effect for High Molecular Weight Polymers in Suzuki-Polycondensation
30.	K. Klahr, D. Schlüns, and J. Neugebauer*	WWU Münster / SFB 858	Geometry Optimizations in a Subsystem DFT formalism - A Test of Two Independent Analytical Gradient Implementations

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31.	M. Klika Skopic, B. Wagner, K. Jung, D. dos Santos, N. Krause,* and A. Brunschweiger*	Technische Universität Dortmund	Synthesis of DNA-pyrazoline conjugates by Au(I)-catalyzed A^3 multicomponent reaction
32.	M. Körner and N. Krause*	Technische Universität Dortmund	Synthesis of Cryptochiral Allenes
33.	L. J. Kost and H. D. Mootz*	WWU Münster / SFB 858	Structure and dynamics of SUMO chains
34.	L. Legnani and B. Morandi*	Max-Planck-Institut für Kohlenforschung Mülheim	Direct Catalytic Synthesis of Unprotected Amino Alcohols from Alkenes Using Iron(II) Phthalocyanine
35.	J. C. Léon, I. Sinha, and J. Müller*	WWU Münster	Selective Recognition of a Pyrimidine Nucleobase using 6-Pyrazolylpurine as an Artificial Nucleobase
36.	M. M. Lerch, M. J. Hansen, W. A. Velema, W. Szymanski, W. R. Browne, and B. L. Feringa*	Rijksuniversiteit Groningen, NED	Orthogonal Photoswitching in a Multifunctional Molecular System
37.	H.-H. Liao, C.-C. Hsiao, S. Raja, I. Atodiresei, and M. Rueping*	Rheinisch-Westfälische Technische Hochschule Aachen	Harvesting Ortho-Quinone Methides as Latent Intermediates for Asymmetric Brønsted Acid Catalyzed Reactions
38.	L. Liu, M. Leutzsch, Y. Zheng, M. W. Alachraf, W. Thiel, and B. List*	Max-Planck-Institut für Kohlenforschung Mülheim	Confined Acid-Catalyzed Asymmetric Carbonyl–Ene Cyclization
39.	S. Löffler, M. John, J. Lübben, L. Krause, D. Stalke, B. Dittrich, and G. H. Clever	Technische Universität Dortmund / Georg-August-Universität Göttingen	Encapsulation of Neutral Guest Molecules by Interpenetrated Coordination Cages
40.	S. Manna and A. P. Antonchick*	Max-Planck-Institut für Molekulare Physiologie / TU Dortmund	Metal Free C-H Bond Functionalization: A Novel Method for Synthesis of Heterocycles

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Nr.	Authors	Institution	Title
41.	R. Matsidik, H. Komber, and M. Sommer	Albert-Ludwigs-Universität Freiburg	Rational Use of Aromatic Solvents for Direct Arylation Polycondensation: C-H Reactivity versus Solvent Quality
42.	P. Mehlmann and F. Dielmann*	WWU Münster / SFB 858	Imidazolin-2-ylidenaminophosphines: highly electron-rich phosphines with an additional basic site
43.	M. Meier, M. Böhmer, and F. E. Hahn*	WWU Münster / SFB 858	Preparation of heteronuclear metal complexes
44.	J. B. Metternich and R. Gilmour*	WWU Münster	One Photocatalyst, *n* Activation Modes Strategy for Cascade Catalysis: Emulating Coumarin Biosynthesis with (–)-Riboflavin
45.	J. Moratz, T. Otremba, and B. J. Ravoo*	WWU Münster / SFB 858	Multivalent Recognition on Membrane-Surfaces by Synthetic Receptors
46.	M. Moselage, N. Sauermannm, and L. Ackermann*	Georg-August-Universität Göttingen	C–H Alkenylations with Alkenyl Acetates, Phosphates, Carbonates and Carbamates by Versatile Cobalt Catalysis at 23 °C
47.	F. Muttach and A. Rentmeister*	WWU Münster	A biocatalytic cascade reaction for versatile one-pot modification of RNA
48.	C. Nienberg, A. Retterath, and J. Jose*	WWU Münster	Click Chemistry for Site Directed Labeling of Surface Displayed Proteins on *Escherichia coli*
49.	G. Prina Cerai and B. Morandi*	Max-Planck-Institut für Kohlenforschung Mülheim	Atom-Economical Cobalt-Catalyzed Regioselective Coupling of Epoxides and Aziridines with Alkenes
50.	I. Pyka, D. Ryvlin, and S. R. Waldvogel*	Johannes Gutenberg-Universität Mainz	Rigidity-controlled Supramolecular Affinity Materials and their Application for Gravimetric Detection of Hazardous and Illicit Compounds

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Nr.	Authors	Institution	Title
51.	T. Quell, N. Beiser, S. R. Waldvogel*, R. Franke, and K. M. Dyballa	Johannes Gutenberg-Universität Mainz	Selenium dioxide-mediated activation of phenols
52.	L. Rakers, C. Richter, A. Rühling, D. Wang, P. Drücker, D. de Jong-Bruinik, H.-J. Galla*, A. Heuer*, and F. Glorius*	WWU Münster / SFB 858	*N*-heterocyclic carbenes and their salts for membrane interactions and micellar catalysis
53.	K. Rau and A. Rentmeister	WWU Münster / SFB 858	Sequence-specific modification of RNAs
54.	A. L. Rauen, C. Gütz, S. Herold, A. Wiebe, and S. R. Waldvogel*	Johannes Gutenberg-Universität Mainz	Electroorganic Process Development
55.	A. Rühling, K. Schaepe, L. Rakers, B. Vonhören, P. Tegeder, B. J. Ravoo*, and F. Glorius*	WWU Münster / SFB 858	Modular bidentate hybrid NHC-thioether ligands for the stabilization of palladium nanoparticles in various solvents
56.	J. Schieven and N. Krause*	Technische Universität Dortmund	Synthesis of functionalized pyrazolidines by gold-catalysed three-component spirocyclization in micellar systems
57.	J. Schüürmann, F. Lindhorst, and J. Jose*	WWU Münster	NADPH Cofactor regeneration on the cell sur-face: A crucial requirement for pharmaceutical applications of surface displayed P450 enzymes
58.	M. Segler and M. P. Waller*	WWU Münster / SFB 858	Modelling Chemical Reasoning and Creativity to Predict and Invent Reactions
59.	N. Sinha, L. Stegemann, T. T. Y. Tan, C. A. Strassert*, and F. E. Hahn*	WWU Münster	Turn on Fluorescence in Tetraphenylethylene-Bridged Tetra-NHC Ligands by Rigidification in Organometallic Complexes: An Alternative to Aggregation-Induced Emission
60.	N. Soltanmoammadi, P. Lulchev, and D. Klostermeier*	WWU Münster / SFB 858	Molecular understanding of functional cooperation between the helicase and the topoisomerase domain of Thermotoga maritima reverse gyrase in DNA binding and supercoiling

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61.	T. Sperger and F. Schoenebeck*	Rheinisch-Westfälische Technische Hochschule Aachen	C-SeCF_3 Bond Formation *via* Dinuclear Pd(I) Catalysis
62.	A. Galstyan, U. Kauscher, M. C. Grüner, D. Block, S. Niemann, M. Schäfers, B. J. Ravoo,* A. Faust*, C. A. Strassert*	WWU Münster	Conjugated Si(IV) phthalocyanines as light-driven antibiotics
63.	K. F. Taupitz and H. D. Mootz*	WWU Münster / SFB 858	Stabilisation of transient SIM-SUMO mediated interactions by photoinducible crosslinking
64.	M. Tesch, J. A. M. Hepperle, H. Klaasen, M. Letzel, and A. Studer*	WWU Münster / SFB 858	Double Click Functionalization of NMP Based Alternating Copolymers
65.	R. Vidyadharan, L. Li, L. Sorokin, and G. Haufe*	WWU Münster	Synthesis of small molecules for optical and whole imaging of CCR6
66.	D. van der Heiden, E. Detmar, and M. Breugst*	Universität zu Köln	Mechanisms of Iodine-Catalyzed Reactions
67.	B. Wagner, M. Klika Skopic, K. Jung, S. Willems, D. dos Santos, A. Brunschweiger*, and N. Krause*	Technische Universität Dortmund	Development of a three-component spirocyclization to highly functionalized pyrazolidines and access to their DNA-conjugates by Au(I)-catalysis
68.	M. Weers, L. H. Lühning, C. Brahms, V. Lührs, S. Doye*	Carl von Ossietzky Universität Oldenburg	One-Pot Procedure for the Synthesis of 1,5-Benzodiazepines
69.	R. C. Wende, A. Seitz, D. Niedek, S. M. M. Schuler, C. Hofmann, J. Becker, and P. R. Schreiner*	Justus-Liebig Universität Gießen	The Enantioselective Dakin–West Reaction
70.	M. Wiemann, R. Niebuhr, P. Jonkheijm*, and B. J. Ravoo*	Universiteit Twente, Enschede, NED / WWU Münster	Switchable Bioactive Ligands for Supramolecular Surfaces

71.	S. Wilde, M. Cnudde, L. Stegemann, D. Ma, A. Bakker, H. Fuchs, and C. A. Strassert*	WWU Münster	Tetradentate luminophores for platinum(II) complexes
72.	K. Willeke and W. Uhl*	WWU Münster / SFB 858	Donor-functionalized alkenyl-silanes and their reactivity

Heavy atom effect in homobihalogenated BODIPY molecules

Dario G. Abradelo,[a] Yannick Rey,[b] Nico Santschi,[b] Ryan Gilmour*[b] and Cristian A. Strassert*[a]

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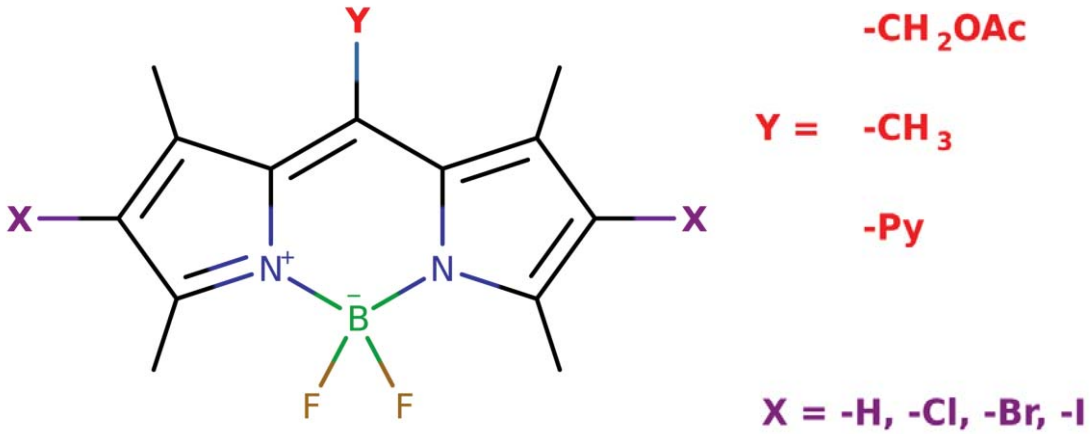
The tuneability of the photophysical properties of fluorescent molecules is fundamental for the development of new photocatalytic and phototherapeutic methodologies involving the photoproduction of highly reactive singlet oxygen (SO). This phenomenon requires an efficient intersystem crossing (ISC) from the singlet to the triplet manifold, and relies on a favorable fast spin-orbit coupling (SOC). In this work, we assess the effect of heavy atoms on the SOC and, therefore, on the intersystem crossing efficiency. The photophysical properties of ten BODIPY dyes with modifications in positions 8 (CH_3, CH_2OAc or Py) and *bis*-2,6 (H, Cl, Br or I) were investigated by absorption spectroscopy. Fluorescence excitation and emission spectra were acquired in solution and in frozen matrices at 77 K, as well as absolute photoluminescent quantum yields (PLQY) and time-resolved luminescence decays to evaluate the excited state lifetimes. As the direct determination of k_{isc} (ISC rate constant) is often hampered by the concomitant occurrence of other non-radiative processes, it was assumed that collisional deactivation of the singlet state is negligible in frozen matrices. A plot of $ln\left(k_{nr\,X}^{77K}/k_{nr\,Y}^{77K}\right)$ *vs.* $ln\left(Z_X/Z_Y\right)$, where X and Y represent the substituents at the positions 2 and 6 of the fluorophore, and Z stands for the correspondent atomic numbers, showed a straight line with a slope close to four (4.4 - 4.7), in correspondence with the SOC-related correlation between k_{isc} and Z. The same slopes (3.6-3.8) were observed for the SO quantum yields, which confirmed the direct dependence of the triplet quantum yield on the atomic number. Compounds with H did not follow the trend, as expected, due to their small SOC and different triplet state properties.



References

1. Wang, H. L. *et al., Phys. Rev. Lett.* **112**, 197201 (2014).

2. Du, C. *et al., Phys. Rev. B* **90**, 140407 (2014).

3. Tserkovnyak, Y. *et al., ChemInform* **36**, (2005).

4. Sarma, D. D. *Proc. Indian Acad. Sci. - Chem. Sci.* **90**, 19 (1981).

Cooperativity effects in multivalent systems – A case study

Larissa K. S. von Krbek, Andreas J. Achazi, Marthe Solleder, Marcus Weber, Beate Paulus, Christoph A. Schalley

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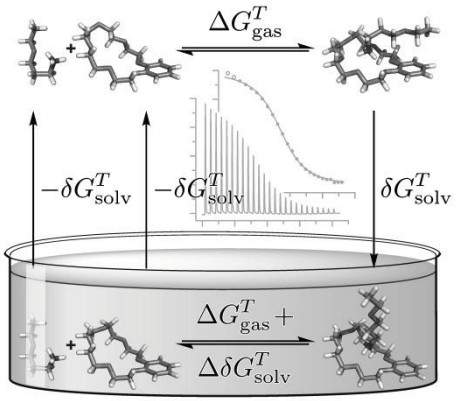
The particularly strong as well as reversible interaction in multivalent systems arises increasing interest, especially as it is progressively used in the fields of supramolecular and medicinal chemistry. To understand and quantify the unique enhancement of the binding constant *K* in multivalent systems, different cooperativity effects have to be considered individually. Besides, various possible unbound, bound and partly bound states occur during the association process of a multivalent guest to a multivalent host. The number of these states influences the value of the over-all binding constant *K* of the multivalent system by statistical factors. Hence, these statistical factors have to be quantified prior to any experimental analysis of the association process. Subsequently, a *double mutant cycle* analysis[1] may be used to quantify all cooperativity effects in the multivalent system.



We use this approach to study the cooperativity effects of divalent crown-ammonium-complexes in different solvent mixtures. Isothermal titration calorimetry is the only tool to directly and simultaneously determine the binding constant *K* as well as the binding enthalpy Δ*H* and thus derive the Gibbs energy Δ*G* and the entropy Δ*S*. Furthermore, we compare our experimental data with DFT[2] and molecular-dynamics calculations which give further insight into the processes occurring upon multivalent binding in solution.

References:

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3. *L. K. S. von Krbek, A. J. Achazi, M. Solleder, M. Weber, B. Paulus, C. A. Schalley,* ***2016****, submitted.*

Fluorinated Boronic acid-appended Pyridinium Salts for Diol Recognition & Discrimination in Water using ^{19}F NMR Barcodes

Joerg Axthelm[a] **and Alexander Schiller**[a]

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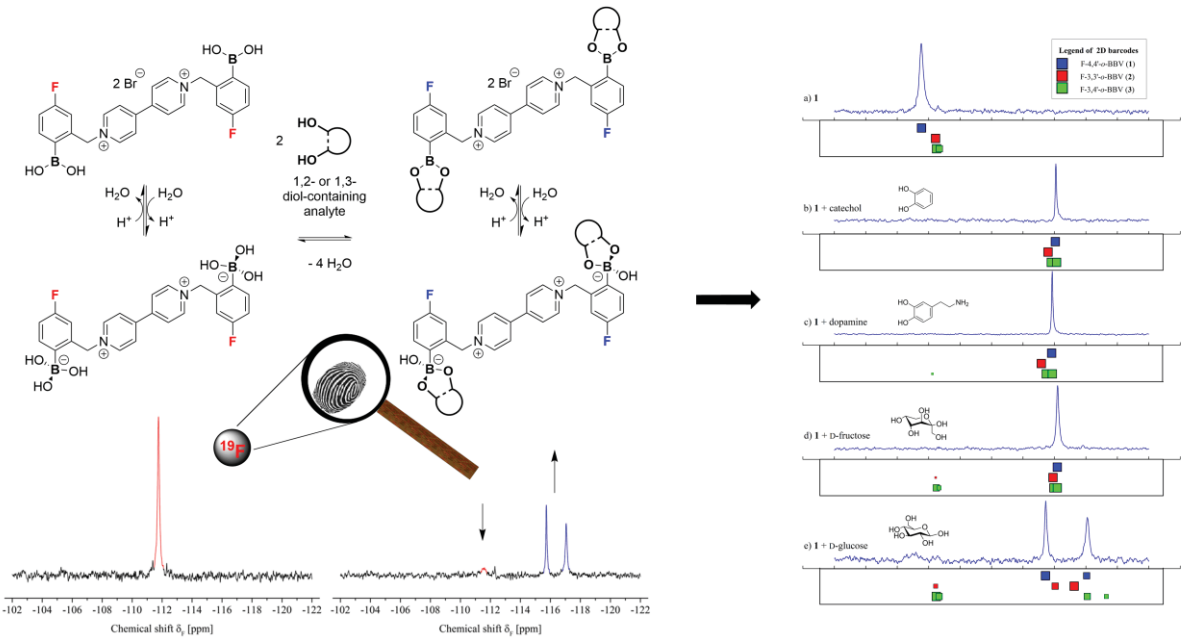
Boronic acid-appended bipyridinium salts are well known receptors for sensing carbohydrates via fluorescence spectroscopy.[1-4] Compared to fluorescence - ^{19}F NMR spectroscopy, particularly used for sensing biological events, is currently growing to be a valuable tool.[5] For instance, nearly no disturbing background signals are present and characteristic and easy to readout ^{19}F NMR shifts can be recorded due to the high environmental sensitivity of the fluorine probe without the need of e.g. an external reporting molecule. Herein, we demonstrate a new sensing concept for diol-containing analytes in water via fluorinated boronic acid-appended pyridinium salts and ^{19}F NMR spectroscopy. ^{19}F NMR fingerprints are produced by the remarkable sensitivity of the ^{19}F probe which recognizes bound analytes at the boronic acid binding site. With this property in hand, we used an array of three water-soluble boronic acid receptors in combination with ^{19}F NMR spectroscopy to discriminate diol-containing bioanalytes such as D-fructose, -glucose, -glucose-6-phosphate, -galactose and catechol derivatives at low mM concentrations.[6] Highly characteristic ^{19}F NMR fingerprints can be interpreted as two-dimensional barcodes without the need of multivariate analysis techniques. The power of this method is a clear and unambiguous detection and quantification of diol-containing analytes. In addition, our approach was successfully applied in screening glucose in a urine matrix and as well in monitoring enzyme catalyzed reactions such as sucrose phosphorylase.



Sensing of diols using fluorinated boronic acid-appended bipyridinium salts and ^{19}F NMR spectroscopy: Left, equilibrium and corresponding ^{19}F NMR spectra of unbound F-4,4′-*o*-BBV and in presence of D-glucose (Conditions: F-4,4′-*o*-BBV (4 mM) and D-glucose (40 mM) in 100 mM HEPES buffer pH 7.4, 10% D_2O). Right, ^{19}F NMR spectra of F-4,4′-*o*-BBV in presence of selected diols and resulting receptor-analyte 2D barcodes underneath each corresponding spectrum obtained by the array of receptors **1**-**3**.

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Gas-phase binding study of dodecaborate dianions and receptors with hydrophobic binding pockets

V. A. Azov, J. Warneke, M. Plaumann

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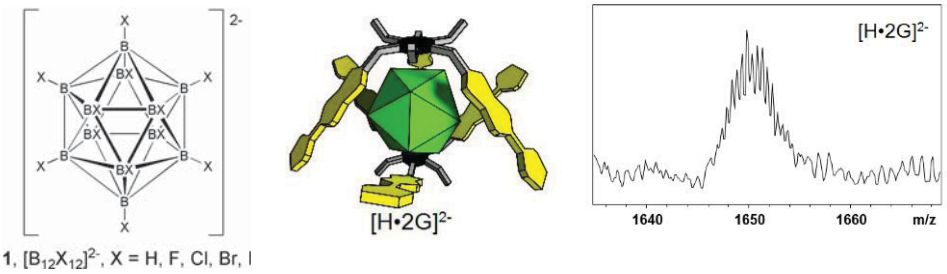
Halogenated *closo*-dodecaborates[1] **1** are inorganic dianions with icosahedral molecular symmetry. The extremely weak binding affinity of the *closo*-dodecaborates with cationic species led to new records in superacidity and allowed stabilization of highly reactive cations. On the other hand, potential for formation of intermolecular complexes of dodecaborates with organic molecules has been so far overlooked. The only recent study on molecular recognition of *closo*-dodecaborates with non-charged organic hosts reports very strong binding of **1** with cyclodextrins (CDs) in aqueous solutions[2] that was explained by the influence of the chaotropic effect.

Using ESI mass-spectrometry as an analytical tool, we investigated complex formation between dodecaborates and organic hosts in the gas phase,[3] where possible solvent effects are excluded. Several organic molecular hosts with hydrophobic binding pockets (tripodal tetrathiafulvalene (TTF) receptors, cyclodextrins, several calix[4]arenes derivatives, and calix[4]azulene) have been tested for their binding affinity to halogenated anionic dodecaborates.[4]



1, $[B_{12}X_{12}]^{2-}$, X = H, F, Cl, Br, I

We have observed a significant intrinsic binding affinity between these seemingly non-complementary molecules combined with binding selectivity. Dodecaborates displayed preference for the large molecular hosts with deep hydrophobic polarizable pockets, as in the case of tripodal TTF receptors, or spherical cavities of complementary shape, as with cyclodextrins. Using the TTF-based receptor, we have devised the host-guest system that can be switched between two binding modes based on different types of interactions (dispersion or electrostatic) upon oxidation/reduction of the TTF-containing host. Moreover, we have demonstrated that cyclodextrin complexes of dodecaborates can be employed for the translocation of boron cluster into the fast growing cell lines, including cancer cells.

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Unique Insertion- and Oligomerisation Reactions of Aluminium-Nitrogen Based LEWIS Pairs

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Recently we reported on the synthesis of aluminum-nitrogen based LEWIS pairs. They were obtained by hydroalumination of ynamines or hydrazones with different dialkylaluminum hydrides[1, 2]. These bifunctional LEWIS pairs are able to activate small molecules or can be used as catalysts for unprecedented oligomerisation reactions [3].

A unique reactivity was achieved by the activation of isocyanates and isothiocyanates. We isolated a wide variety of products by the application of functionalized LEWIS pairs and different isocyanates and isothiocyanates. Figure 1 shows two different insertion reactions depending on the heteroatom.

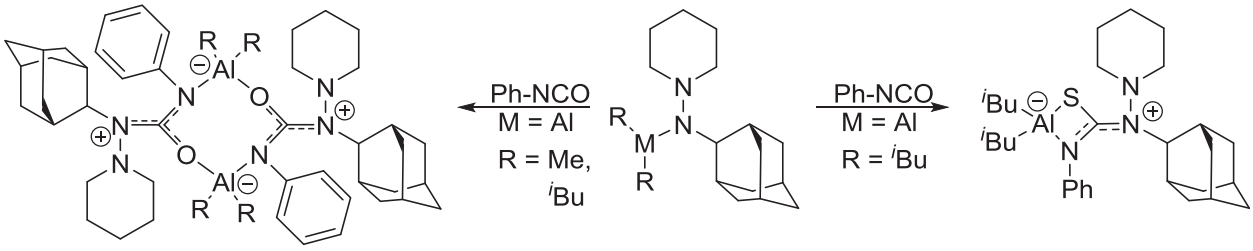

Figure 1: Activation of phenyl isocyanate depending on the heteroatom.

In case of the Al-N based LEWIS pair shown in Figure 2 we investigated the oligomerisation reaction of 4- morpholine carbonitrile. Activation of *tert*-butyl isocyanate afforded an unprecedented reaction course with pseudo dimerisation of the LEWIS pair by condensation and formation of two new C-C bonds.

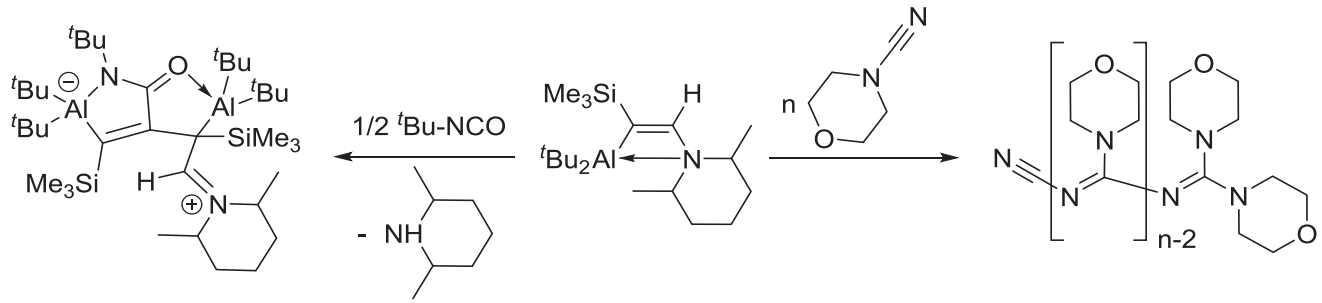

Figure 2: Examples for reactions of an Al-N based LEWIS pair with isocyanates and oligomerization of a carbonitrile.

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Light as a Multi-Tool for Zeolite L Modification and Assembly

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Zeolite L crystals are optically transparent, non-toxic and under physiological conditions stable microcontainers with nanoporous structure. Due to their one-dimensional, strictly parallel channels it is possible to functionalize the particle surface site-specifically.[1] Previously, we established the thermally induced dynamic nitroxide exchange reaction as an efficient method for chemical surface modification or even to assemble particles in chain-like structures.[2]

Herein, a novel type of zeolite/polymer hybrid material is presented. Zeolite L crystals were used as macro initiators to synthesize particle-based polymer brushes *via* surface initiated polymerization processes. (Co)polymerization of a photocleavable styrene derivative and subsequent spin trapping of functionalized nitroxides leads to a broad variety of highly modified zeolite L based core-shell particles (Figure 1).[3]

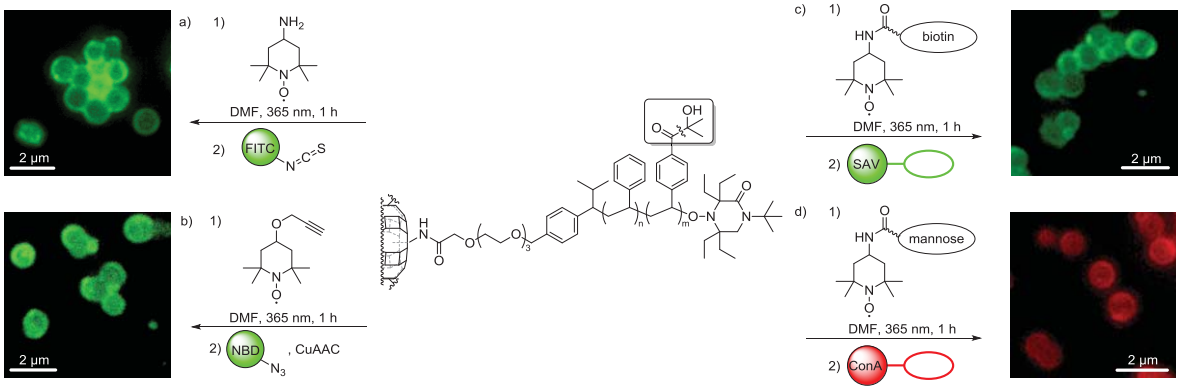

Figure 1: Postmodification of polyacyloin brush particles *via* light induced spin trapping of nitroxides.

Currently, the three-dimensional assembly of these particles by using holographic optical tweezers (HOT) is investigated. The objective is to form sophisticated aggregates or even ´bio-hybrid micro-shuttles´ by attaching living an self-propelling bacteria to zeolite L surfaces.[3,4]

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Radical Reactions in the Synthesis of Trideuteromethylated Compounds

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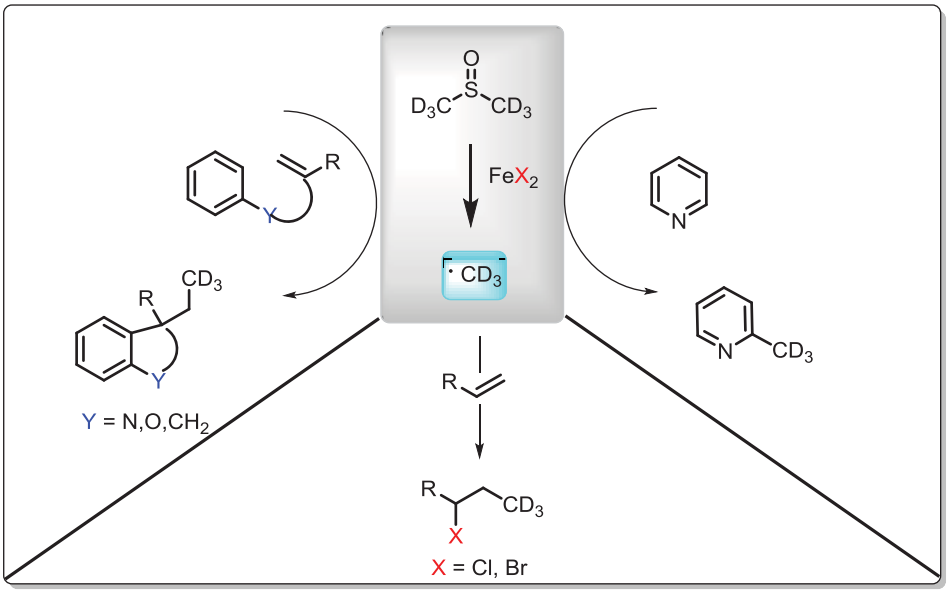
The growth potential of deuterated pharmaceuticals is being widely demonstrated since several deuterium-containing drugs have reached clinical trials. Adding a neutron, to create deuterium, entails such a big change with appreciable chemical effect. Indeed, deuterium can change properties of compounds, such as absorption, distribution and toxicology, while retaining its original potency and selectivity[1]. Above all occurring functional groups in bioactive compounds, methyl group has been considered for long time as one of the most privileged. Herein, we report radical cascade transformations for the synthesis of trideuteromethylated products using dimethyl sulfoxide-D_6 as source of deuterium.



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COMPUTATIONAL STUDY OF THE EFFECT OF THE ACYL MOIETY ON THE ENANTIOSELECTIVITY OF *Candida antarctica* Lipase B (CalB) CATALYZING HYROLYSIS OF (*R,S*)-PROPRANOLOL ESTERS

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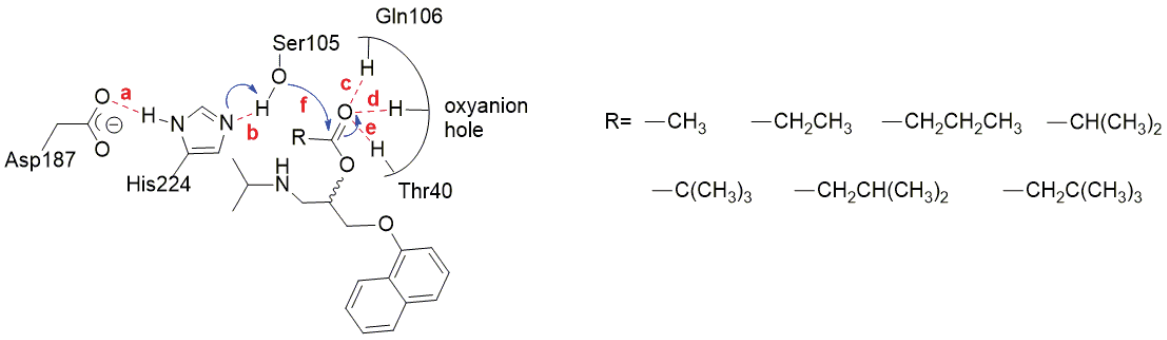
Propranolol (1-iso-propylamino-3-(1-naphthoxy)-2-propanol), a beta-adrenergic blocking agent commonly used for treating hypertension, is commercially available as a racemic mixture. However, only the *S*-enantiomer has the desired therapeutic effect, and administration of the racemic propranolol mixture may even cause side effects such as bronchoconstriction or diabetes. Obtaining the *S*-enantiomer with high purity will enhance the therapeutic potential of propranolol and is therefore an active area of research. Kinetic resolution catalyzed by lipases has been established as a versatile method to achieve this goal.

In this work, we have carried out a computational study of the effect of the acyl moiety on the enantioselectivity of *Candida antarctica* lipase B (CalB) catalyzing hydrolysis of propranolol esters. The following acyl groups were tested: acetyl, propanoyl, butanoyl, isobutyryl, pivaloyl, isovaleryl and 3,3-dimethylbutanoyl. The reaction is a two-step process. The enantioselectivity originates from the first step when the propranolol ester transfers its acyl group to the catalytic serine (Ser105) of CalB, yielding an acylated enzyme (AcCalB) and propranolol (acylation step). In the second step AcCalB reacts with water and CalB is recovered along with the formation of a carboxylic acid (deacylation step). Acylation as well as deacylation proceed via an initial noncovalent enzyme substrate complex (Michaelis complex; MCC) and an oxyanionic tetrahedral intermediate (TI). The latter is stabilized through hydrogen bond interactions by the residues of the so-called oxyanion hole (Thr40 and Gln106).

We have applied a molecular docking protocol to model the MCCs of the acylation step. This docking protocol involved three stages: 1) preparation of the structure of CalB (the docking target) by explicit solvent molecular dynamics (MD) in water, 2) docking of the propranolol esters against CalB and 3) optimization of the poses with the highest interaction free energy from the docking procedure. The analysis of the MCCs was focused on the interatomic distances important for the catalytic process (**Scheme 1**) and the enzyme-substrate interactions involved in the binding modes of the substrate. Based on this analysis the reactivity of the *R*- and *S*-enantiomer of the propranolol esters was estimated.



Scheme 1. MCCs between CalB and propranolol esters. **a-f** are the most important interatomic distances for the catalytic process.

Redox-Responsive Polymer Nanocontainers with Tunable Surface Functionalization

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Synthetic vesicles allow the development of biomimetic soft materials, drug delivery systems and microreactors. Previously, we reported on polymer shelled vesicles based on templates of amphiphilic cyclodextrin derivatives. Adamantane terminated poly(acrylic acid) was anchored on cyclodextrin vesicles via host-guest recognition followed by crosslinking of carboxylic acid groups. The resulting nanocontainers were highly stable and effective for encapsulation of small hydrophilic molecules.[1]
In this project a redox-responsive release of a hydrophilic payload from modified polymer shelled vesicles is realized. Therefore, a reductively cleavable cystamine linker is used for crosslinking and the release of cargo is studied in reducing environments. Moreover it is shown that the surface of these stimulus-responsive nanocontainers can be easily functionalized via amide coupling. By using several ligands or short polymers a facile engineering of surface properties is possible. For example the immobilization of sugars enables highly specific recognition of lectins at the nanocontainer surface. Currently we are investigating the capacity of these nanocontainers as a delivery system for hydrophilic cargo into cells.

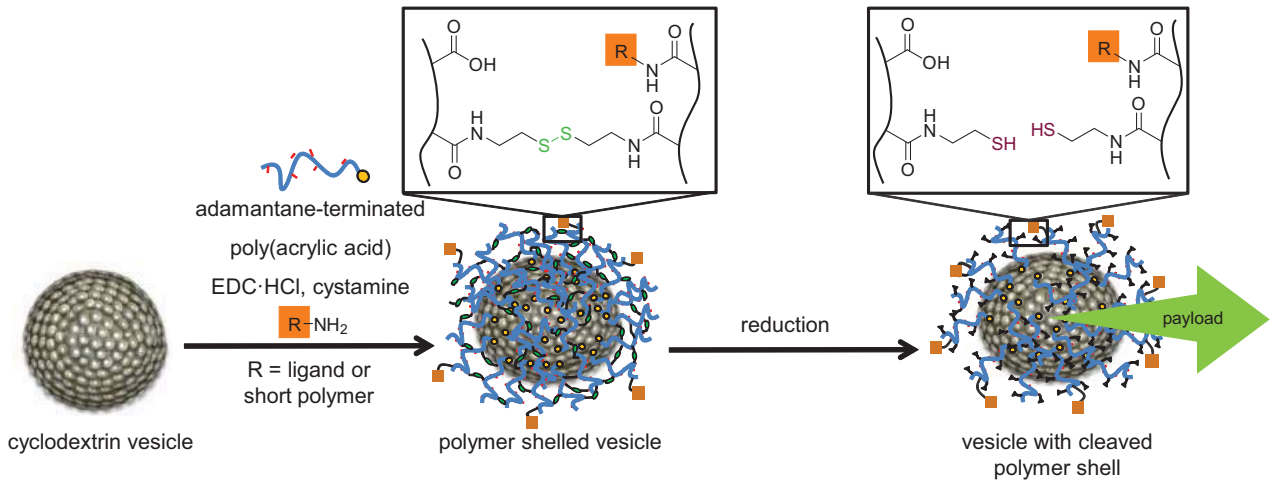

Figure 1: Synthesis of redox-responsive polymer shelled vesicles with facile surface functionalization.

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Photoinduced Insertion of Isonitriles into the C-F Bonds of Perfluorinated Arenes

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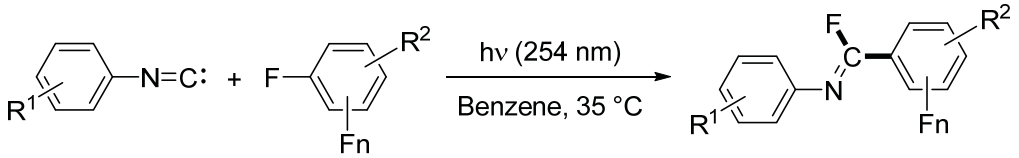
Fluorine is one of the most important elements of the periodic table and has drawn great attention from researchers in recent times. [1] It plays an important role in the development of various agrochemicals, pharmaceuticals and novel organic materials because the strong electronegativity of fluorine alters the properties of compounds to a great extent. [1] One of the challenging pathways to make partially fluorinated compounds is C-F bond activation of its polyfluorinated analogues due to the strong bonding ability of fluorine with almost any other element. Along with transition-metal catalyzed processes [2], elegant Lewis acid mediated methods for C-F activation also made their way into the literature. [3] A more challenging transformation from the synthetic point of view is C-F insertion i.e. squeezing one or more atoms into the C-F bond. The most commonly used reagents for this purpose are complexes of transition-metals (e.g. Ni, Pd, Pt) which form stronger bonds with fluorine. [4] Herein, we present organic isonitriles as carbon sextet reagents to furnish insertion of its low-valent carbon atom into the C-F bonds of perfluorinated arenes. [5]



26 examples, 34-98% yield

Strong UV (254 nm) irradiation was required to activate the isonitrile, but the reaction did proceed at ambient temperature (35 °C) and under air atmosphere. The method tolerated a broad range of functionalities on both reaction partners with moderate to excellent yields. DFT calculations suggested involvement of triplet isonitrile species and an unprecedented radical mechanism. The method established in this work is also a novel one-step procedure to prepare imidoyl fluorides.

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Black Box *ab initio* Prediction of the Magnetism of Verdazyl Radical Crystals

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We present an easily usable method to calculate the temperature-dependent magnetic susceptibility and heat capacity starting from nothing more than a crystal structure. In this way, we can not only predict the magnetic character, *i.e.* ferro- or antiferromagnetic, and the transition temperature to the paramagnetic phase, but we also gain insight into the microscopic interactions which lead to the macroscopically observable magnetic behavior.
We make use of the *first-principles bottom-up* approach[1,2], in which finite magnetic model spaces are set up to describe the infinite periodic crystal. For each model space a Heisenberg Hamiltonian is constructed, which can be easily parametrized with results from *broken symmetry*[3] calculations. After diagonalization of the Hamiltonian, the Boltzmann distribution can be applied to yield temperature-dependent properties like the magnetic susceptibility and the heat capacity.
Especially for molecular crystals based on organic radicals like verdazyl the identification of all unique interacting radical pairs is a complicated and error-prone task. Likewise, a proper definition of the magnetic unit cell, which is essential to obtain correct results,[1] is far from trivial, except for special cases.
Among others, these critical steps have been automatized as presented on this poster. We applied the procedure to several verdazyl-based radical systems and obtained excellent agreement with experiments without any post-processing of the results.

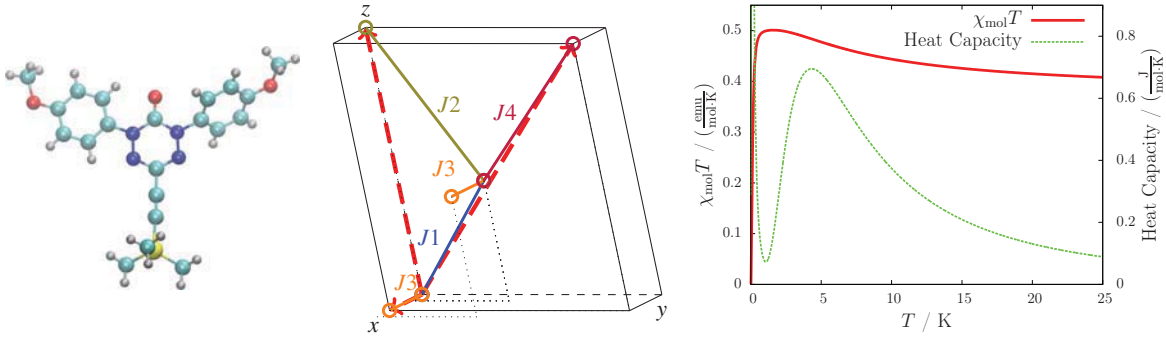

Figure 1: Structure (left), magnetic unit cell (center) and temperature-dependent magnetic susceptibility and heat capacity curves (right) of a verdazyl-based radical.

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MS_CEC 2016 Poster session application

- *Title of the poster:* Boron-Catalyzed Regioselective Deoxygenation of Terminal 1,2-Diols to 2-Alkanols.
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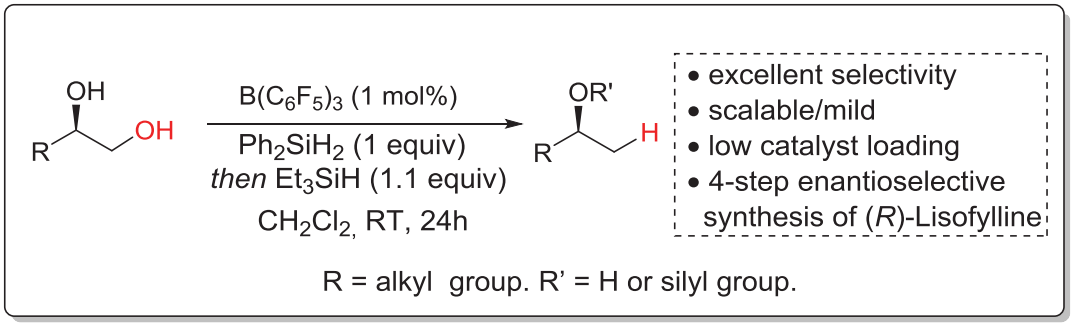
- *Address:* Max-Planck-Insitut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr, Germany.
- *E-Mail:* Drosos@mpi-muelheim.mpg.de
- *Abstract:* The selective deoxygenation of polyols is a frontier in our ability to harness the stereochemical and structural complexity of natural and synthetic feedstocks. Herein, we report a highly active and selective boron-based catalytic system for the selective deoxygenation of terminal 1,2-diols at the primary position, a process enabled by the transient formation of a cyclic siloxane. The method provides an ideal complement to well-known catalytic asymmetric reactions to prepare synthetically challenging, chiral 2-alkanols in nearly perfect enantiomeric excess, as illustrated in a short synthesis of the anti-inflammatory drug (R)-Lisofylline.
- *Figures:*



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N. Drosos, B. Morandi, *Angew. Chem. Int. Ed*. **2015**, *54*, 8814–8818

Synthesis of SF_5CF_2-containing allylic alcohols and investigation of instability of this group in specific chemical environments and reaction conditions

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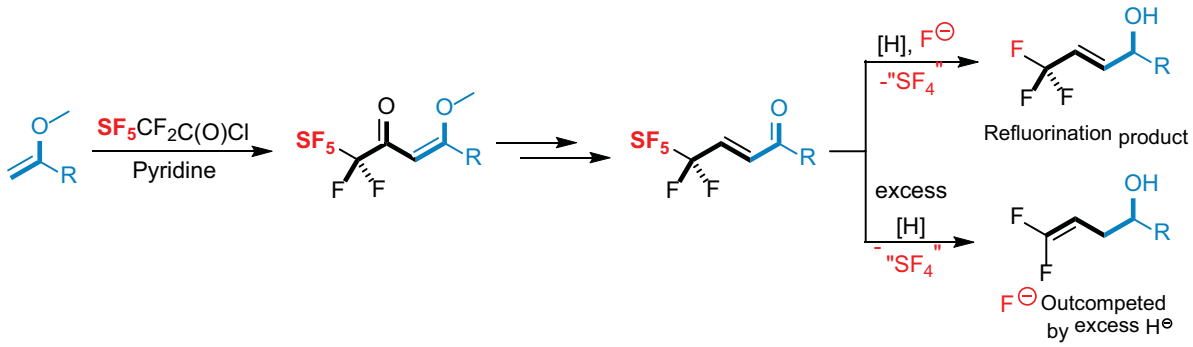
The chemistry of the SF_5 group has witnessed noticeable advances in the recent years.[1] The chemistry of the SF_5CF_2 moiety, however, remains underdeveloped.[2] We focused our investigations on synthesis of SF_5CF_2 substituted allylic alcohols which can serve as useful building blocks for further modifications, including [3,3]-sigmatropic rearrangements.



Starting from SF_5CF_2COOH and enol ethers, through several steps, we synthesized SF_5CF_2 substituted enones destined for the final reduction to the target allylic alcohols. Unfortunately, all our attempts led to elimination of the SF_5 group followed by secondary reactions, including formation of CF_3 substituted allylic alcohols, instead. This work presents investigations of the nature of the undesired transformations and opportunities to avoid them. Hence gained knowledge might be useful for designing synthesis of new SF_5CF_2 substituted compounds.

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Nickel-catalyzed Trifluoromethylthiolation of C_{sp}^2–O Bonds: A Case of Computational Assistance of Method Development

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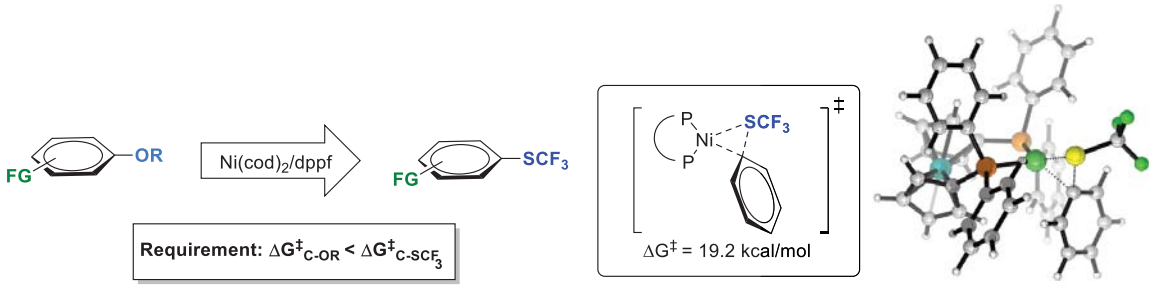
Incorporation of fluorine or fluorine-containing moieties into organic molecules significantly impacts several physical properties, including lipophilicity, polarity, bioavailability and metabolic stability. Consequently, a large number of agrochemicals and pharmaceuticals on the market contain fluorine.[1] In this context, the SCF_3 group is of high current interest.

While several methods have successfully been developed to incorporate the SCF_3 group into small molecules at a later stage in the synthesis, C_{sp}^2-O bonds had remained inaccessible.[2] This poster describes a combined computational and experimental approach to the development of the trifluoromethythiolation of C_{sp}^2-O bonds (vinyl and aryl) under homogeneous nickel catalysis.[3]

Nickel's remarkable reactivity towards relatively unreactive functional groups, even unactivated aryl ethers, has recently been elegantly showcased for the formation of inert C-C and/or C-H bonds.[4] On the other hand, this poster emphasizes that when harnessing Nickel's activity to introduce potentially reactive groups, such as SCF_3, the reactivity of the functional groups in the starting material and in the product require matching in order to prevent deactivation side-reactions. In this context, computational chemistry allowed us to identify the match/mismatch functionalities and guide the substrate scope.



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Synthesis of carbamates from carbon dioxide

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Carbon dioxide is an attractive, abundant and renewable C_1 building block, therefore it is desirable to utilize a small part of the excessive amount of this greenhouse gas for chemical reactions.[1] In the last decades, most approaches relied on stoichiometric amounts of organometallic reagents, due to high thermodynamic stability and low reactivity of CO_2.[1] *Nolan et. al.* has shown that gold(I) complexes bearing strong donor ligands are able to carboxylate aromatic C-H bonds, affording the corresponding carboxylic acids.[2] Recently, a substantial advance was made in the development of direct C-H carboxylations catalyzed by coinage metal salts.[1,3]

Another promising field for carbon dioxide utilization is the synthesis of carbamates. They are important is building block in target-oriented synthesis, as well as for polymer chemistry. The preparation usually requires use of highly toxic and corrosive phosgene, therefore use of carbon dioxide as non-toxic and non-corrosive building block would is desirable.[4]

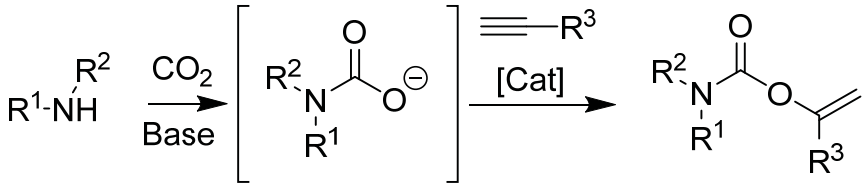

Abb. 1. Synthesis of carbamates from carbon dioxide

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Oxidative Coupling Reactions Using Mo^{V} Reagents

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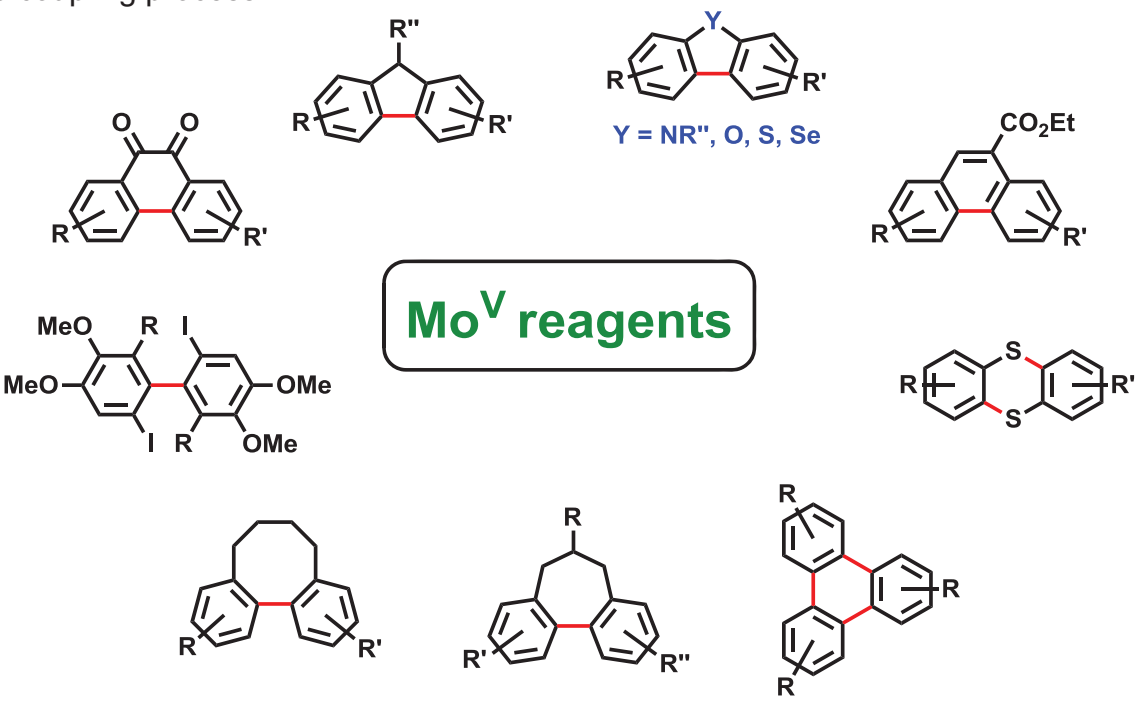
The formation of aryl-aryl bonds is one of the most important reactions in organic chemistry. Although reductive transformations requiring transition metal catalysis are well established, the direct dehydrogenative coupling of aryls gained the attention of many research groups in the past decades.[1]
Molybdenum pentachloride is a readily available molybdenum salt with a strong lewis acid property. The high oxidation potential leads to very fast transformations. Therefore, a variety of labile moieties like iodo groups or acetals are tolerated during the coupling process.[2]



Scheme 1: Overview of the substance classes accessible by using molybdenum(V) reagents.[2,3,4]

However, some substrates (in particular very electron rich aryls) are prone to the formation of chlorinated byproducts. The use of chlorine scavengers e.g. $TiCl_4$ can reduce, but not completely suppress these undesired side reactions. We report the development of a novel molybdenum(V) reagent with a reduced chlorine content which leads to a siginificant depression of the chlorination.[5]

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Four-State Nanomechanical Switch Controlled Sequential Reaction in an ON/OFF Manner

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Abstract:

The field of switchable catalysis has received huge attention over past decade because of their capability of performing well defined tasks such as mechanical work,[1] regulation of catalysis[2] and synthesis of small molecules.[3] However, regulation of sequential catalysis which consists of multiple substrates in one compartment is unprecedented in the literature. The nanomechanical switch **1** with its three orthogonal binding motifs, the zinc(II)-porphyrin, azaterpyridine and shielded phenanthroline stations,[4] is quantitatively and reversibly toggled back and forth between four different states by means of addition and removal of appropriate metal ion inputs. Each switching state is fully characterized by NMR, UV-vis, ESI-MS spectroscopy and elemental analysis. Two of the four switching states direct catalytic transformations (ON states), while the two other states shut down any reaction (OFF states). In brief, the cyclic switching protocol commands the sequential transformation **A**+**B**+**C** → **AB** + **C** → **ABC**, which evolves stepwise along the switching states OFF1 → ON1 (click reaction: **A**+**B** → **AB**) → OFF2 → ON2 (Michael addition: **AB** + **C** → **ABC**) → OFF1. Two consecutive cycles were realized without loss in activity in the two-step sequential catalysis requiring the supreme orthogonality of eleven components.

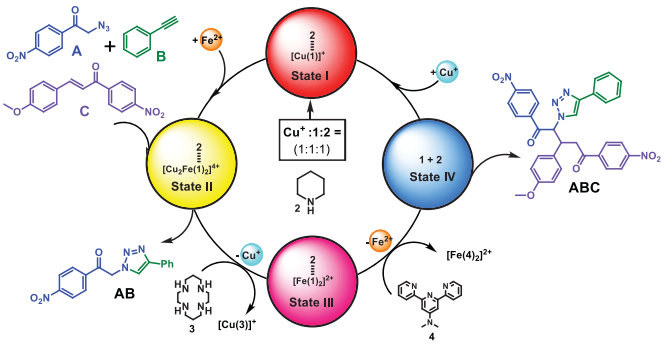

Figure **1**. Schematic representation of the switching cycle of nanoswitch **1** with the catalytic transformation of **A**+**B**+**C** → **AB** + **C** → **ABC** occurring stepwise in states II and IV.

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Asymmetric Lewis acid organocatalysis of the Diels – Alder reaction by a silylated C – H acid

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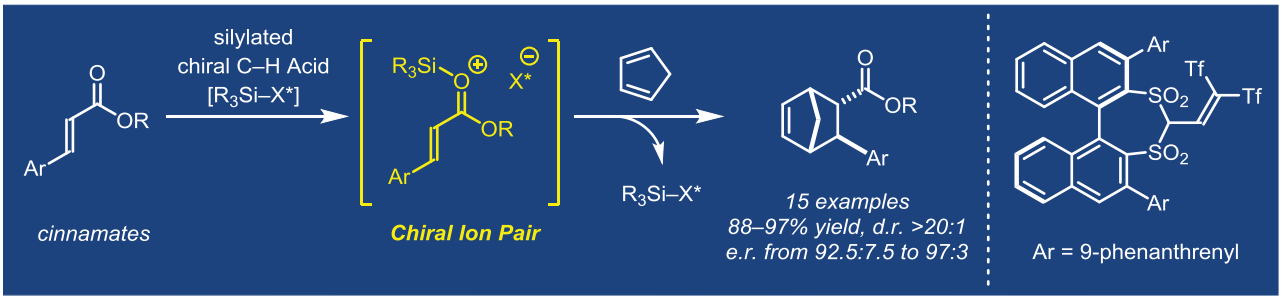
Silylium ions have shown promise as Lewis acid catalysts for a range of important C–C bond forming reactions. While conventional chiral Lewis acids typically consist of a metal(loid) complex with chiral ligands or substituents, we previously demonstrated that achiral silylium ions can be combined with chiral anions to achieve asymmetric transformations. Here we describe novel chiral C–H acid catalysts that upon in situ silylation generate silylium ion equivalent – carbanion pairs, which are extremely active Lewis acid catalysts for enantioselective Diels–Alder reactions of cinnamates with cyclopentadiene. Enantiomeric ratios of up to 97:3 and diastereomeric ratios of more than 20:1 are observed across a diverse set of substitution patterns with 1 mol% of C–H acid catalyst and 10 mol% of a silicon reagent. Mechanistic studies indicate the involvement of ionic species and a catalytic cycle based on the concept of asymmetric counteranion-directed catalysis (ACDC). The results bode well for broad applications of this silyl ion pair motif in asymmetric Lewis acid catalysis.



Literature:
T. Gatzenmeier,[+] M. van Gemmeren,[+] Y. Xie, D. Höfler, M. Leutzsch, B. List, Science 2016, 351, 6276, 949-952 ([+] = equal contribution)

Glowing Chemistry: Fluorescent Labeling of *E. coli* and Surface Exposed Proteins

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The tracking and analysis of gram negative bacteria, like *E. coli,* using fluorescence microscopy or flow cytometry is possible due to fluorescent dyes and fluorescently-labeled proteins. In this work, three different methods for successful labeling of *E. coli* are presented. In the first, *E. coli* cells were stained with carboxyfluorescein succinimidyl ester (CFSE). CFSE is a cell-permeable fluorescein derivate, which is cleaved by esterases after entering living cells. Subsequently, it starts to emit light and forms covalent bonds with intracellular proteins [1]. This staining technique can be applied for other bacteria and for eukaryotic cells as well.

In the second method, binding domain four of the low-density lipoprotein receptor-related protein 1 (LRP1-IV) [2] was surface displayed on *E. coli* cells via Autodisplay [3] and labeled with fluorescein-5-maleimide (FM). For this purpose “Cystope tagging” [4] was used, by which the reduced cysteine residues of the LRP1-IV coupled covalently via Michael addition to the FM double bond. Because natural *E. coli* outer membrane proteins do not contain accessible cysteines, “Cystope tagging” can be used to certify the surface exposure of any recombinant protein, if it contains at least one accessible cysteine.

The third method exploited the affinity of apolipoprotein E3 (ApoE3) to surface exposed LRP1-IV. ApoE3 was coupled to FM before binding (ApoE3-FM). Compared to control cells without receptor, cells displaying LRP1-IV showed a highly increased fluorescence, due to ApoE3-FM binding. These three simple methods, based on one-pot chemical reactions, enable the fluorescent labeling of *E. coli* and recombinant proteins on its surface.

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Synthesis of amphiphilic tetrylenes

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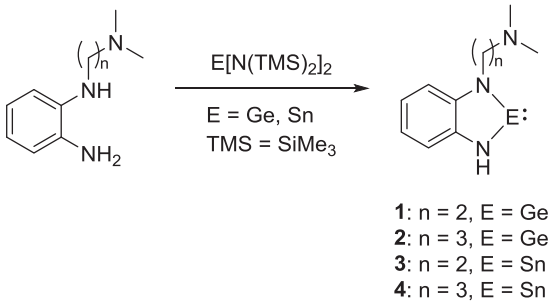
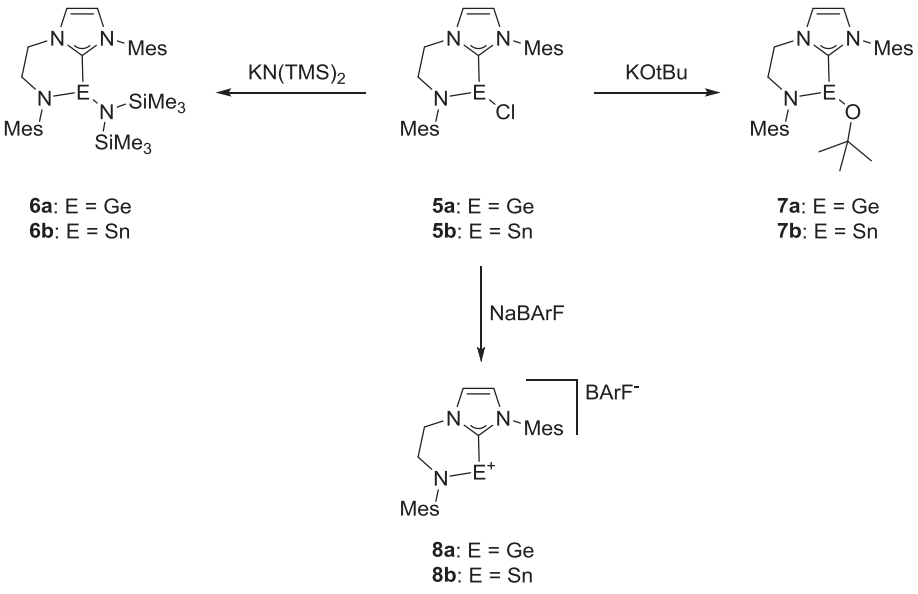
The heavier analogues of N-heterocyclic carbenes (NHCs), N-heterocyclic tetrylenes (NHEs, E = Si, Ge, Sn, Pb), have been known for years[1] even before the first successful isolation of a stable free NHC by Arduengo[2]. However, tetrylenes gained less attention. Here we present the synthesis and characterization of N-donor functionalized protic NHEs **1**–**4** (Scheme 1).



Scheme 1: Synthesis of protic NHEs **1**–**4**.

In addition, NHC-stabilized tetrylenes **5a** and **5b** have been synthesized and the anion exchange has been studied by NMR experiments (Scheme 2).



Scheme 2: Anion exchange of NHC-stabilized germylenes and stannylenes.

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On-Surface Domino Reactions: Glaser Coupling and Dehydrogenative Coupling of a Biscarboxylic Acid to Form Polymeric Bisacylperoxide

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Playing domino on gold! We present on-surface dehydrogenative coupling of the carboxylic acid functionality in 6,6′-(1,4-buta-1,3-diynyl)-bis(2-naphthoic acid) (BDNA) on two different gold surfaces, a reaction which is currently unknown in solution phase chemistry that offers a valuable extension to the "reaction toolbox" for on-surface synthesis.[1] By using this approach we were able to prepare linear bisacylperoxide connected polymer chains with a length of up to over 100 nm. This unprecedented on-surface reaction can be combined with a Glaser coupling step[2] representing the first on-surface domino reaction sequence. This allows the readily accessible 6-ethynyl-2-naphthoic acid (ENA) to be used as a starting material for polymerization. We have found that the Au-surface topography and the surface coverage influence the reaction outcome. Formation of the bisacylperoxide functionality was verified by comparing STM images and XPS data with those obtained for an *ex situ* synthesized reference bisacylperoxide compound.

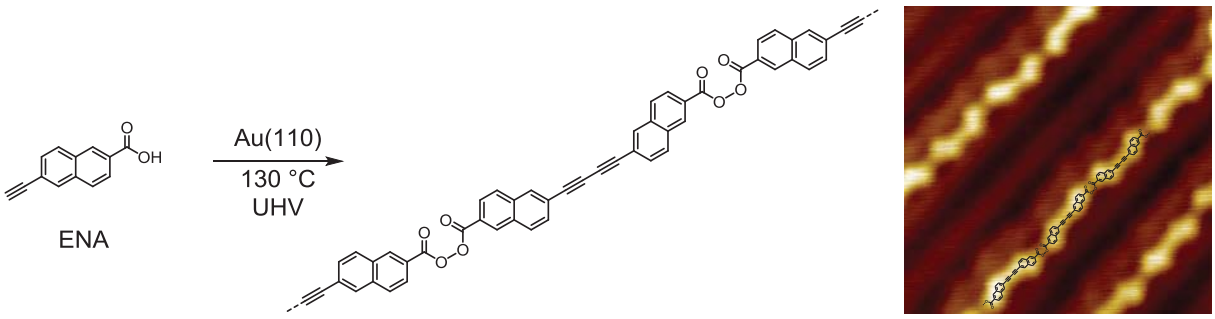

Figure 1: Polymeric bisacylperoxide formation via Glaser coupling and dehydrogenative coupling of a bis-carboxylic acid.

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Fluoroalkyl-substituted Diazoalkanes – Powerful Reagents for the Synthesis of Fluorinated Heterocycles

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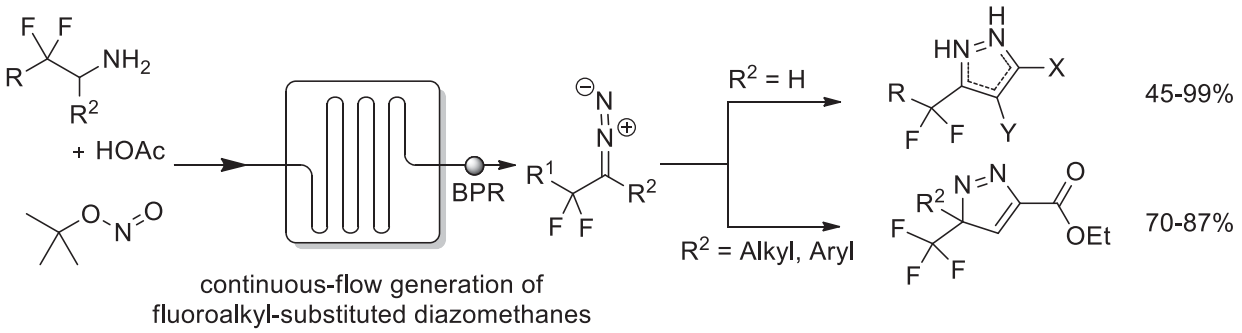
Fluoroalkyl-substituted pyrazoles and pyrazolines represent a versatile class of heterocycles and can be found in a range of different pharmaceuticals, e.g. COX inhibitors Celecoxib and Deracoxib contain fluoroalkylated pyrazoles as the central aromatic ring. The efficient synthesis of these heterocycles still represents a major challenge for organic chemists, typically the pyrazole ring is built up using hydrazine analogues.[1]

Small fluoroalkyl-substituted diazomethane analogues have long been neglected in organic synthesis. Recently, Carreira and co-workers and Mykhailiuk reported on the synthesis of fluoromethylated diazomethanes and their application in organic synthesis.[2]

Herein, we describe the utilization of simple and practical microreactors and their utilization in a general protocol for the synthesis of fluoroalkylated diazomethanes and their subsequent application in the synthesis of fluoroalkylated pyrazoles and pyrazolines. This protocol not only provides an easy-to-use and safe method for the preparation of novel fluoroalkyl-substituted diazomethanes but also allows an operationally simple access to versatile heterocycles.[3]



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Intermolecular Hydrogen Bonds Control Stereoselectivity in Allene-Enone (3+2) Annulations Catalyzed by a Bifunctional, Amino Acid Derived Phosphine Catalyst[1]

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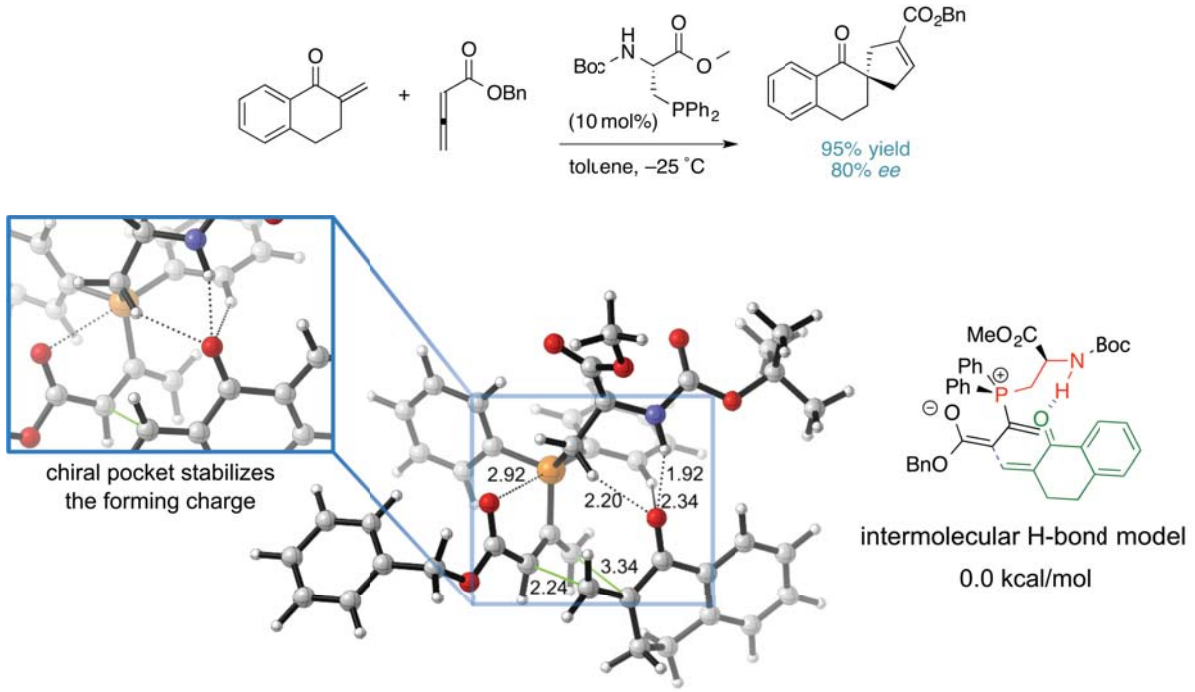
Results:

The seminal example of a (3+2) annulation reaction catalyzed by an amino acid derived phosphine catalyst reported by Miller[2] was studied using DFT calculations. Consistent with previous studies on the achiral variant of this reaction using PMe_3,[3] the first step of the reaction is the addition of the catalyst to the allenoate resulting in a zwitterionic intermediated. Subsequently, the zwitterion reacts with the enone by stepwise formation of the two C–C bonds. The first C–C bond formation is higher in energy than the second and is thus stereocontrolling. In the corresponding transition state, an intermolecular hydrogen bond was found to be key for facial selectivity. This intermolecular hydrogen bond activates the enone of the substrate and stabilizes the forming negative charge as the addition proceeds. The transition state leading to the minor product was found to be 3.0 kcal/mol higher in energy due to distortion into a more unfavorable conformation to allow for an optimal hydrogen bonding pattern. The transition state model for this important transformation will be helpful in the design of related reactions.



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Accelerated Discovery in Photocatalysis using a Mechanism-based Screening Method

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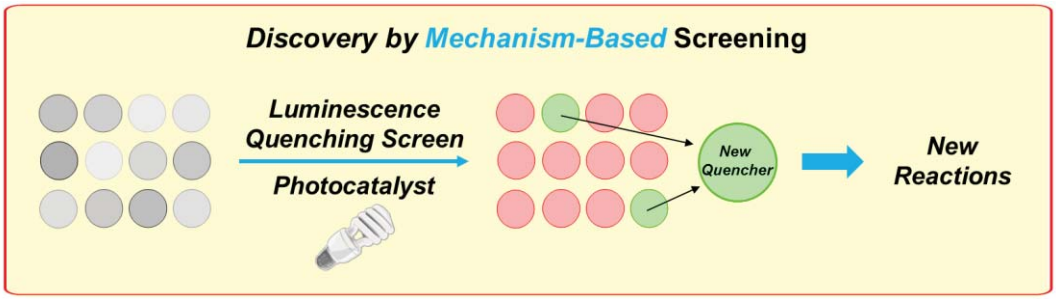
New chemical transformations often result from experimental serendipity. The discovery of these chance findings can be accelerated by using screening technologies, in which substrates, solvents or other conditions are systematically varied in a fast and efficient manner. Most screening approaches are "reaction-based" and look for the formation of an overall reaction product.[1] Treating chemical transformations as discrete entities in this way allows for the detection of complete working reactions but provides little insight as to why unsuccessful combinations failed. As an alternative screening concept, we have developed a "mechanism-based" method,[2] which instead focuses on a single key mechanistic step central to a general reaction class. This approach provides complementary information to that obtained through "reaction-based" screening and reveals catalyst and substrate combinations, which could be applied in a range of new transformations.



Using luminescence spectroscopy as a fast and simple method to investigate the key quenching step in photocatalysis,[3] 100 potential substrate compounds were tested with a representative iridium photocatalyst and two promising substrate classes, phenols and benzotriazoles, were discovered. In a more focused second screen involving the evaluation of different catalysts and substrate analogues, mechanistic insights were obtained, which aided the development of two light-promoted reactions involving the discovered quenchers.[4]

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Structure-Based Design of 3-(4-Aryl-1*H*-1,2,3-Triazol-1-yl)-Biphenyl Derivatives as $P2Y_{14}$ Receptor Antagonists

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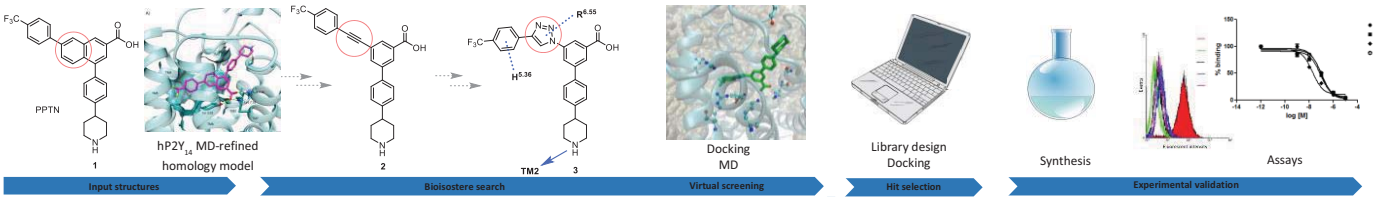

$P2Y_{14}$ receptor ($P2Y_{14}R$) is a G-protein-coupled receptor (GPCR),[1] that modulates cell functions related to inflammation,[2] diabetes,[3] and asthma.[4] Only a limited set of $P2Y_{14}R$ antagonists are currently known. A computational pipeline was set up to suggest alternatives to the naphthalene ring of the $P2Y_{14}R$ antagonist PPTN (**1**) by means of docking and molecular dynamics (MD) simulations on a human (h) $P2Y_{14}R$ homology model. Two non-naphthalene alternatives, *p*-F_3C-phenyl-acetylene (**2**) and *p*-F_3C-phenyl-triazole derivative (**3**) were prepared. Compound **3** was found to be more potent than the corresponding alkyne **2**. Thus, a library of additional triazole-based derivatives was designed. Compounds, predicted to be potential hits by virtual screening, were prepared and assayed in a convenient flow cytometric fluorescence competition assay in $P2Y_{14}R$-CHO cells.

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Nickel-Catalyzed Trifluoromethylthiolation of Aryl Chlorides: Fundamental Studies Revealing the Active Catalytic Species and the Key Roles of Ligand and Additive

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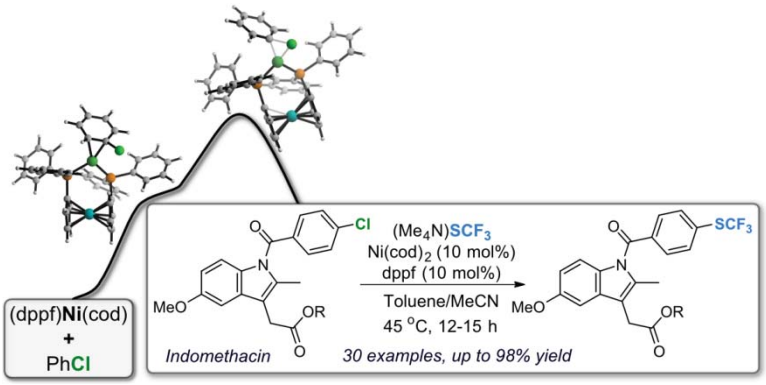
There is an increasing interest to develop efficient and sustainable catalytic processes. Catalytic processes based on nickel, which is frequently seen as a cheaper and less precious analog of palladium, is therefore of considerable current interst.[1] However, controlling the reactivity and selectivity in Ni catalysis is burdened by numerous challenges, such as multiple potential oxidation states, ligation states and reactive intermediates. A thorough fundamental mechanistic understanding might help in making progress towards improved catalysis and novel catalytic methodologies. This poster describes the combination of computational and experimental methods as an efficient way of gaining this knowledge.[2]

The first direct catalytic trifluoromethylthiolation of aryl chlorides will be presented as case study.[3,4] As a result, the importance of ligand properties and its implications on the active species of the catalyst, along with the role and beneficial effect of an additive and the characterization of key intermediates are highlighted. Ultimately the functionalization of a large variety of aromatic and heteroaromatic chlorides is achieved. Furthermore, this methodology is also shown to be applicable in the late-stage modification of active pharmaceutical ingredients.



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Selective C6-metalation of purine nucleobases *via* oxidative addition

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Purine nucleobases are essential building blocks of DNA and RNA, which provide important binding sites in nucleic acids. They are excellent ligands for metal ions and usually form Werner-type complexes using the N-donor atoms of the nucleobase skeleton. A detailed understanding of the coordination chemistry of purines is due to the important role of metal complexes in cancer therapy[1] currently the subject of intensive investigations. Most recently, the regioselective C-metalation of purines like caffeine and 9-methyladenine has been reported,[2] which is one of the rare examples of a C8-metalated purine nucleobase synthesized by oxidative addition.

Here we show that monochlorinated purines such as 6-chloro-9-methylpurine react with $[M(PPh_3)_4]$ (M = Pd^0, Pt^0) under oxidative addition of the C6–Cl bond to the metal center. This produces both the mononuclear purine metal complexes as well as dinuclear compounds (Figure 1, top).[3] In contrast, dichlorinated purines such as 2,6-dichloro-9-methylpurine selectively react at the C6–Cl bond, but no formation of the dinuclear purine metal complexes was observed (Figure 1, bottom).

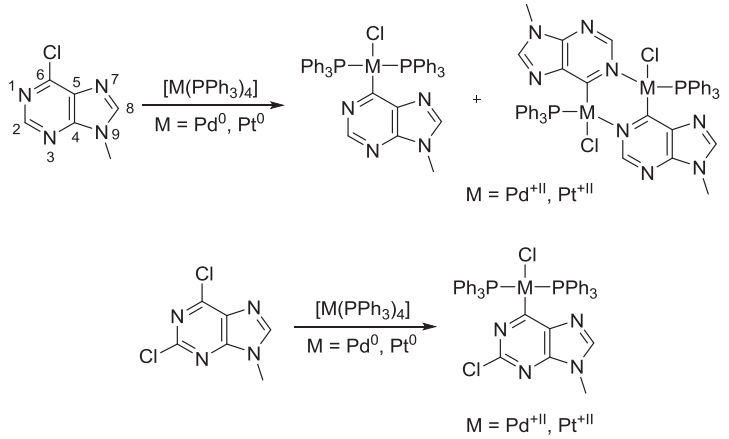

Figure 1: Synthesis of C6-metalated purine nucleobase complexes by oxidative addition.

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Title: Sequence-Specific Detection of RNA in Two Colors Using a Genetically Encodable System

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Abstract: The ability to detect several individual RNAs simultaneously is of high importance when analyzing RNA localization and involvement in different cellular processes. Most common multiplexing methods either make use of fluorescently labeled probes that necessitate transfection of cells, or they require prior tagging of the target-RNA.[1]

We expanded the tetramolecular fluorescence complementation (TetFC) system, which is based on the sequence-specific binding of two proteins to a target RNA, and subsequent complementation of the green fluorescent protein (GFP).[2] By introducing substitution T203Y into our reporter molecule,[3] we were able to detect and distinguish between two closely related RNAs, using green and yellow fluorescence signals.[4] Importantly, all molecules required for our systems could be produced by the cellular machinery, making it a promising tool for dual detection of endogenous RNAs *in vivo*.

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Cooperative Ligand Effect for High Molecular Weight Polymers in Suzuki-Polycondensation

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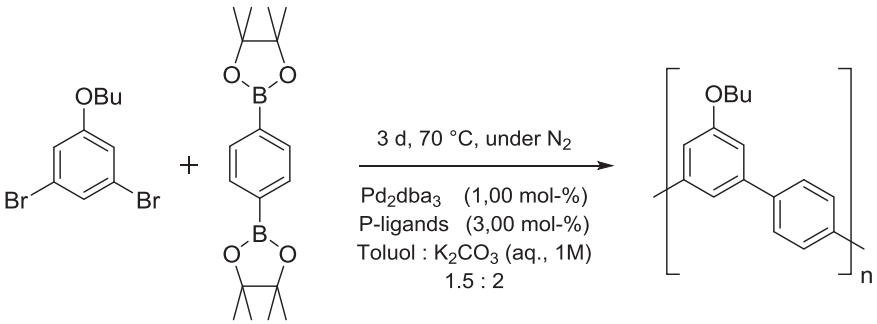
The combination of two different phosphine ligands resulted in a drastic increase of twice the molecular weight for *m,p*-polyphenylenes compared to single phosphine ligand catalysis. Careful analysis for the separate P-ligands showed that $^{t}Bu_2MeP$ produces overall low molecular weight polymers (≈ 30 000 g/mol), but always contains small fractions of high molecular weight (> 10^5 g/mol, ≈ 1 wt-%). In contrast, the Buchwald ligand S-Phos on its own produces medium molecular weights (≈ 60 000 g/mol) without any high molecular weight fractions.

We hypothesised that $^{t}Bu_2MeP$ on its own favours the formation of cyclic polymers over linear polymers, causing the reaction to terminate at an early stage due to the absence of functional groups on chain ends. In contrast, S-Phos seems to produce mainly linear polymers but is not reactive enough for high molecular weights > 10^5 g/mol. Therefore we concluded that the addition of minimal amounts of $^{t}Bu_2MeP$ to S-Phos (1 : 50) should allow for further polymerisation in the final stages once the S-Phos catalysis has slowed down. The data with combined $^{t}Bu_2MeP$ and S-Phos catalysis show precisely this cooperative ligand effect resulting in polymers with twice the peak molecular weight compared to the best single ligand reactions.



P-Ligand		M_p / g/mol
$^{t}Bu_2MeP \cdot HBF_4$		33 000
S-Phos		62 000
S-Phos + $^{t}Bu_2MeP \cdot HBF_4$	$\frac{50}{1}$	121 000

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Geometry Optimizations in a Subsystem DFT formalism - A Test of Two Independent Analytical Gradient Implementations

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Subsystem DFT (sDFT), a subsystem approach to density functional theory which uses Frozen Density Embedding (FDE), is an efficient alternative to Kohn-Sham density functional theory (KS-DFT) for complex chemical systems [1-4]. By partitioning the total electron density $\rho_{tot}(\boldsymbol{r})$ into a set of smaller subsystem densities, the ansatz introduces linear scaling with the number of subsystems. In an FDE calculation, instead of treating all subsystems on an equal footing, one subsystem is considered to be embedded in an effective environment potential. This embedding potential is used to describe its effects on the embedded systems' electronic structure. Self-consistency is achieved by successive interchange of active- and environment subsystems.

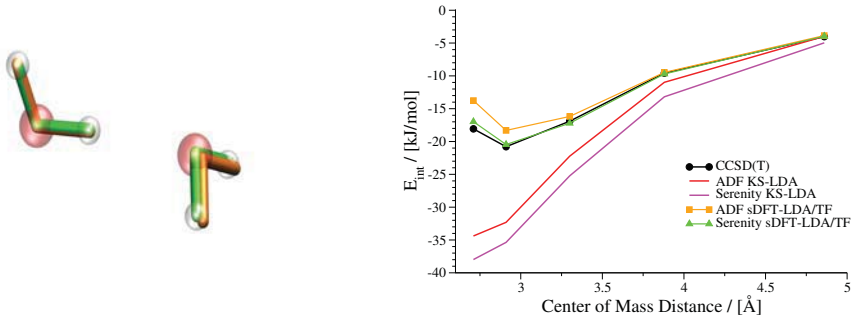

Fig 1: Comparison of an sDFT water dimer optimization in ADF (orange) in TZ2P basis and Serenity (green) in Def2-TZVPP with a CCSD(T)-CBS extrapolated Geometry.

Here, we are going to present an implementation of analytical sDFT gradients into our in-house Quantum Chemistry program Serenity as a prerequisite for a succesful implementation of a subsystem-based Molecular Dynamics scheme, as well as an independant implementation [5] in the Slater-Type-Orbital based professional Quantum Chemistry program ADF [6]. Numerical gradients and results of previously successful implementations of DFT gradients based on subsystem approaches [7-8] serve as a reference for testing the embedding gradients.

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Synthesis of DNA-pyrazoline conjugates by Au(I)-catalyzed A^3 multicomponent reaction

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The screening of large, pooled DNA-encoded small molecule libraries (DELs) is a validated technology for the target-based identification of bioactive compounds.[1] DELs consist of small organic molecules covalently coupled to DNA sequences serving as PCR-amplifiable identification bar codes. DELs are synthesized by iterative, combinatorial organic synthesis and encoding steps. Therefore, DNA-compatibility of reactions is prerequisite for library synthesis. Synthesis methodology meeting this requirement is very limited. Chief reason for the inaccessibility of many catalytic systems for DEL synthesis is the reactivity of the purine nucleotides: Purine nucleotides bind to many transition metal ions; they are easily oxidized; and they are depurinated under acidic conditions. We hypothesized that the use of oligopyrimidine-sequences as adapter oligonucleotides in the first step of DEL synthesis might broaden the spectrum of applicable catalysts in the initial step of DEL synthesis. Thus, we developed the "**TIDEC"** (oligo**T**hymidine **I**nitiated **D**NA-**E**ncoded **C**hemistry) strategy for DEL synthesis. TIDEC employs a solid phase-bound 5'-aminolinker-modified hexathymidine sequence as adapter oligonucleotide that tolerates a surprisingly broad spectrum of catalysts and reaction conditions.[2] Here, we demonstrate the applicability of Au(I) catalysis to furnish TIDEC-conjugates of highly substituted pyrazolines[3] from readily accessible starting materials. The TIDEC-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 yielding the TIDEC-pyrazoline **4**. The scope of the reaction was broad with respect to the aldehyde and the substitution of the benzylhydrazide. We were able to ligate coding DNA sequences to TIDEC-pyrazoline conjugates. We are currently synthesizing DNA-encoded screening libraries based on the pyrazoline scaffold **4**.

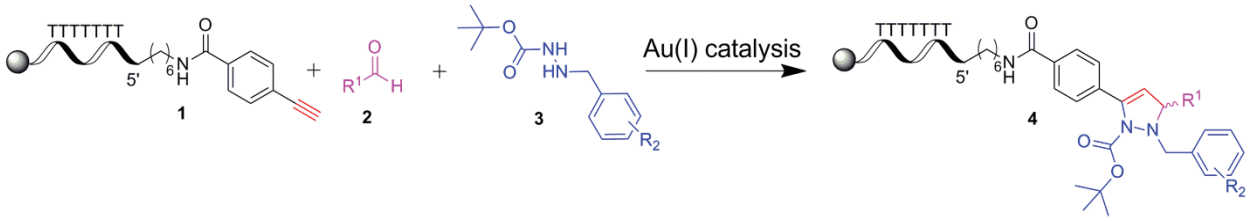

Fig. 1: Gold-catalyzed A^3 multicomponent reaction to synthesize hexa-T oligonucleotide-pyrazoline conjugates.

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Synthesis of Cryptochiral Allenes

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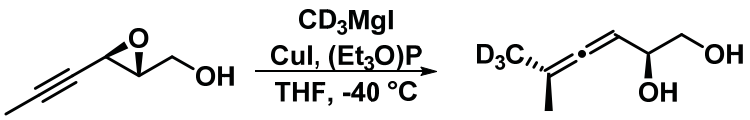
The use of organometallic reagents for the synthesis of allenes is highly developed, and several fundamentally different methods are now well established. Copper enjoys a rich history in organometallic chemistry and plays an important role in organic synthesis.[1]

The S_N2'-substitution of propargylic electrophiles with organometallic reagents is one of the most efficient method for the stereoselective synthesis of allenes. The transformation of propargyl oxiranes with organocopper compounds, which are the nucleophiles of choice, give allenes with high *anti*-stereoselectivity.[2] Likewise, an *anti*-selective S_N2'-reduction of propargyl oxiranes using an NHC-stabilized copper hydride catalyst has been developed.[3]

Based on these results, we report the first synthesis cryptochiral allenes. Cryptochiral compounds arising from the replacement of hydrogen atoms by deuterium are of interest in organic chemistry and biochemistry. These chiral compounds have a non-measurable optical rotation.[4] We used deuterated magnesium cuprates, which are formed *in situ* form a Grignard reagent and copper(I) salt in present of triethylphosphite, for the *anti*-selective S_N2'-substitution of enantiomerically enriched propargyl oxiranes (Scheme 1).



Scheme 1: Synthesis of a cryptochiral allene by S_N2'-substitution.

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Structure and dynamics of SUMO chains

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Many cellular processes are regulated by posttranlational protein modifications. In the SUMOylation process SUMO (small ubiquitin-related modifier) is linked *via* an isopeptide bond involving a lysine residue side chain of the target protein and its own carboxy terminus. SUMO regulates many cellular processes, including transcription, DNA repair, signal transduction and cell-cycle control.[1] 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.[2] Proteins with multiple SIMs like RNF4 (RING finger protein 4) have a high affinity towards SUMO chains.[3] The study of protein-protein interactions is quite challenging, this is due to the weak, mostly non-covalent binding.
Our current aim is to find out more about structure and dynamics of SUMO chains and their interaction with different binding partners. Therefore we developed a linear SUMO dimer which is labeled with two organic dyes using bioorthogonal reactions. By employing FRET (Förster-resonance energy transfer) we are investigating the influence of interaction partners on the conformation of the SUMO dimer.

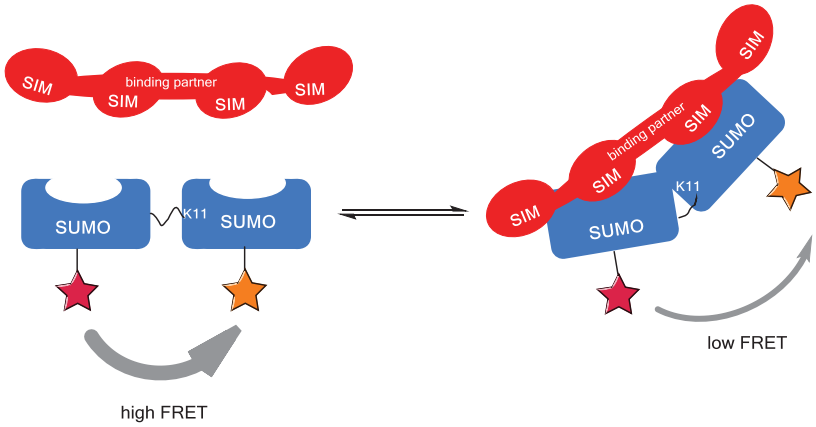

Figure 1: Investigation of conformational dynamics of the SUMO dimer using FRET.

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MS_CEC 2016 Poster – Luca Legnani

- Title of the poster: ***Direct Catalytic Synthesis of Unprotected Amino Alcohols from Alkenes Using Iron(II) Phthalocyanine***

- Full given and surnames of all contributors: *Luca Legnani (presenting author), Bill Morandi**

- Full address of your institution: *Max-Planck-Institut für Kohlenforschung - Kaiser-Wilhelm-Platz 1 - D-45470 Mülheim an der Ruhr*

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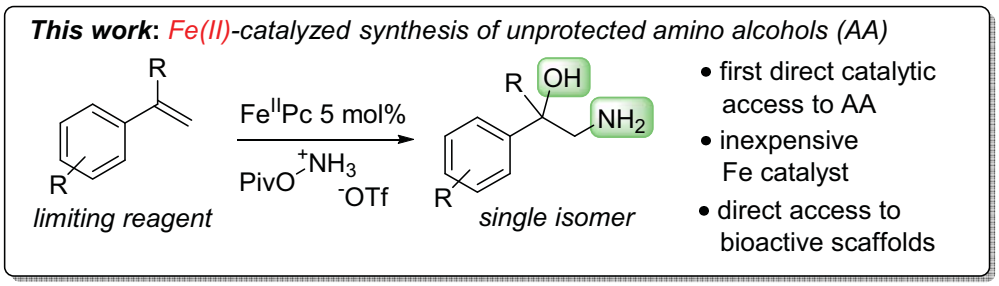
- The abstract paragraph: *Aryl-substituted amino alcohols are privileged scaffolds in medicinal chemistry and natural products. Herein, we report that an exceptionally simple and inexpensive Fe(II)-complex can efficiently catalyze the direct transformation of simple alkenes into unprotected amino alcohols in good yield and perfect regioselectivity. This new catalytic method was applied in the expedient synthesis of bioactive molecules and could be extended to aminoetherification.*

- Scheme for illustration:



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Selective Recognition of a Pyrimidine Nucleobase using 6-Pyrazolylpurine as an Artificial Nucleobase

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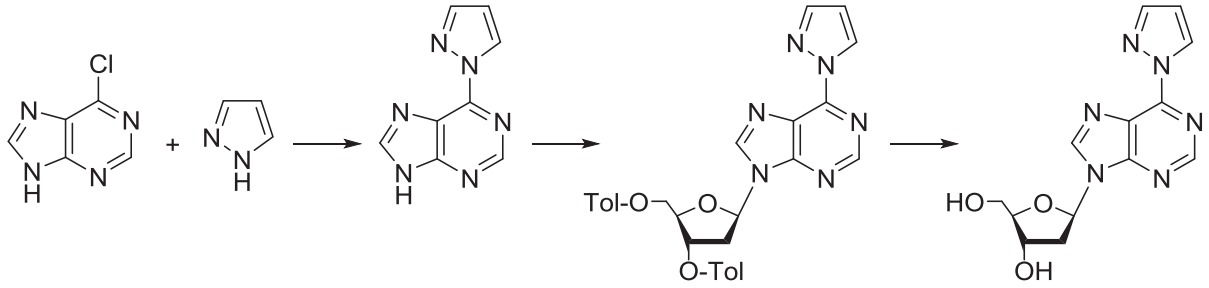
Nucleic acids are increasingly being used as building blocks in nanotechnology, owing to their superb and highly predictable self-assembly, their stiffness, and the ease of their modification.[1] The artificial nucleobase 6-pyrazol-1-yl-purine (6PP) has been investigated with respect to its applicability in metal-mediated base pairing. As was shown by temperature-dependent UV spectroscopy, 6PP may form weakly stabilizing 6PP–Ag(I)–6PP homo base pairs. Interestingly, 6PP can be used to selectively recognize a complementary pyrimidine nucleobase. The addition of Ag(I) to a DNA duplex comprising a central 6PP:C mispair (C = cytosine) leads to a slight destabilization of the duplex. In contrast, a stabilizing 6PP–Ag(I)–T base pair is formed with a complementary thymine (T) residue. In order to exclude conformational changes within the duplexes CD, spectroscopy was used.[2]



Acknowledgments
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Orthogonal Photoswitching in a Multifunctional Molecular System

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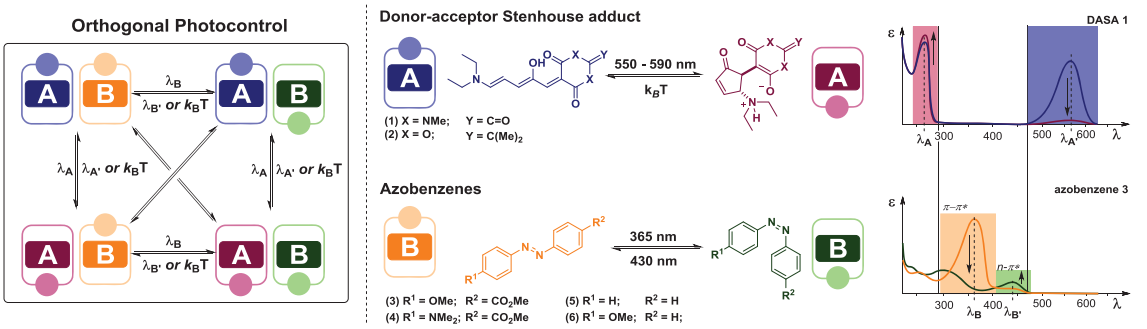
Selective and reversible control is crucial for the successful application of photochemical tools in complex systems. We present the development of wavelength orthogonal control of two independent photoswitches[1] in the same solution based on rational, spectrum-guided design. The reported intermolecular system is highly robust and modular. Its basis is set through the photochromic compatibility of two different classes of molecular photoswitches: a donor-acceptor Stenhouse adduct (DASA)[2] and an azobenzene. Both classes of photoswitches can be reversibly and independently addressed in parallel. Differently functionalized photoswitches are tolerated, which allows for spectral fine-tuning and convenient incorporation into functional systems. Recent non-orthogonal applications of independent switches in the same solution highlight the general potential of this approach.[3;4] Further, more complex applications would be enabled by a more thorough understanding of the DASA photoswitching mechanism and therewith a toolbox for tuning photoswitch properties.



KEYWORDS: photochromism; orthogonality; photoswitches

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Harvesting Ortho-Quinone Methides as Latent Intermediates for Asymmetric Brønsted Acid Catalyzed Reactions

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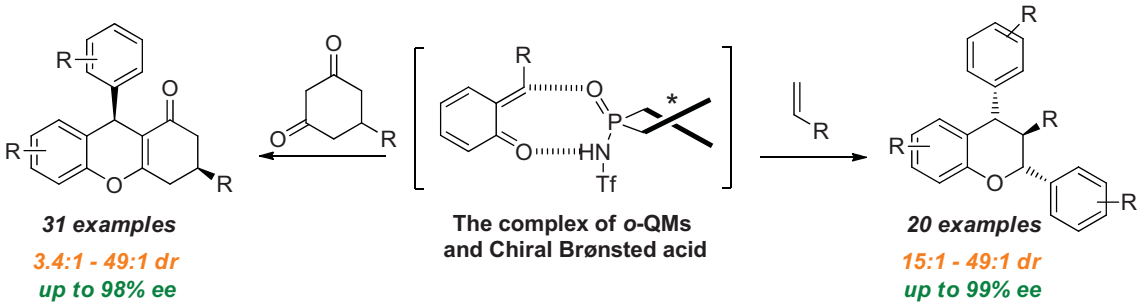
The development of simplified and atom economic strategies for rapid access to complex enantiomerically enriched structural motifs featured in natural products is one of the main tasks in synthetic chemistry. For example, chromane and chromene frameworks are intriguing core structure widely present in many fascinating natural products with remarkable biological and pharmacological properties.[1] However, efficient ways to access these frameworks in an straightforward and enantioselective fashion are still rare.

ortho-Quinone methides (*o*-QMs) are highly reactive, transient intermediates which are used in the synthesis of natural products and bioactive compounds.[2] Although *o*-QMs are a class of useful intermediates that has attracted the attention of organic chemists, the transient nature of *o*-QMs leads to difficulties in asymmetric synthesis applications. Nevertheless, with the recent development of organocatalysis, highly reactive *o*-QMs have successfully been applied in metal free enantioselective reactions. Here, we developed an efficient protocol for the highly enantioselective synthesis of chiral chromanes and chromenes bearing multiple stereogenic centers. A chiral BINOL-based N-triflylphosphoramide proved to be an effective catalyst[3] for the in situ generation of ortho-quinone methides (o-QMs) and their subsequent cycloaddition reaction with unactivated alkenes or activated 1,3-cyclohexanedione provided chromans or chromenes with excellent diastereo- and enantioselectivities.[4]



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Confined Acid-Catalyzed Asymmetric Carbonyl–Ene Cyclization

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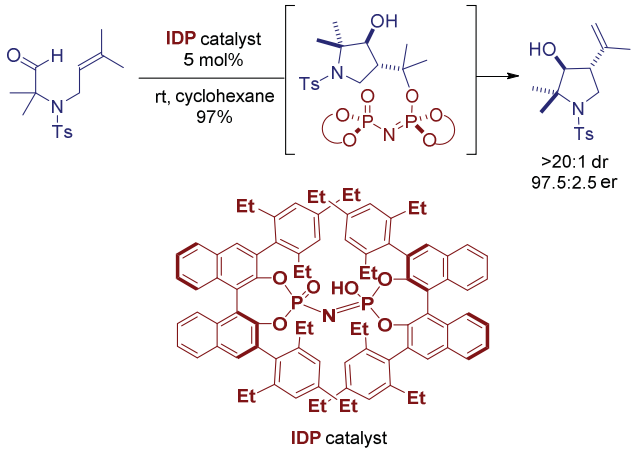
A highly enantioselective confined chiral Brønsted acid C_2-symmetric imidodiphosphates catalyzed intramolecular carbonyl-ene reaction of olefinic aldehydes has been developed. Using a confined imidodiphosphate catalyst, the reaction delivers diverse *trans*-3,4-disubstituted carbocyclic and heterocyclic five-membered rings in high yields and with good to excellent diastereoselectivities and enantioselectivities. ESI-MS, NMR, and DFT mechanistic studies reveal that the reaction proceeds via a stepwise pathway involving a novel covalent intermediate.



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Encapsulation of Neutral Guest Molecules by Interpenetrated Coordination Cages

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Supramolecular coordination cages have become a popular research area, due to their versatile usage. The cavity of self-assembled cages can serve as container for guest molecules or as environment for catalytic reactions similar to enzymatic processes. Interpenetrated double cages are of special interest, because they offer three mechanically coupled cavities, which are able to incorporate anionic guest molecules.[1]

In this poster we will present the formation of an interpenetrated double cage based on a new acridone derives ligand, which is capable of allosteric anion binding in their outer two pockets. Surprisingly, halide binding enables the double cage to encapsulate neutral guest molecules, such as benzene or norbornadien in its central pocket.[2]

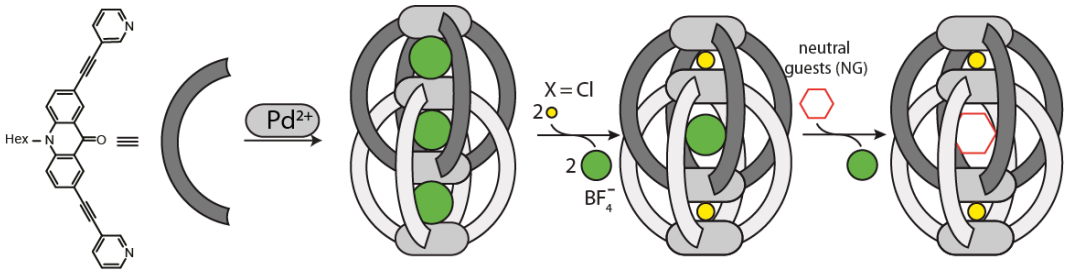

Fig 1. Schematic representation of the halide binding in the outer pockets of the double cage that triggers the uptake of neutral guest molecule in the central pocket.

We furthermore will show that the introduction of a bulky adamantyl group to this acridone ligand prevents dimerization and results in the clean formation of a monomeric cage [Pd_2L_4]. The ligand shows a flipping dynamic between two energetically degenerated conformers in the free ligand and astonishingly in the cage.[3]

Currently, we are studying the application of those systems in the context of double-input receptors, molecular logic gates and switchable catalysis inside confined cavities.

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Metal Free C-H Bond Functionalization: A Novel Method for Synthesis of Heterocycles

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Metal free C-H bond functionalization has emerged over the last few decades and represents as an attractive method to the diverse range of synthetically useful transformation to the natural products and biologically active compounds. However, nitrogen containing heterocycles are ubiquitous in nature and widely applicable in biological studies. Interestingly, isoquinolones and benzimidazole represent important scaffolds in many natural products and drug. Several attractive synthetic routes to isoquinolones and benzimidazole have been developed using transition-metal-catalyzed [1]. However, economical and environmental aspect, synthesis of biologically important heterocycles via metal free method is highly demanding. We have developed completely new approach to the synthesis of heterocycles under simple organocatalyzed[2] and mild metal-free conditions[3]. Simple method offers a novel straightforward approach for the synthesis of isoquinolones and benzimidazole at ambient temperature and mild reaction conditions.

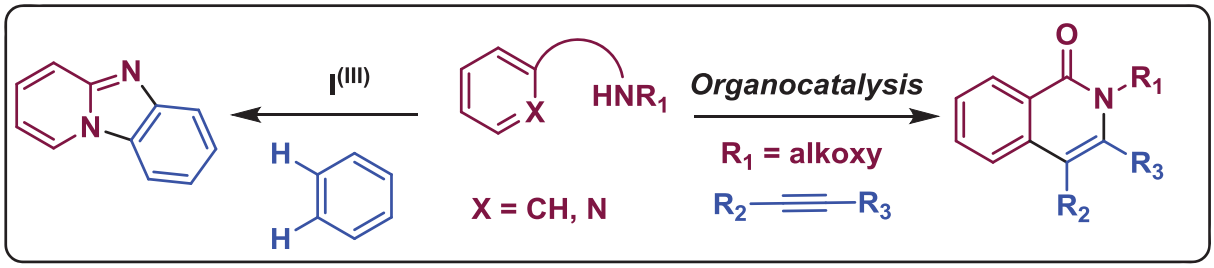

Figure 1. Metal free heterocycles synthesis.

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Rational Use of Aromatic Solvents for Direct Arylation Polycondensation: C-H Reactivity versus Solvent Quality

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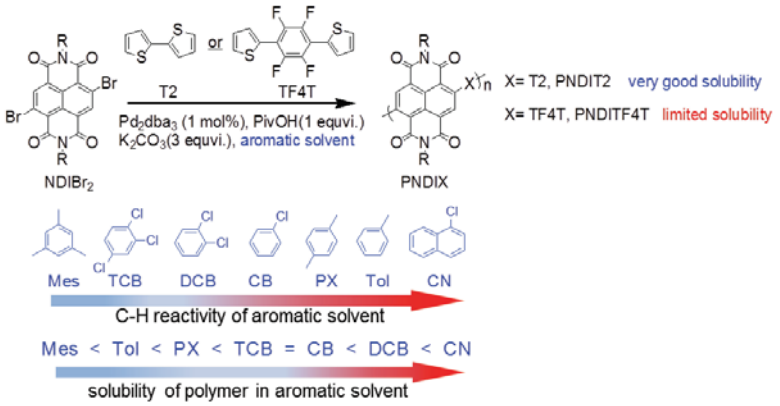
The solvent is an important parameter for organic reactions. In direct arylation polycondensation (DAP), dimethylacetamide is often used albeit being not a particularly good solvent for conjugated polymers.[1] Especially for conjugated polymers exhibiting reduced solubility, the choice of solvent decides on the maximum molecular weight that can be achieved, hence good aromatic solvents are generally desirable. However, the C-H bonds of aromatic solvents can in principle react under DAP condition as well, leading to in-situ solvent end-capping which either limits or controls molecular weight.[2] Thus, characterizing aromatic solvents with respect to their dissolving capabilities and C-H reactivities is central to the development of optimized DAP protocols allowing for the preparation of well-defined copolymers with both controlled and high molecular weight. Here, we evaluate C-H reactivity and solvent quality of seven aromatic solvents for the DAP of high electron mobility defect-free naphthalene diimide (NDI)-based polymers of different solubility, namely PNDIT2 and PNDITF4T.[3] C-H reactivity of aromatic solvents is strongly reduced with increasing degree of substitution for both methyl and chlorine substituents. For NDI copolymers with good solubility (PNDIT2), C-H reactivity of the solvent mostly controls molar mass by in-situ end-capping, whereby lower C-H reactivities generally result in higher molar masses. The situation is different for NDI copolymers with limited solubility (PNDITF4T). Here solvent quality is more important than its C-H reactivity to maximize molar mass.



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Imidazolin-2-ylidenaminophosphines: highly electron-rich phosphines with an additional basic site

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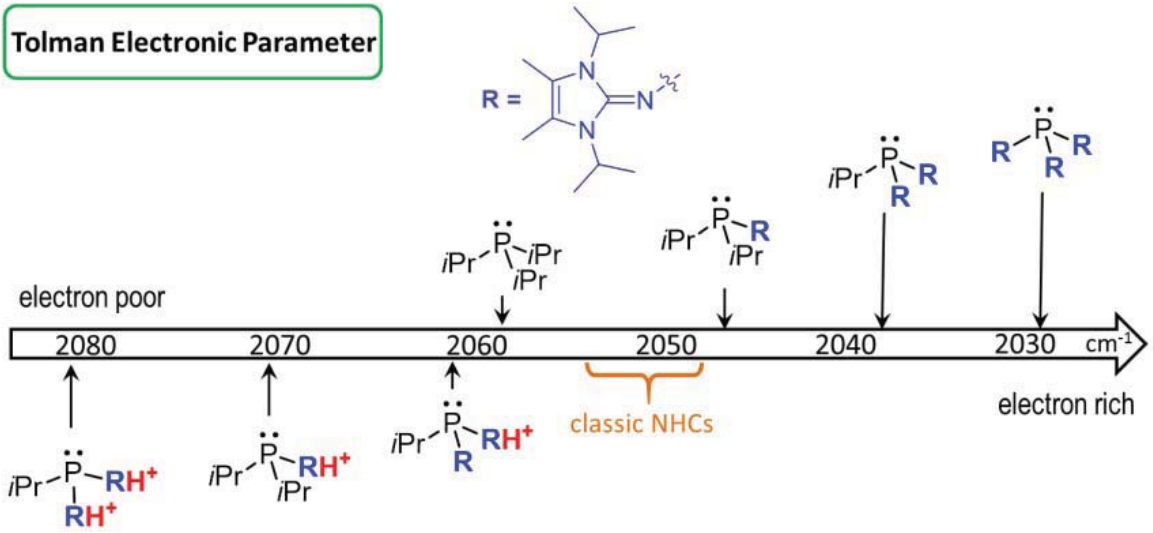
Phosphine ligands (PR_3) are widely used in transition metal-catalyzed reactions. One of their many attractive features is the fact that their steric and electronic properties can be easily adjusted in a predictable manner by variation of the R substituents. As a consequence, their application as ancillary ligands in catalysis has led to major breakthroughs in many fields of academic and industrial research. Specifically, strong electron-donating alkylphosphines are the ligands of choice when electron-rich metal centers are required. As part of our program to enhance the donor strength of phosphines we report a new approach to highly electron-rich phosphines based on the use of imidazolin-2-ylidenamino groups directly attached to the phosphorus atom.[1] These imidazolin-2-ylidenaminophosphines (IAPs) depict excellent donor abilities, which exceed that of N-heterocyclic carbenes.

An excellent performance of the ligands was observed in the palladium-catalyzed Suzuki-Miyaura cross-coupling reaction of non-activated aryl chlorides. Furthermore, protonation experiments of the basic imino-N atoms of IAPs resulted in remarkable changes of their donor strength and demonstrate their potential as cooperative ligands for bifunctional substrate activation strategies.



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Preparation of heteronuclear metal complexes

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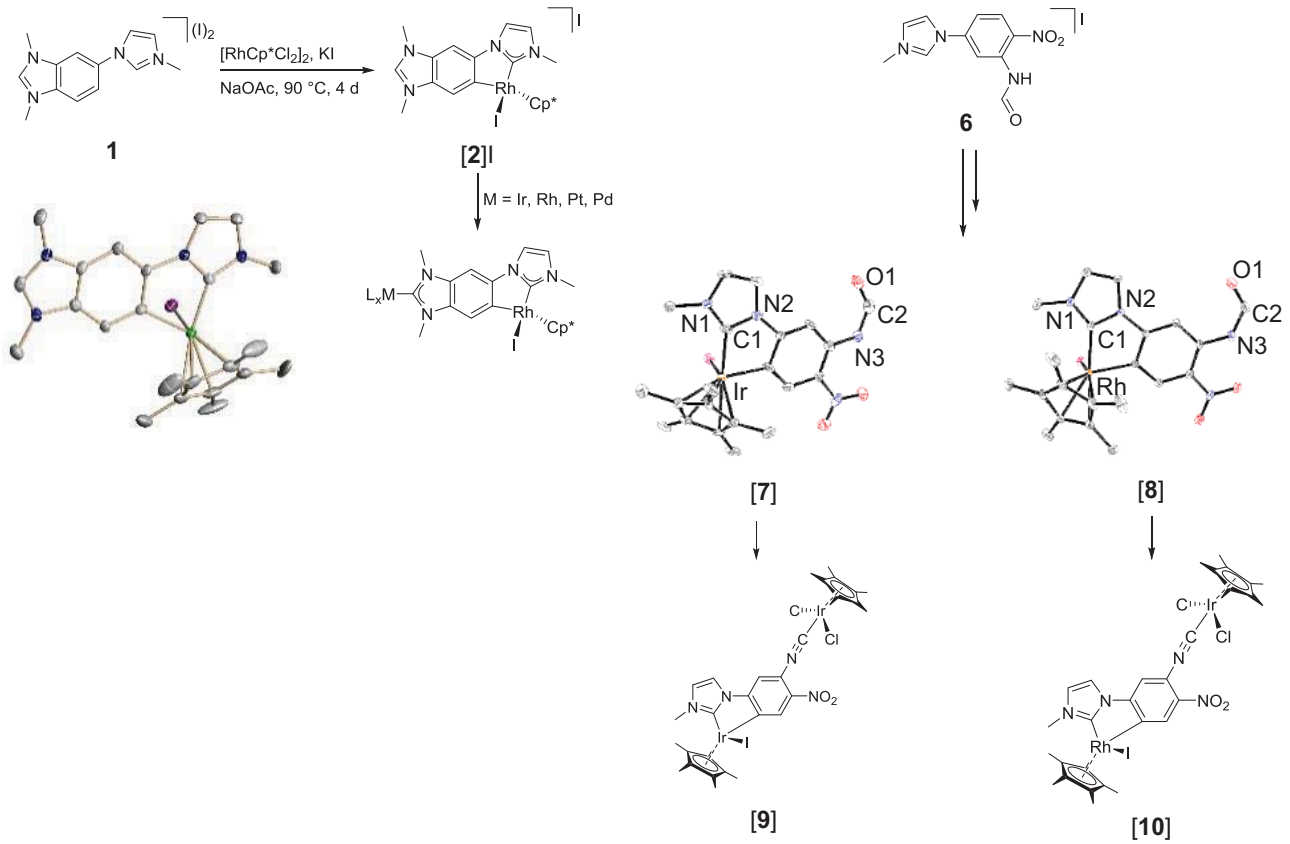
The interest in heteronuclear metal complexes has been increasing in the last few years due to their novel approach in tandem catalysis.[1] The possibility of placing two metal ions in a certain distance in one complex molecule allows the investigation of new cooperative effects. Most heteronuclear complexes are generated by the sequential metallation of polyazolium salts.[2] The introduction of other metal atoms is enabled by a different acidity of the azolium salts (bis(azolium salt) **1**). The application of *β*-functionalized isocyanides constitutes an innovative idea in the preparation of polynuclear metal complexes. Heteronuclear metal complexes can be synthesized by a stepwise deprotonation and metalation of **1** or by the combination of a *β*-functionalized isocyanide and an azolium unit for the selective introduction of metal complex fragments to the ligand precursors (see **6**, Scheme 1).



Scheme 1: Synthesis of heteronuclear metal complexes featuring an unsymmetrical bis-NHC ligand or by the coordination chemistry of isocyano / azolium ligand precursors.

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One Photocatalyst, *n* Activation Modes Strategy for Cascade Catalysis: Emulating Coumarin Biosynthesis with (–)-Riboflavin[1]

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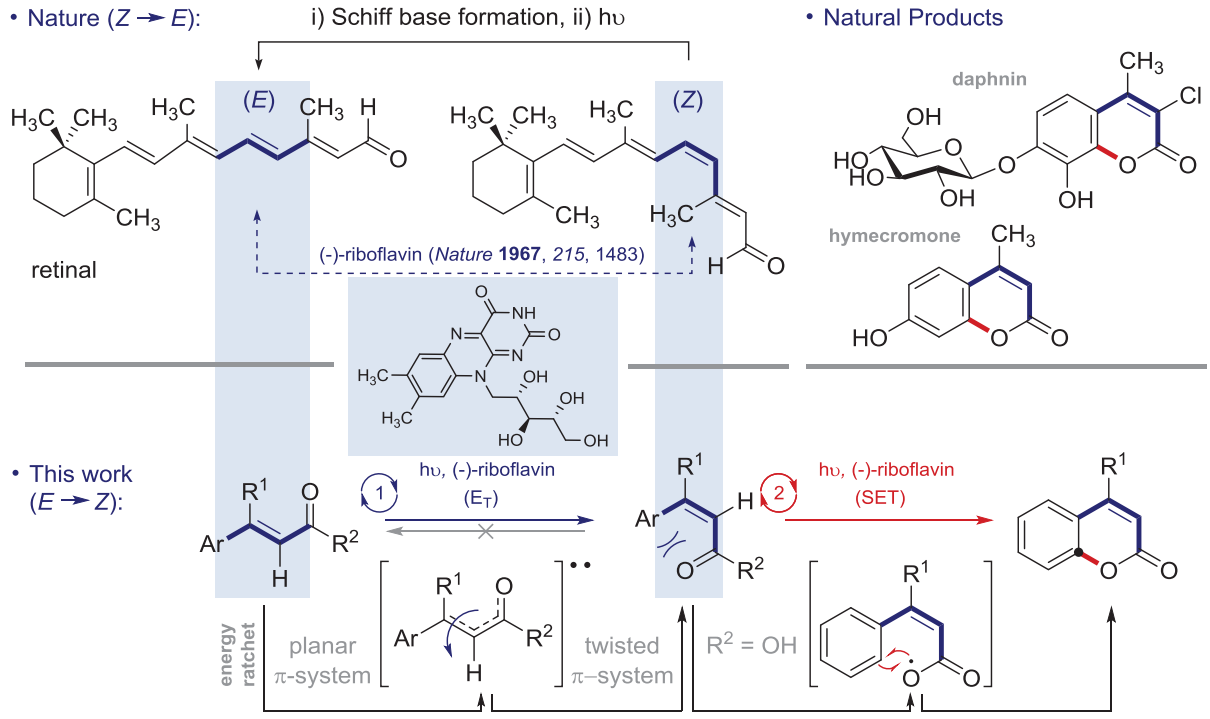
The bio-inspired *E*→*Z* isomerization and photo-cascade cyclization of activated olefins catalyzed by (–)-riboflavin will be presented.[1] In an effort to extend the scope of photosensitized isomerization and employ cheap, commercially available organic photosensitizers,[2] Nature's photochemical (*Z*→*E*) isomerization of retinal was taken as a blueprint for reaction design.[3] The transformation is generally applicable to substrates in which the cinnamaldehyde motif is embedded including differentially substituted esters, ketones, Weinreb amides and carboxylic acids. In this latter case, the method can be extended to directly generate substituted coumarins. By harnessing the two discrete photochemical activation modes (–)-riboflavin, it is possible to sequentially induce isomerization and cyclization by energy transfer and SET activation pathways, respectively. This catalytic approach mimics the photochemical isomerization in the biosynthesis of these important compounds[5] and demonstrates the synthetic utility of (–)-riboflavin as a cheap, commercially available photocatalyst for organic synthesis.



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Multivalent Recognition on Membrane-Surfaces by Synthetic Receptors

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In biology, many recognition processes take place on cell surfaces. In order to understand and manipulate these phenomena it is crucial to develop synthetic model systems. In the past we established vesicles of amphilic cyclodextrins (CDV) as a versatile tool to study recognition processes on the membrane surface.[1,2] We now designed a supramolecular system based on these vesicles of amphililic cyclodextrins, a functional guest and multivalent receptors with a defined amount of binding sites to investigate the kinetics of multivalent recognition on membrane surfaces (Figure 1).

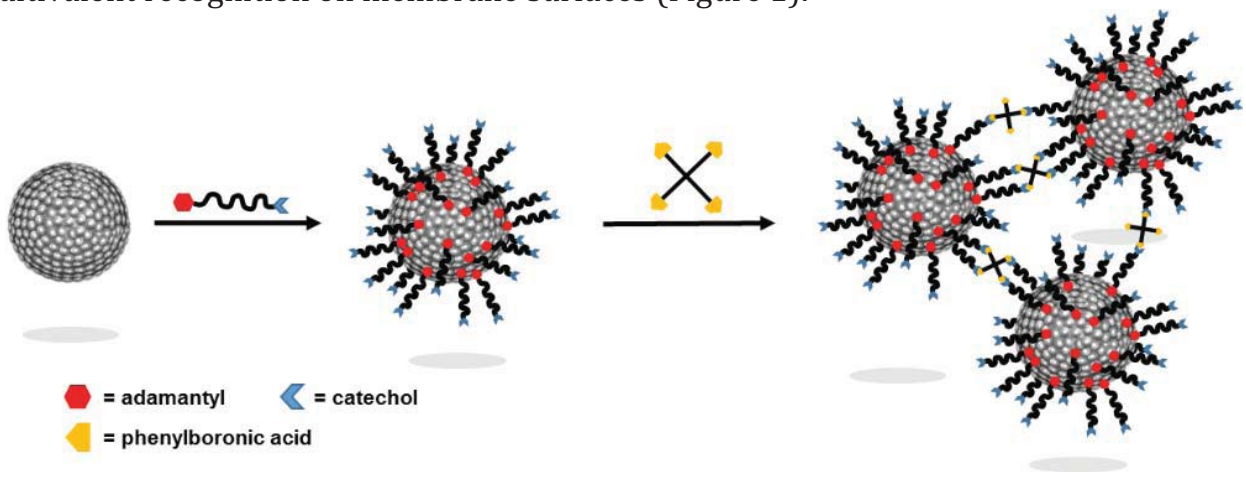

Figure 1: Multivalent complexation of CDV, linker molecules and phenylboronic acid based multivalent receptors.

In addition, we applied the functionalization of liposomes via covalent, dynamic hydrazone-chemistry to decorate liposomes with carbohydrate and catechol derivatives, creating a model glycocalyx.
Future focus will lie on exploring these systems capacity to simulate dynamic recognition processes on membranes by multivalent receptors and to investigate the kinetics of these interactions.

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C–H Alkenylations with Alkenyl Acetates, Phosphates, Carbonates and Carbamates by Versatile Cobalt Catalysis at 23 °C

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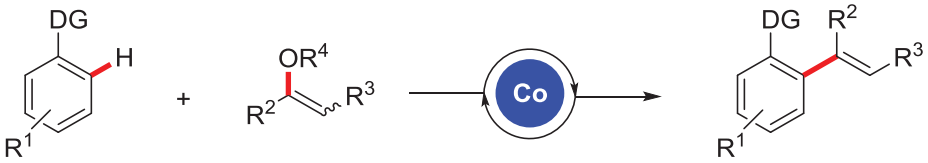
Cobalt-catalyzed C–H activation represents a powerful tool for the sustainable synthesis of biologically active compounds and functional materials,[1] which were as of yet mostly achieved by the use of more expensive second row transition metal-complexes. In recent years, considerable success has been accomplished with the development of C–H arylations, alkylations and benzylations with organic electrophiles by low-valent cobalt catalysis.[2] As of yet, cobalt-catalyzed olefinations were solely accomplished by hydroarylations of alkynes.[3] Despite significant advances, this method faces considerable limitations, including the restriction to the synthesis of acyclic alkenes.

Herein, we present a cobalt-catalyzed C–H olefination with easily accessible enol derivatives.[4] Notable features of our isohypsic strategy are nor limitied to a predictable regio-control, challenging C–H/C–O functionalizations with unactivated alkenyl acetates, phosphates, carbonates, and carbamates in a stereo-convergent fashion, as well as oxidant-free olefinations under remarkably mild conditions at 23 °C.



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A biocatalytic cascade reaction for versatile one-pot modification of RNA

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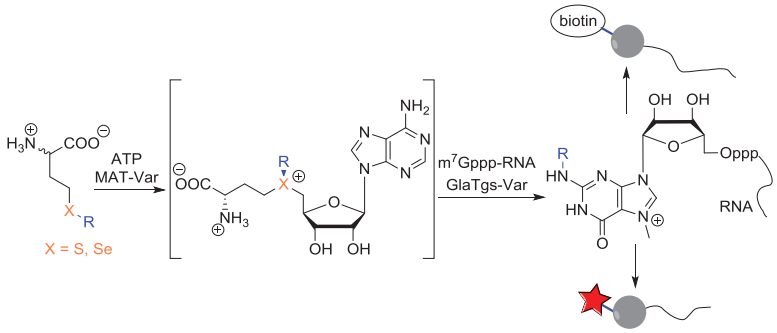
Labelling and visualization of mRNA becomes increasingly important for numerous applications in cell biology and biomedicine.[1] Chemo-enzymatic strategies are appealing for the modification of biological structures as they combine the specificity of enzymatic recognition and modification with the high selectivity of bioorthogonal chemistry.[2] While a small tag such as an alkyne or azide is first appended enzymatically to the molecule of interest, the subsequent bioorthogonal reaction allows for the insertion of a larger reporter molecule.

To date there is a lack of chemo-enzymatic strategies for the site- or sequence specific labelling of an mRNA molecule. Our group has recently reported on a chemo-enzymatic approach for the site-specific modification of the mRNA cap. The trimethylguanosine synthase GlaTgs from the protozoan *Giardia lamblia* transfers methyl groups to the exocyclic amine (N^2) in the mRNA cap, using *S*-adenosyl-L-methionine (AdoMet) as methyl donor.[3] In our lab a variant of GlaTgs was generated which showed remarkable promiscuous activity towards AdoMet analogues bearing various functional groups in their side-chains.[4]

However, this AdoMet-based approach suffers from several drawbacks including limited stability and lacking cell permeability of AdoMet analogues. We here present a novel biocatalytic cascade strategy to overcome these limitations.[5] Starting from methionine analogues we were able to generate AdoMet analogues enzymatically using a methionine adenosyltransferase (MAT) variant. AdoMet formation was directly coupled to its consumption by our GlaTgs variant, giving access to alkene-, alkyne- and azido-modified 5'-capped RNA in one pot (Scheme 1). Further reaction with fluorophores or biotin proved to be an efficient strategy for mRNA labelling. This study paves the way for AdoMet-based RNA labelling inside cells.



Scheme 1: One-pot modification of 5'-capped RNA based on methionine analogues.

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Click Chemistry for Site Directed Labeling of Surface Displayed Proteins on *Escherichia coli*

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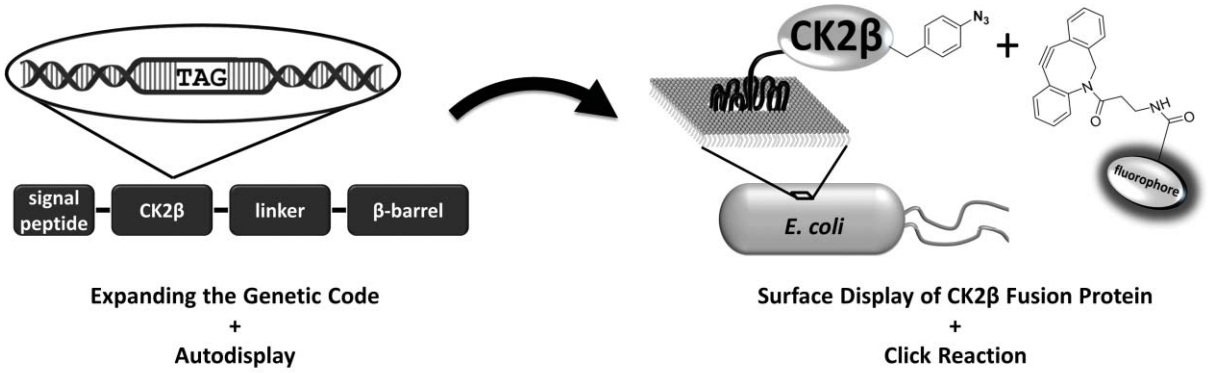
The Autodisplay technology is based on the natural secretion mechanism of autotransporter proteins on the surface of bacterial cells [1]. The surface display of human protein kinase CK2 on *Escherichia coli* has previously been shown [2]. Combining this technique with the incorporation of an unnatural amino acid into proteins facilitates bioorthogonal reactions and expands the capabilities of protein chemistry.



This study reports the successful incorporation of an unnatural amino acid into the surface displayed fusion protein CK2β followed by a bioorthogonal click reaction. CK2β was used as a model protein and is the regulatory subunit of the human protein kinase CK2. The DNA triplet encoding Tyr108 of CK2β was chosen and mutated to the amber DNA stop codon, TAG. By suppression of the mutation with an amber suppressor tRNA, the unnatural amino acid para acidophenylalanine (pAzF) [3] could be incorporated at this position. Performing the SPAAC click reaction (Strain-Promoted Alkyne-Azide Cycloaddition) [4] using a dibenzylcyclooctyne-fluorophore (DBCO-fluorophore) resulted in a side specific labeling of CK2β fusion protein on the surface of *E. coli*, which was evaluated by flow cytometry and SDS-PAGE. The functionality of the obtained regulatory CK2β subunit activating the catalytically active CK2α subunit was confirmed by capillary electrophoresis. This innovative procedure of labeling proteins on the outer membrane of bacterial cells could be a significant advancement for screening assays or protein interaction studies with whole cells, cell lysates or isolated outer membrane proteins.

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MS_CEC 2016 Poster – Gabriele Prina Cerai

Title of the poster**:** ***Atom-Economical Cobalt-Catalyzed Regioselective Coupling of Epoxides and Aziridines with Alkenes***

- Full given and surnames of all contributors: <u>*Gabriele Prina Cerai*</u> *(presenting author), Bill Morandi*

- Full address of your institution: *Max-Planck-Institut für Kohlenforschung - Kaiser-Wilhelm-Platz 1 - D-45470 Mülheim an der Ruhr*

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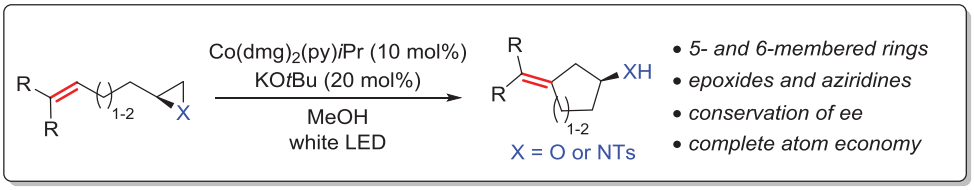
- The abstract paragraph: *A simple cobalt complex can regioselectively couple epoxides and aziridines with alkenes to generate valuable homoallylic alcohols and amines. The reaction exhibits complete atom economy and is particularly efficient for the preparation of 5- and 6-membered rings. Promising results regarding the development of an intermolecular process using both epoxides and aziridines are reported, as well as preliminary mechanistic studies suggesting a radical mechanism.*

- Scheme for illustration:



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Rigidity-controlled Supramolecular Affinity Materials and their Application for Gravimetric Detection of Hazardous and Illicit Compounds

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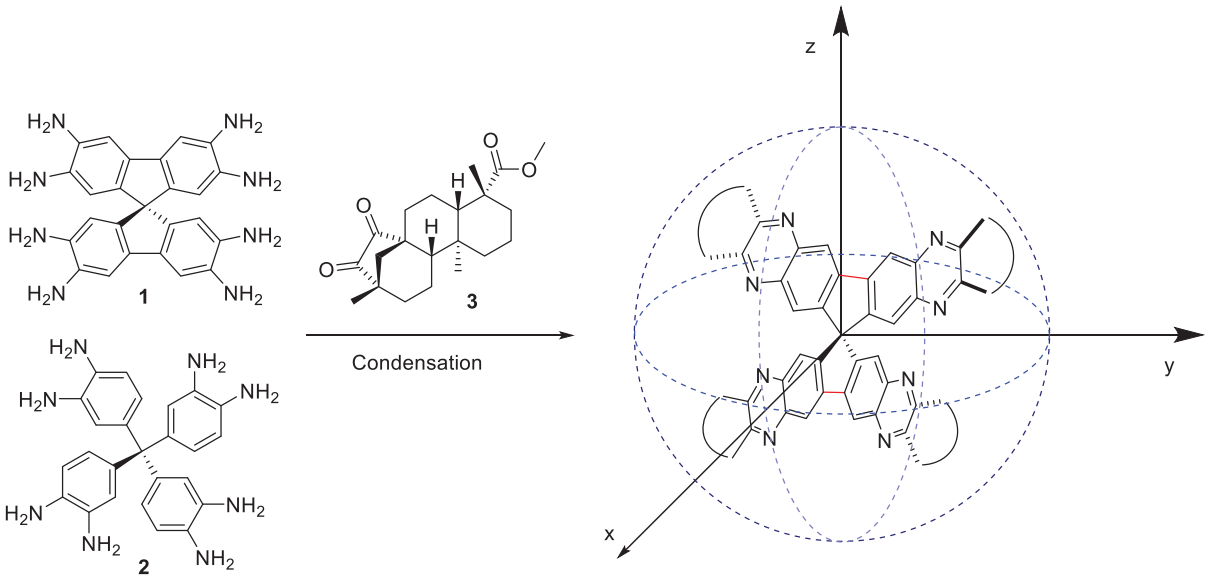
The selective and sensitive detection of volatile organic compounds (VOCs) is a contemporary research topic.[1] Quartz crystal microbalances (QCMs) are a powerful tool for those detections. They can be coated with size-exclusive organic affinity materials by a well-known electrospray protocol.[2] The choice of the deposited material on the electrode effects the interaction with the airborne analyte and determines the selectivity and sensitivity of the detection.

9,9'-Spirobifluorene **1** and tetraphenylmethane **2** derivatives differ only in two bonds. However, the structural properties change significantly. Both compounds represent unique building blocks for the synthesis of affinity materials due to their rigid symmetric scaffolds. A multiple functionalization of the core and its combination with different sidearms, i.e. the naturally occurring diterpene (−)-isosteviol **3**,[3] provides the opportunity to generate novel supramolecular hosts. These symmetric compounds feature a unique three-dimensional structure (scheme 1) with electron-rich and persistent cavities for the analyte interactions.

This presentation will demonstrate the influence of rigidity and their capabilities in sensor applications by comparing 9,9'-spirobifluorene and tetraphenylmethane based affinity materials.[4]



Scheme 1: Supramolecular hosts based on (−)-isosteviol.

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Selenium dioxide-mediated activation of phenols

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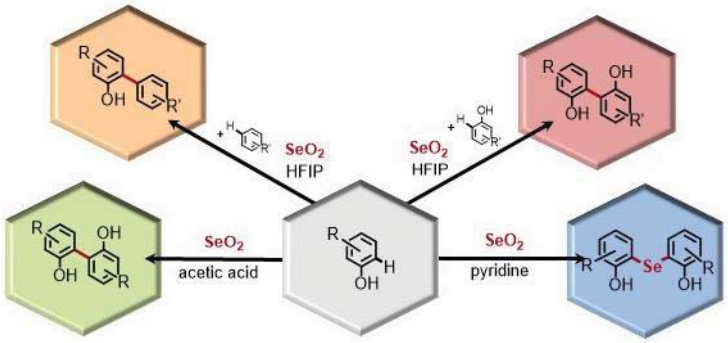
Symmetric and non-symmetric biphenols are important structure motifs for ligand systems in organic catalysis and therefore included in the category of so called “privileged ligands”.[1] We have developed a novel synthetic pathway to construct these structures by use of selenium dioxide, a stable, powerful and commercially available oxidizer.[2] Our innovative, and easy to perform protocol gives rise to biphenols and diaryl selenides depending on the solvent employed. Oxidative treatment of phenols in acetic acid yields the corresponding biphenols, whereas conversion in pyridine results in the preferred formation of diaryl selenides. Additionally the use of 1,1,1,3,3,3-Hexafluoro-2-propanol as solvent provides an easy acces to non-symmetric biaryls. Such non-symmetric motifs are well established ligands whereas the diaryl selenides could act as pincer-like ligands with further applications in organic synthesis or as ligands in transition metal catalysis.[3]



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N-heterocyclic carbenes and their salts for membrane interactions and micellar catalysis

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N-heterocyclic carbenes (NHCs) are well established ligands in organometallic chemistry, which results from their electron-rich character and directed steric demand towards the metal leading to strong transition metal to carbon bonds.[1] Despite the great success of NHCs, comparable little attention was paid to their salts. In 2014 we designed a NHC with long alkyl chains in the backbone to stabilize palladium nanoparticles.[2] Realizing the structural compliance with lipids we decided to investigate the biological activities of these salts. Biophysical measurements indicated an interaction of the salts with Dipalmitoylphosphatidylcholine (DPPC) membranes which was dependent on the chain length[3] Computational investigations elucidated the mode of interaction between NHC salts and DPPC membranes.[4] Inspired by the membrane interactions we investigated the corresponding gold and palladium complexes for micellar and lipophilic catalysis.[5,6]

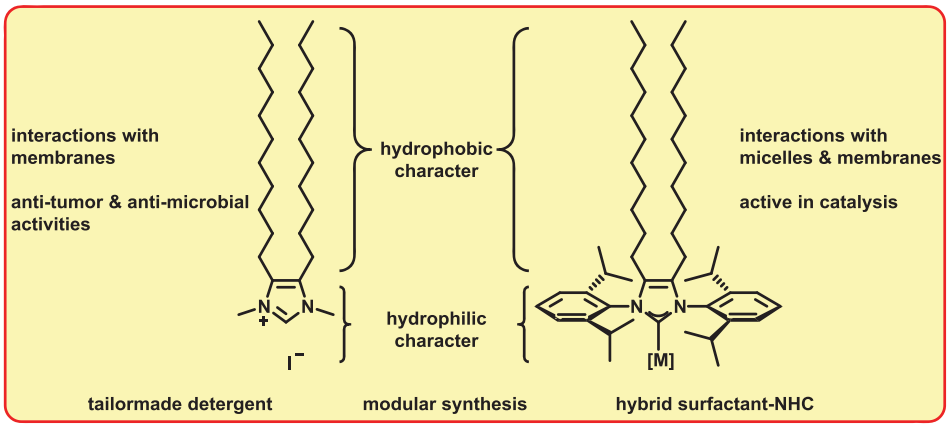

Figure 1: Schematic representation of the imidazolium salts and the corresponding metal complexes.

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Sequence-specific modification of RNAs

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The study of specific modifications of RNAs is becoming a new exciting research field. Especially mRNAs are in the focus, because of their essential role in cells. Such modifications could affect the transport, stability and translation of mRNAs. N^6-methyladenosine (m^6A) is the most common mRNA modification. Different approaches exist to detect m^6A, but its role is still unrevealed [1, 2]. The methylation is performed through an enzyme complex of METTL3, METTL14 and WTAP [3]. FTO and AlkBH5 remove the methyl group [4, 5]. Specific demethylations of m^6A sites in mRNAs could identify the role of these methylations. To reach this specificity two RNA-binding proteins are chosen as fusion partners: dCas9 and λN.

dCas9 is the nuclease-deficient form of Cas9 that is part of the CRISPR-Cas Type II system [6]. Currently the system is used for genome editing, but it was also modified to bind RNAs. For the RNA recognition a guide RNA matching the target RNA sequence and a protospacer adjacent motif-containing DNA oligonucleotide (PAMmer) is necessary [7].

λN is a small peptide of 22 amino acids originating from λ-phage. It binds to a 17 nt boxB RNA hairpin with nanomolar affinity [8]. The incorporation of boxB into a guide RNA targets λN to the complementary RNA sequence [9].

Through the fusion of dCas9 and λN, respectively, FTO and AlkBH5 could be guided to specific mRNAs by different guide RNAs. The cloning of all fusion proteins with different linkers was successful, but not every variant could be expressed, purified and was active. The produced fusion proteins of λN and FTO comprise wildtype activity. With different guide RNAs the specific demethylation will be measured by HPLC followed by experiments in eukaryotic cells. There the demethylation could be measured through m^6A sequencing [1, 2].

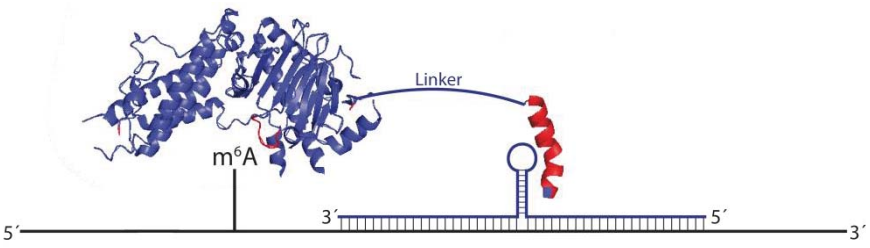

Figure 1: Concept of site-specific mRNA modification. λN (red) is fused with a linker to FTO (blue). λN binds to boxB in the guide RNA (blue) complementary to the mRNA with m^6A.

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Electroorganic Process Development

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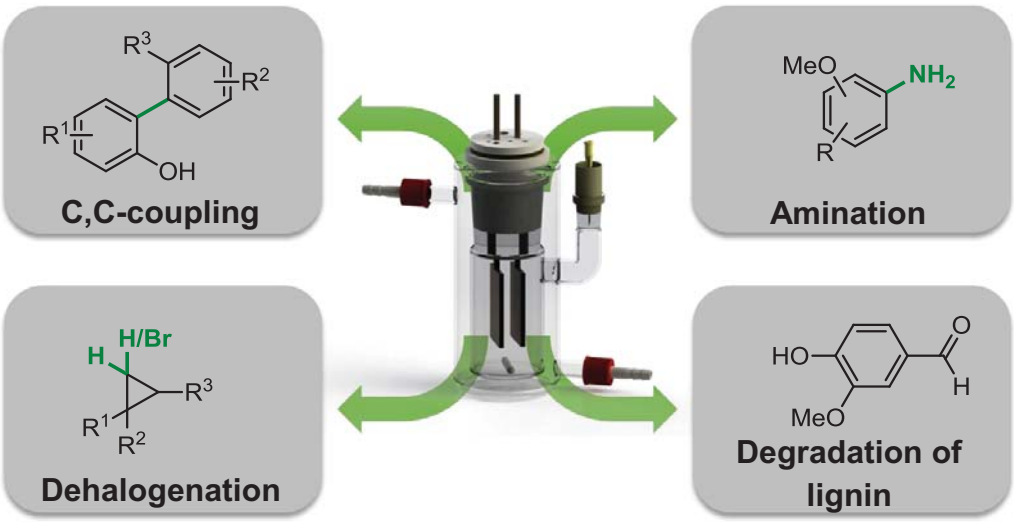
Electroorganic synthesis offers a highly attractive alternative to classic oxidation or reduction reactions. The major benefit of electrochemistry is the use of electrons as reagent. In a “green chemistry” approach, electrons can be generated by renewable energy sources.

Over more than a decade we acquired know-how in the development of electroorganic syntheses to produce fine chemicals or pharmaceutically interesting compounds. Our efforts usually start on a microscale screening level, to save chemicals, and continue with optimization on the preparative level. For highly relevant targets we already optimized reaction conditions up to multi-molar scale in batch or flow cells. Our current electrochemical process developments are a reagent-free C,C-coupling-reaction,[1] the amination of less activated aromatic compounds,[2] mono or double dehalogenation reactions for cyclopropane derivatives,[3] and the anodic degradation of lignin to vanillin.[4]



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Modular bidentate hybrid NHC-thioether ligands for the stabilization of palladium nanoparticles in various solvents[1]

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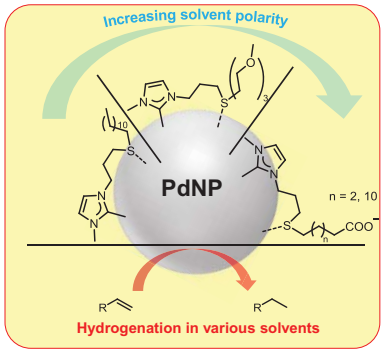
During the last decade the interest in nanoparticles (NP) has grown significantly, especially in the field of materials and catalysis.[2-3] However, a common challenge in these research fields is the NP's stabilization, as agglomeration would render them "inactive". NPs are normally stabilized by ligands such as thiols and thioethers.[4] However, N-heterocyclic carbenes (NHCs),[5] which are superb ligands in organometallic chemistry, are an emerging class of ligands for NP stabilization.[6] In 2014 we reported on a tailor-made NHC, bearing two long alkyl chains in the backbone for the stabilization of palladium NPs.[7] The drawback of this system was the difficulty to adapt this design to different polarities, which is needed for stability and solubility in various media. Consequently, a broader field of applications could be addressed with a modular design, in which an alternative stabilizing motif is implemented. We envisioned the combination of an NHC ligand with a thioether as a hybrid bidentate ligand would allow us to use the properties of both ligand classes in a synergistic fashion.[8] Such a combinatorial approach simplifies the synthesis of the ligand, and enabling a quick adaption to the polarity and therefore solubility of the NPs on demand.



We synthesized a set of four different NHC-thioether ligands and the corresponding palladium nanoparticles, covering solubility in unpolar and polar solvents. The nanoparticles we analyzed in detail via NMR, TEM and TGA. XPS analysis was identified as a convenient tool to establish the binding mode of the NHC ligand. Furthermore we evaluated the catalytic activity of our palladium nanoparticles via chemoselective hydrogenation in various solvents.

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Synthesis of functionalized pyrazolidines by gold-catalysed three-component spirocyclization in micellar systems

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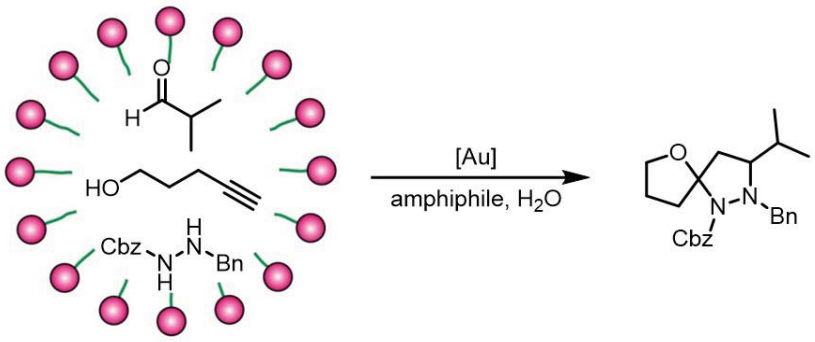
In medicinal chemistry natural products continue to be an inspiration for the design of new drugs. In this context spiroacetals have been found as a key structural unit in many biologically active and structurally diverse natural products.[1] Nevertheless, synthetic approaches to [N,O]-spiroacetals are not well explored. Recently, KRAUSE et al. have developed a gold-catalyzed one-pot approach to functionalized pyrazolidines. With this reaction different kinds of aldehydes, alkynols and hydrazines can be coupled to the corresponding [N,O]-spiroacetals with yields of up to 97%.[2]

Nowadays, preparative transformations are not only judged by efficiency and stereoselectivity, but also by safety and economic and environmental sustainability.[3] One way to improve the environmental sustainability of reactions is the use of micelles in bulk water instead of organic solvents. In these systems both polar and unpolar organic substrates and catalysts are soluble and can react in the nanometer-sized micelles.[4]

Herein, we report the synthesis of functionalized pyrazolidines via gold-catalyzed three-component spirocyclization in micellar systems (Scheme 1).



Scheme 1: Gold-catalyzed three-component spirocyclization in micellar system.

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NADPH Cofactor regeneration on the cell surface: A crucial requirement for pharmaceutical applications of surface displayed P450 enzymes

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Applications of purified enzymes still suffer from costly production processes, stability problems and limited options for reusability. In this regard, whole cell biocatalysts offer significant advantages, but are restricted to cell permeable substrates and products. One solution to circumvent mass transfer problems and possible cross reactions with intracellular enzymes is the presentation of enzymes on the cell surface.

Recently, surface display of active human CYP1A2 using the Autodisplay technology was demonstrated [1]. The technique replaces the passenger domain of a native autotransporter by a peptide or protein of choice, which is then transported to the cell surface [2]. The current project focusses on the display of CYP102A1 from *Bacillus megaterium* for pharmaceutical applications. Surface exposure of the enzyme was confirmed by protease accessibility tests, flow-cytometry analysis and activity measurements. CYP102A1, also known as BM3 is one of the best studied Cytochrome P450s to date and can be engineered to accept many pharmaceutical relevant substances [3]. In a proof-of-principle study we analyzed a small library of substances with the known R47L F87V L188Q mutant displayed on the cell surface of *E. coli*.

However, the project also elucidated a major challenge for the use of the technology in industrial applications. Bringing an enzyme to the cell surface blocks the access to intracellular cofactors, which are too expensive to be added stoichiometrically. Keeping the advantages of a surface displayed catalyst, we also used the Autodisplay technology to present various dehydrogenases on the surface of *E.coli* cells for the regeneration of the essential cofactor NADPH. We aim at a combination with the CYP102A1 whole cell biocatalyst for an efficient system for biotechnological and pharmaceutical applications.

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Modelling Chemical Reasoning and Creativity to Predict and Invent Reactions

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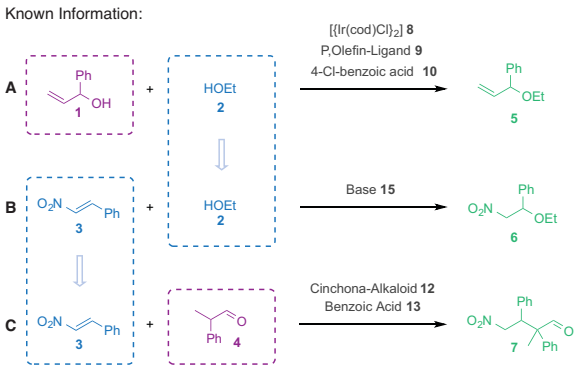
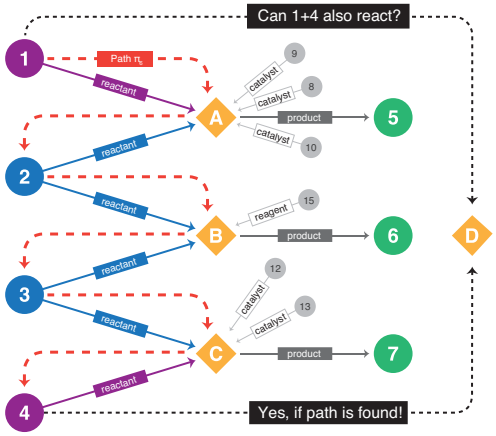
The ability to reason beyond established knowledge allows organic chemists to solve important and intriguing synthetic problems and to invent novel transformations. Both tasks involve the prediction of the outcome of reactions. In synthesis, the problem can be linked to known similar reactions, while in reaction discovery usually an indirect link between seemingly unrelated knowledge has to be established. Here, we propose a model which formalises reaction prediction and discovery as finding missing links in a knowledge graph. This enables computers to infer hypotheses about reactivity and reactions purely driven by data, without entering or extracting reaction rules beforehand. Our model outperforms a rule-based expert system in the reaction prediction task. We show that our model can generalise even beyond known reaction types, thus effectively invent novel transformations, including transition-metal catalysed reactions. Furthermore, we propose an approach to predict catalysts and reagents for reactions.

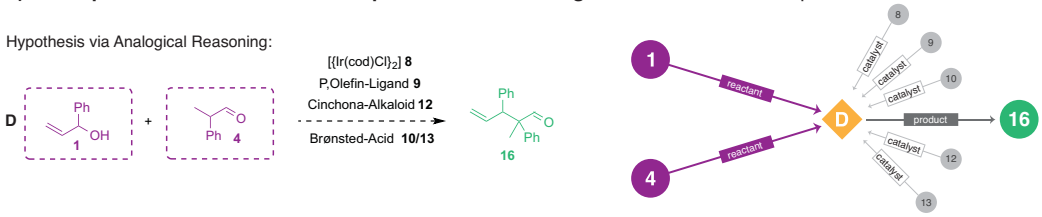
a) Traditional Scheme Representation



b) Graph Representation



c) Conceptual link via mutual reaction partners: Path Finding ⟶ Reaction **D** is plausible!



Turn on Fluorescence in Tetraphenylethylene-Bridged Tetra-NHC Ligands by Rigidification in Organometallic Complexes: An Alternative to Aggregation-Induced Emission

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The search for promising luminescent materials is a topic of great interest due to their versatile applications as fluorescent sensors and probes, light-emitting diodes, bioimaging agents, and so on.[1] N-heterocyclic carbenes (NHCs)[2] have emerged as an important class of ligands due to their applications in various fields like as catalytically active metal complexes, as biologically active compounds, material science, and recently in metallosupramolecular chemistry.[3] Although some organometallic complexes featuring NHC ligands are known to exhibit luminescent properties due to the strong ligand field they provide, most of them feature monodentate or bidentate NHC ligands.[4] Organometallic light-emitting materials featuring poly-NHC ligands are still underdeveloped despite their promising properties as advanced emissive materials.

We designed and synthesized novel tetraphenylethylene (TPE)-bridged tetraimidazolium carbene precursors [**2**-Et]$(PF_6)_4$ and [**2**-Bu]$(PF_6)_4$ which in dilute solution showed fluorescence with quantum yield (Φ_F) of 1%. After metallation, that is, after preparation of the corresponding dinuclear Ag^I/Au^I tetracarbene complexes [**3**-Et]$(PF_6)_2$, [**3**-Bu]$(PF_6)_2$, [**4**-Et]$(PF_6)_2$ and [**4**-Bu]$(PF_6)_2$ the fluorescence quantum yield (Φ_F) went up to 47% in dilute solution, showing a 47 folds increase compared to the free ligand. The fact that no phosphorescence is observed can be related to the lack of participation on the excited state of the heavy transition metal atom, thus minimizing spin-orbit coupling. A high fluorescence quantum yield in very dilute solution was observed due to the locking of phenyl rings rotation by forming dinuclear tetracarbene complexes, a phenomenon that can be ascribed to rigidification.

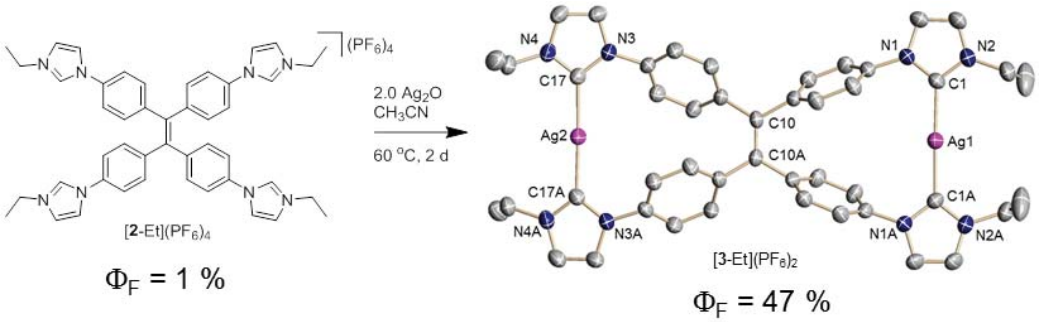

Figure 1. Synthesis of dinuclear Ag^I tetracarbene complex [**3**-Et]$(PF_6)_2$.

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Molecular understanding of functional cooperation between the helicase and the topoisomerase domain of *Thermotoga maritima* reverse gyrase in DNA binding and supercoiling

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Reverse gyrase is a type I DNA topoisomerase that can introduce positive supercoils into DNA in an ATP dependent manner. The protein is found in hyperthermophiles and consists of a helicase and a topoisomerase domain [1]. Both domains interact with the DNA substrate. The cooperative action of the helicase and topoisomerase domains allows for the ATP-dependent positive supercoiling of DNA. Although different models for positive supercoiling by reverse gyrase have been proposed, the molecular mechanism for the functional cooperation between the two domains remains unknown.

T. maritima reverse gyrase contains two zinc fingers, one in the helicase domain, the second in the topoisomerase domain, which are connected by a salt bridge between His9 and Asp631 [2]. The two zinc fingers are thought to cooperate in DNA binding and supercoiling. Therefore, we investigated the influence of the salt bridge on DNA binding, supercoiling activity and stability of reverse gyrase using variants in which either His9 or Ap631 have been replaced by alanines. Our results show that this salt bridge is not necessary for DNA binding or supercoiling, but contributes to reverse gyrase stability. It is currently unclear which elements from helicase and topoisomerase domains contact the DNA substrate at different steps of the catalytic cycle, or how the DNA is oriented in the reverse gyrase/DNA complex. To identify individual elements of reverse gyrase that are involved in DNA binding, we performed UV and chemical crosslinking of reverse gyrase/DNA complexes. Interaction sites can then be identified by mass spectrometric analysis. In ensemble FRET measurements with a bubble DNA substrate that carries an acceptor fluorophore at one end and donor-labeled reverse gyrase, we investigated the orientation of this DNA substrate. Altogether, these experiments will further our understanding of the cooperation of helicase and topoisomerase domains during DNA binding and positive DNA supercoiling.

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C-$SeCF_3$ Bond Formation *via* Dinuclear Pd(I) Catalysis

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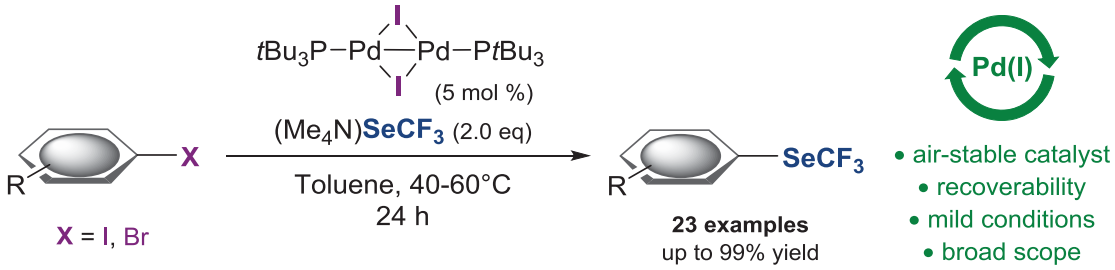
The Pd(I)-catalyzed C-$SeCF_3$ coupling of aryl iodides and bromides is described.[1] Efficient conversion of a wide range of aryl iodides and bromides to the corresponding aryl trifluoromethylselenides under mild reaction conditions is facilitated by the use of an air-stable Pd(I) dimer as a catalyst.

The trifluoromethylselenide moiety presents an interesting functional group in pharmaceutical and agrochemical research due to its promising properties regarding bioavailability and membrane permeability. Hence, direct catalytic access to Ar-$SeCF_3$ would be desirable. While no Pd-based protocol existed, successes have been achieved using Cu and/or activated arenes.[2-4] Based on our previous use of Pd(I) dimers as catalysts for C-X bond formation (X = Br, SCF_3),[5-6] we envisioned the application of this dinuclear cross-coupling principle in the formation of C-$SeCF_3$ bonds. In contrast to commonly employed air-sensitive Pd(0)-catalysts, our approach relies on the formation of air-stable Pd(I) dimers and their direct reactivity with aryl halides. Combined experimental and computational studies are in line with dinuclear catalysis and support the direct reactivity of aryl halides with Pd(I) dimers, thereby leaving the Pd-Pd bond intact. This remarkable stability of the Pd(I)-Pd(I) framework even allows for the recovery of employed catalyst *via* column chromatography or distillation and also for its recyclability and reusability in economic cross-coupling.



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Conjugated Si(IV) phthalocyanines as light-driven antibiotics

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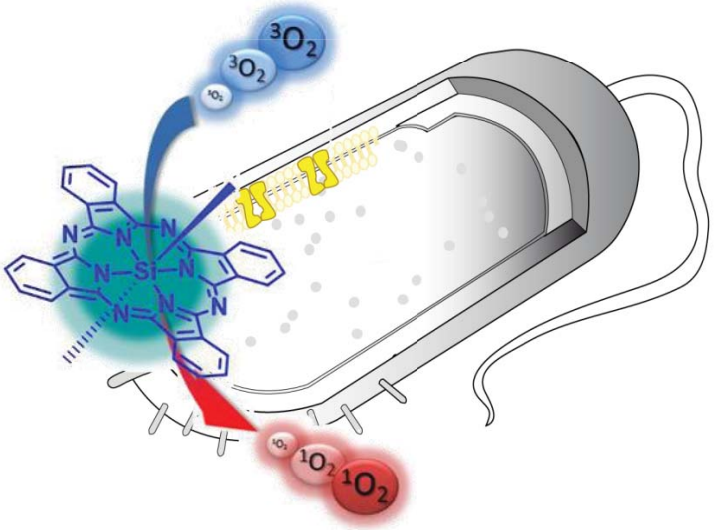
Exponential increase of microbial multidrug resistance in nosocominal infections has been extensively reported in medical practice and has currently emerged as a serious threat to public health. Despite the success of antibiotics, bacteria always try to stay one step ahead by developing resistances, leading to serious infections. A highly promising alternative method to overcome this problem is antimicrobial photodynamic therapy (aPDT), which is a clinically approved therapeutic modality for the treatment of various infectious diseases [1].
Phthalocyanines (Pc) derivatives are efficient theranostic agents due to their low toxicity, high stability, efficient $^1O_2$ generation and intense red light absorption corresponding to the therapeutic window where deep tissues can be reached [2]. Our recent study show that carbohydrate-conjugated silicon(IV) phthalocyanines are able to label and to inactivate pathogens with different degrees of selectivity for Gram-positive bacteria on the basis of the attached carbohydrate [3]. In another study we aimed at controlling the aggregation of the photosensitizer, and to tune its photophysical and photochemical properties. For this purpose, a host-guest complex of a tailored Si(IV)Pc with supramolecular β–cyclodextrin vesicles (CDV) was prepared [4]. This nanostructured array is capable of efficiently photoinactivating Gram-positive species, despite their antibiotic resistance.



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Stabilisation of transient SIM-SUMO mediated 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, stability, 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 modified by small proteins such as ubiquitin or ubiquitin-like proteins (Ubls), e.g. SUMO (small ubiquitin-related modifier). Hundreds 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, Parkinson's or Huntington'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 precise role of SUMOylation is often difficult to study.

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.

This approach will contribute to a better understanding of the consequences of SUMOylation for new and altered protein-protein.

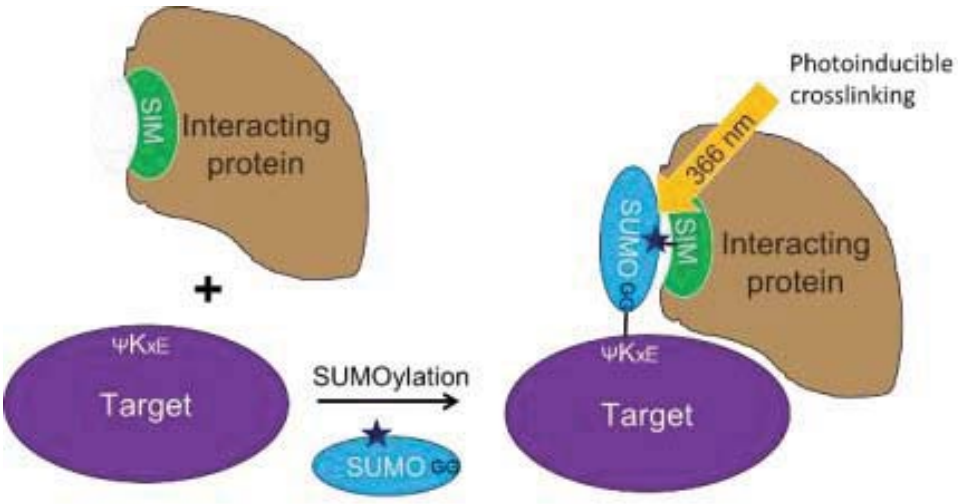

Figure 1: Concept of photoinducible crosslinking as a tool to study SIM-SUMO mediated interactions in multi protein complexes.

Double Click Functionalization of NMP Based Alternating Copolymers

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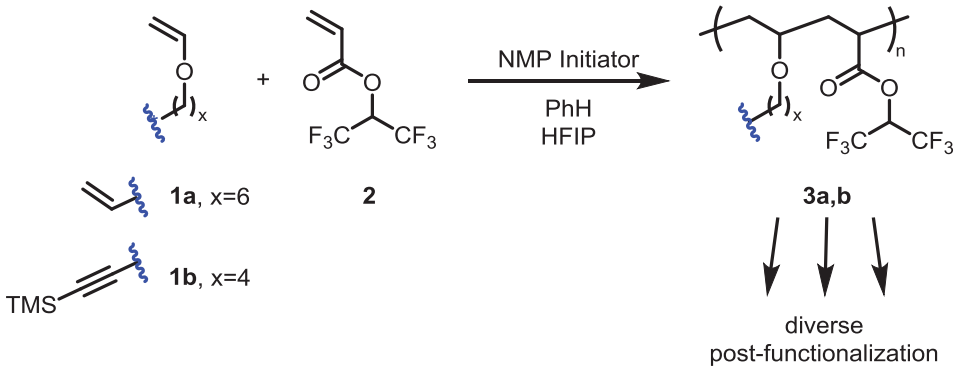
Nature creates structure as well as function by controlling the monomer sequence of proteins and nucleic acids. Accordingly, sequence control in synthetic polymer chemistry has gained a lot of interest during the past years and has been identified as "The Next Holy Grail" in polymer science.[1] Most strategies towards controlling the sequence of polymers either require tedious step-wise syntheses or the complexity of the sequence is limited to simple repetitive patterns.[2] Our approach comprises an alternating sequence of two electronically distinct monomers with the possibility to post-functionalize both of them in a modular way *via* orthogonal click chemistry (Scheme 1).[3]



Scheme 1: Alternating copolymerization of functional vinyl ethers **1** and HFIP acrylate **2** *via* NMP.

The vinyl ether monomer features either a terminal alkene (**1a**) which can be addressed by a radical thiol-ene reaction or a TMS-protected alkyne (**1b**) which can undergo a Cu-catalyzed cycloaddition with azides. Hexafluoroisopropyl acrylate **2** is prone to amidation in the presence of amines or can be hydrolyzed to yield the corresponding acrylic acid derivative. Using this modular post-functionalization approach, a single type of alternating copolymer **3** with defined molecular weight and narrow PDI can be transformed into various alternating polymers bearing different functionalities.

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Synthesis of small molecules for optical and whole body imaging of CCR6

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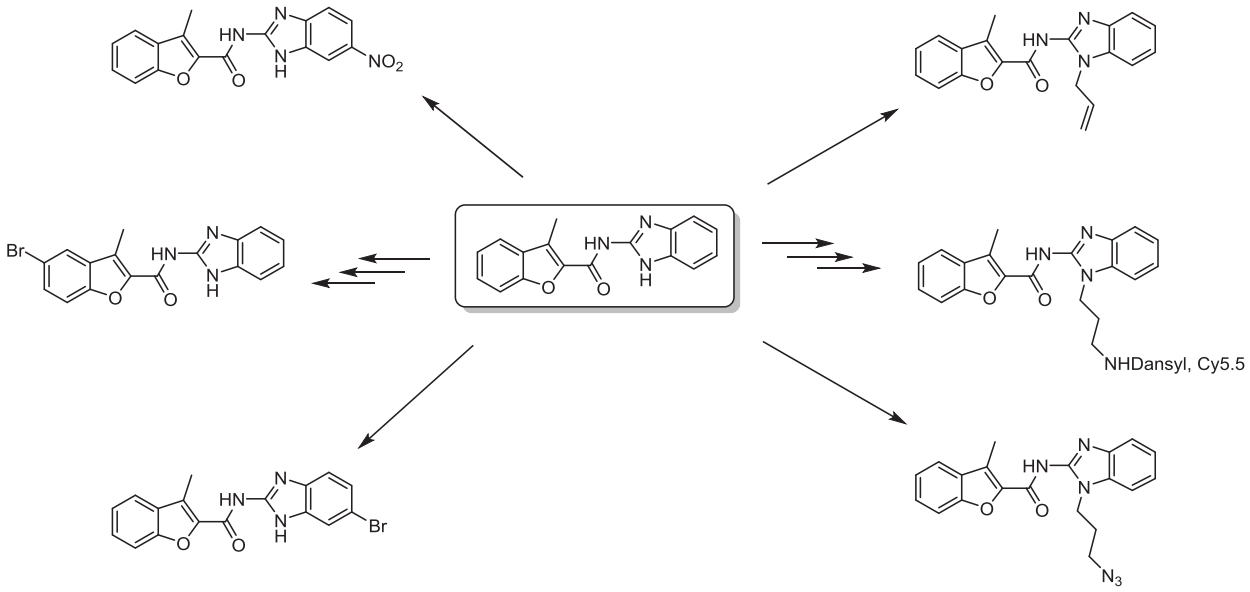
Chemokine Receptor 6 (CCR6) and its exclusive ligand CCL20 have been found to play an important role in signaling for regulating the migration and recruitment of antigen-presenting and immunocompetent cells during inflammatory and immunological responses.[1] Previous studies have successfully established that the CCR6 knockout mice had defects such as leukocyte homing to the intestinal mucosa, impaired humoral immunity and altered responses to contact hypersensitivity.[2]

A lead structure was identified from the compounds screened by the NIH via docking studies.[3] The lead structure was modified at different sites to assess the difference in activity. The compounds were evaluated for their activity using a transmigration assay.



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Mechanisms of Iodine-Catalyzed Reactions

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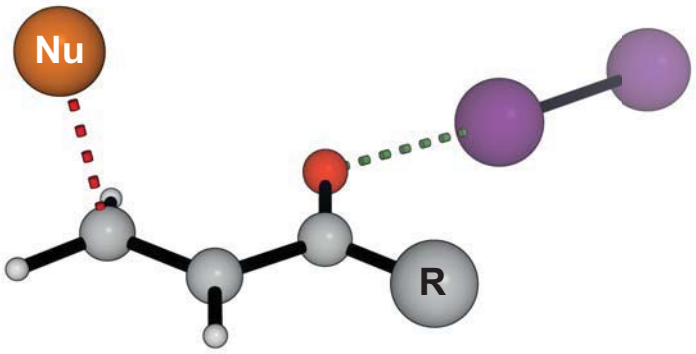
The catalytic potential of molecular iodine is known since 1915, when Hibbert first reported an iodine-catalyzed dehydration reaction employing tiniest amounts (0.01 mol-%) of I_2.[1] Over the last decades, numerous reactions have been published that rely on the catalytic properties of molecular iodine.[2] Despite these successful reports, the underlying reaction mechanism and mode of activation remain widely unknown.

In the light of the recent developments in the field of halogen bonding,[3] we have now analyzed several iodine-catalyzed reactions using experimental and computational techniques. Our results indicate that molecular iodine acts as a halogen-bond donor to activate the electrophiles and that hidden Brønsted-acid catalysis is less likely.



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Development of a three-component spirocyclization to highly functionalized pyrazolidines and access to their DNA-conjugates by Au(I)-catalysis

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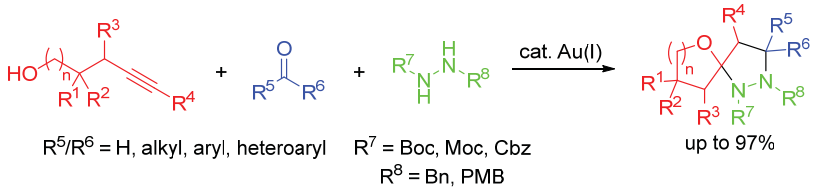
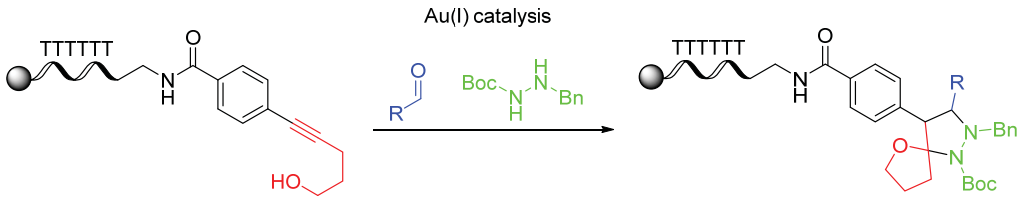
As a carbophilic Lewis-acid, gold has the ability to activate alkenes and alkynes for nucleophilic attack to form C-C-, C-O-, C-N- or C-S-bonds.[1] The obvious advantages of gold catalysis are mild reaction conditions at oftentimes room temperature, tolerance against different functional groups and its low toxicity.
We now disclose a new access to spiro acetals by a one-pot approach in the presence of a gold catalyst (Scheme 1).[2] In this reaction a coupling of alkynols with *N*,*N*'-disubstituted hydrazines and aldehydes or ketones takes place.[3] With this efficient method we are able to form numerous spirocyclic pyrazolidines in high yield.



Scheme 1. Gold-catalyzed three-component spirocyclization to highly functionalized pyrazolidines.

The screening of large, pooled DNA-encoded small molecule libraries (DELs) is a validated technology for the target-based identification of bioactive compounds.[4] DELs consist of small organic molecules covalently coupled to DNA sequences serving as PCR-amplifiable identification bar codes. DELs are generated by iterative organic synthesis and encoding steps. Currently, DNA-compatible reaction methodologies are very limited.
In our newly developed "**TIDEC**" (oligo**T**hymidine **I**nitiated **D**NA-**E**ncoded **C**hemistry) strategy, we now demonstrate the first application of Au(I) catalysis to furnish TIDEC-conjugates of highly substituted spirocyclic pyrazolidines (Scheme 2).[5]



Scheme 2. Gold-catalyzed three-component reaction to synthesize hexa-T oligonucleotide-heterocycle conjugates.

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One-Pot Procedure for the Synthesis of 1,5-Benzodiazepines

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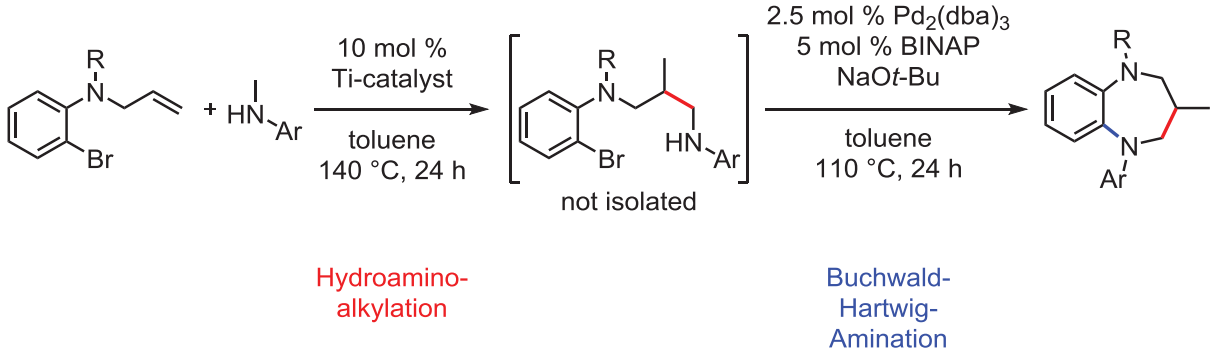
During the past decade, the hydroaminoalkylation of alkenes was the subject of intense research because it represents a useful approach to synthesize amine building blocks from alkenes and secondary amines.[1] Another important method for the formation of aromatic amines is the well-established Buchwald-Hartwig-Amination.[2] By combining the highly regioselective titanium-catalyzed hydroaminoalkylation of *N*-allyl-2-bromoanilines with *N*-methylanilines with a subsequent intramolecular Buchwald-Hartwig-Amination we were able to synthesize 1,5-benzodiazepines using a high-yielding one-pot procedure. Due to the ability of 1,5-benzodiazepines to interact with the central nervous system, these seven-membered-rings are of immense interest for the pharmaceutical industry.[3]



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The Enantioselective Dakin–West Reaction

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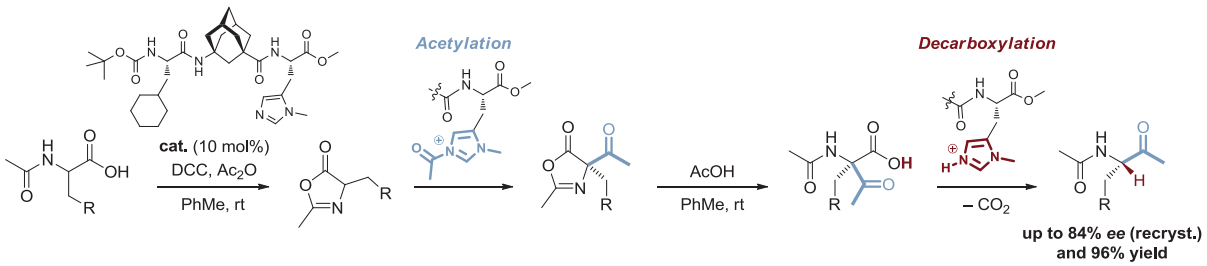
Even though the Dakin-West reaction dates back to 1928,[1] it is still one of the most effective synthetic procedures to prepare α-acylamido ketones directly from the corresponding primary α-amino acids.[2] Generally, the treatment of an amino acid with an acid anhydride and a base, typically pyridine, at elevated temperature provides the desired product upon liberation of CO_2. Although numerous modifications were subsequently developed *no* asymmetric variant has been reported, restricting the use of this important reaction in modern synthetic chemistry.[2]

Very recently, we reported the first enantioselective Dakin–West reaction making use of a synthetic oligopeptide as catalyst under well-defined reaction conditions.[3] The catalytically active π-methyl histidine acts as Lewis base for the acetyl transfer and concurrently as Brønstedt base in the terminal decarboxylative protonation,[4] thus enabling the use of a single catalyst for the entire reaction sequence. Starting from racemic *N*-acetyl amino acids valuable α-acetamido methylketones form with up to 58% *ee* with good to excellent yields under mild reaction conditions. Two of the products were recrystallized once to achieve up to 84% *ee*. We propose a dispersion-controlled reaction path that determines the asymmetric reprotonation of the intermediate enolate after the decarboxylation.



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7th Münster Symposium On Cooperative Effects in Chemistry

Switchable Bioactive Ligands for Supramolecular Surfaces

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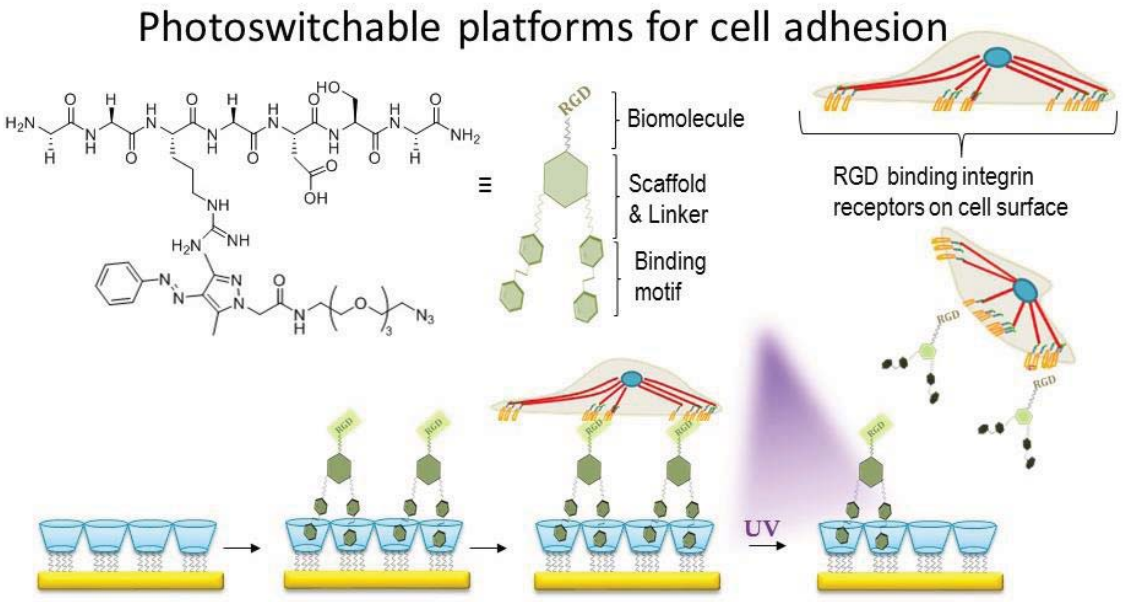
Abstract

Bioactive switchable ligands have recently attracted much interest since they allows the immobilization of cells and bacteria to supramolecular surfaces. Host-guest chemistry is therefore a valuable tool because the concept is inspired by nature. The interactions are non-covalent, reversible and are fulfilling a number of biological requirements.[1]

We are using arylazopyrazoles (AAPs) derivatives as novel switchable ligands for cell immobilization on surfaces. AAPs have promising switching properties and are easy to modify further for biological application.[2] This supramolecular approach based on host-guest interaction of the AAP moiety with curcurbit[8]uril and b-cyclodextrin (bCD). Basic interaction studies are investigated by NMR, ITC and UV/Vis spectroscopy, as well as a first trial on gold surfaces. The AAP binding molecule is modified with an integrin binding peptide for biocompatibility. The adhesion and release of the cells can be controlled by applying UV-light as an external trigger.



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Tetradentate luminophores for platinum(II) complexes

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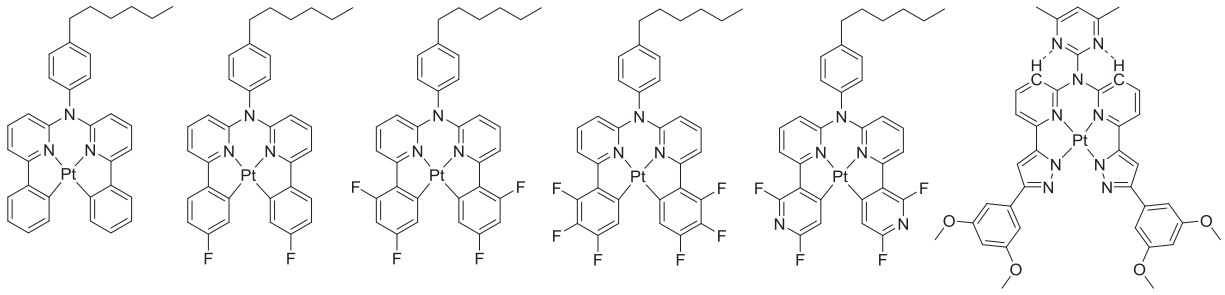
Luminescent Pt(II) complexes have gained major attention in recent times for their use in organic light emitting diodes (OLEDs) [1,2]. They have a d^8-electron configuration and therefore exhibit a square planar geometry, allowing d-d-orbital interactions upon formation of aggregates with new photophysical properties. Herein, we present six tailored cyclometallated platinum(II) complexes bearing tetradentate luminophores. The electron density on the aromatic part of the chelates was modulated by the introduction of electron withdrawing groups (phenyl *vs.* fluorophenyl), as well as by the introduction of heterocyclic rings (difluoropyridine *vs.* dilfuorophenyl). Correlating with the decreasing electron density, an enhanced tendency to Pt-Pt interactions could be observed. The aggregation behaviour also led to a phosphorescence shift from blue-green to orange. The solubility of the complexes follows the same pattern as the aggregation tendency, as a drop of the electron density leads to a lower solubility. The processability of the complexes was further enhanced by the introduction of a hexyl chain at the bridging aniline of the tetradentate ligands. The introduced chain not only enhances the solubility of the complexes, but also represents a key factor for the self-assembly observed at the Au(111) interface, which was measured by STM. Two of those complexes were processed to build OLEDs in collaboration with the Tsinghua University. The measurements showed promising results by combination of the monomer and aggregate emission in the realization of warm WOLEDs.



Stable deep-blue emitting species are still subject of intensive research, and with the aid of scanning tunnel microscopy (STM), a better knowledge of stabilities, frontier orbital localization and energies can be gained [2,3]. Since a high degree of planarization facilitates such measurements, the aniline bridge was replaced by aminopyrimidine units that could lead to intramolecular hydrogen bonding. Pt(II) complex **6** has been already synthesized and characterized, and is object of ongoing research efforts.

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Donor-functionalized alkenyl-silanes and their reactivity

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Hydroalumination of sterically shielded and donor-functionalized alkynyl-silanes affords the corresponding alkenyl-silanes in equimolar quantities of dialkylaluminum hydrides and leads to the reduction of a C≡C triple bond in highly regio- and stereoselective reactions (*cis* addition). These alkenyl derivates feature a strong intramolecular interaction between the coordinatively unsaturated aluminum atom and the donor atom (X) (Figure 1).

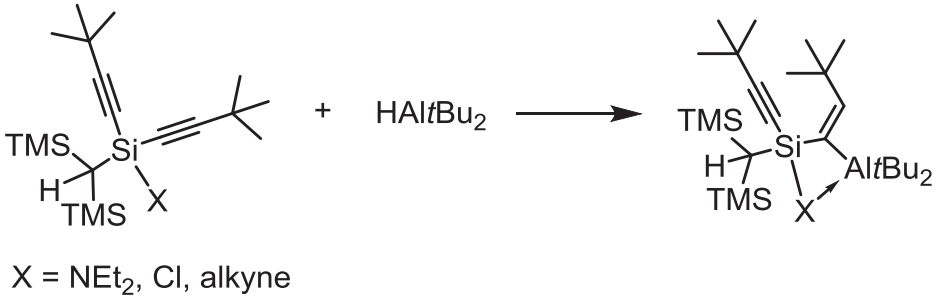

Figure 1. Synthesis of donor-functionalized alkenyl-alkynyl-silanes.

The Al-X interactions result in an activation of the Si-X bond (e.g. X = NEt_2), as demonstrated by the reaction with heterocumulenes and the facile insertion into the Si-N bond (Figure 2).

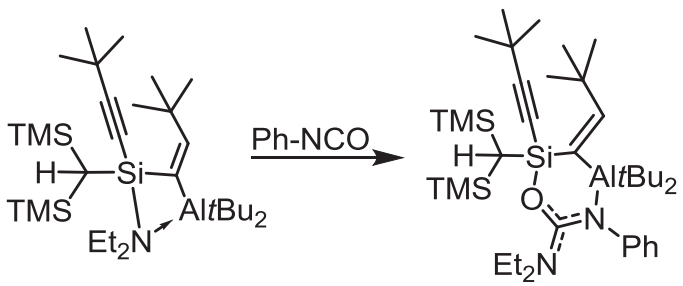

Figure 2. Reaction of one equivalent Ph-NCO with a donor-functionalized alkenyl-alkynyl-silane.

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