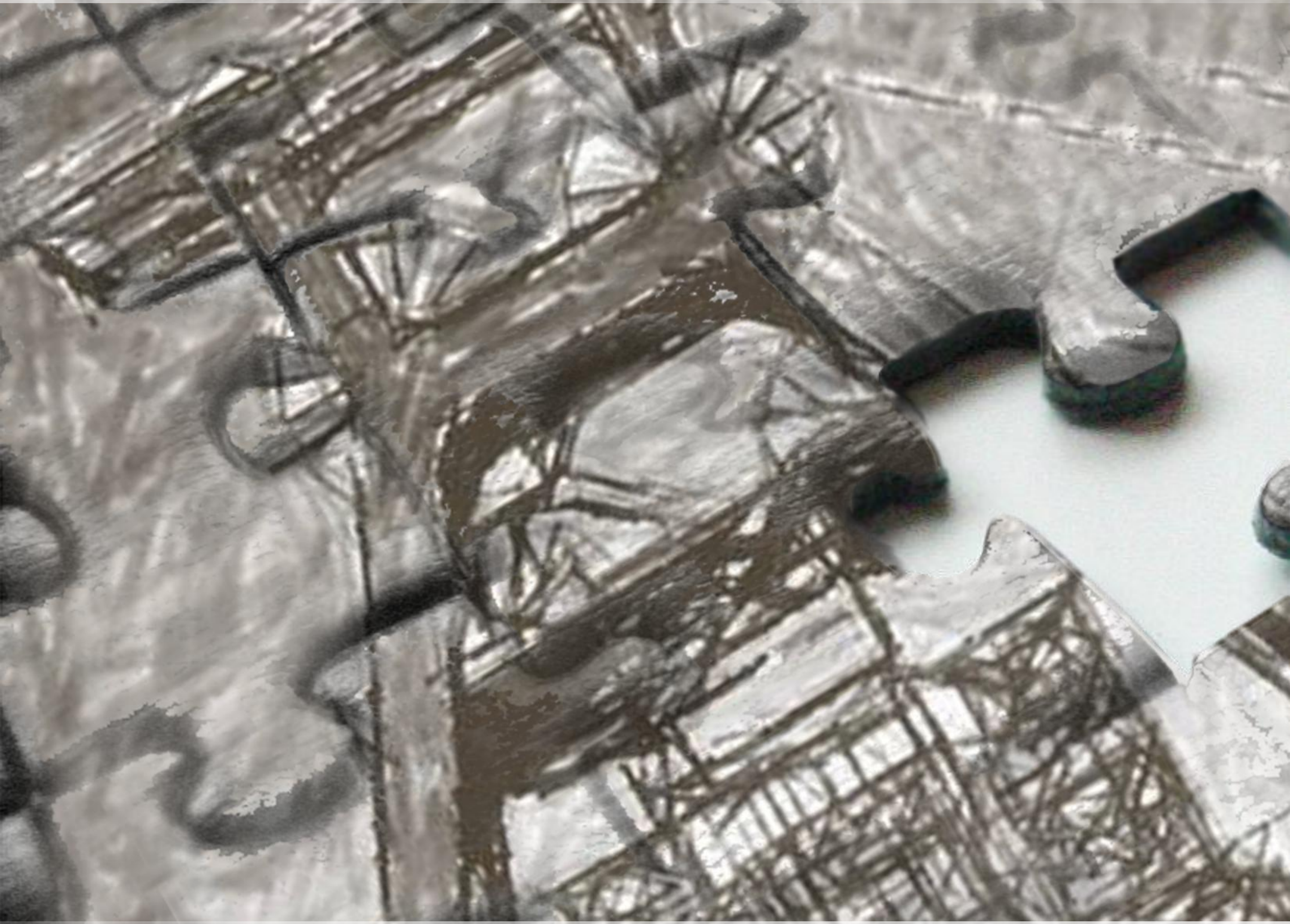
Abstracts

February 24th - 25th 2011



SupraChem

Symposium in Supramolecular Chemistry

Contents

Abstracts

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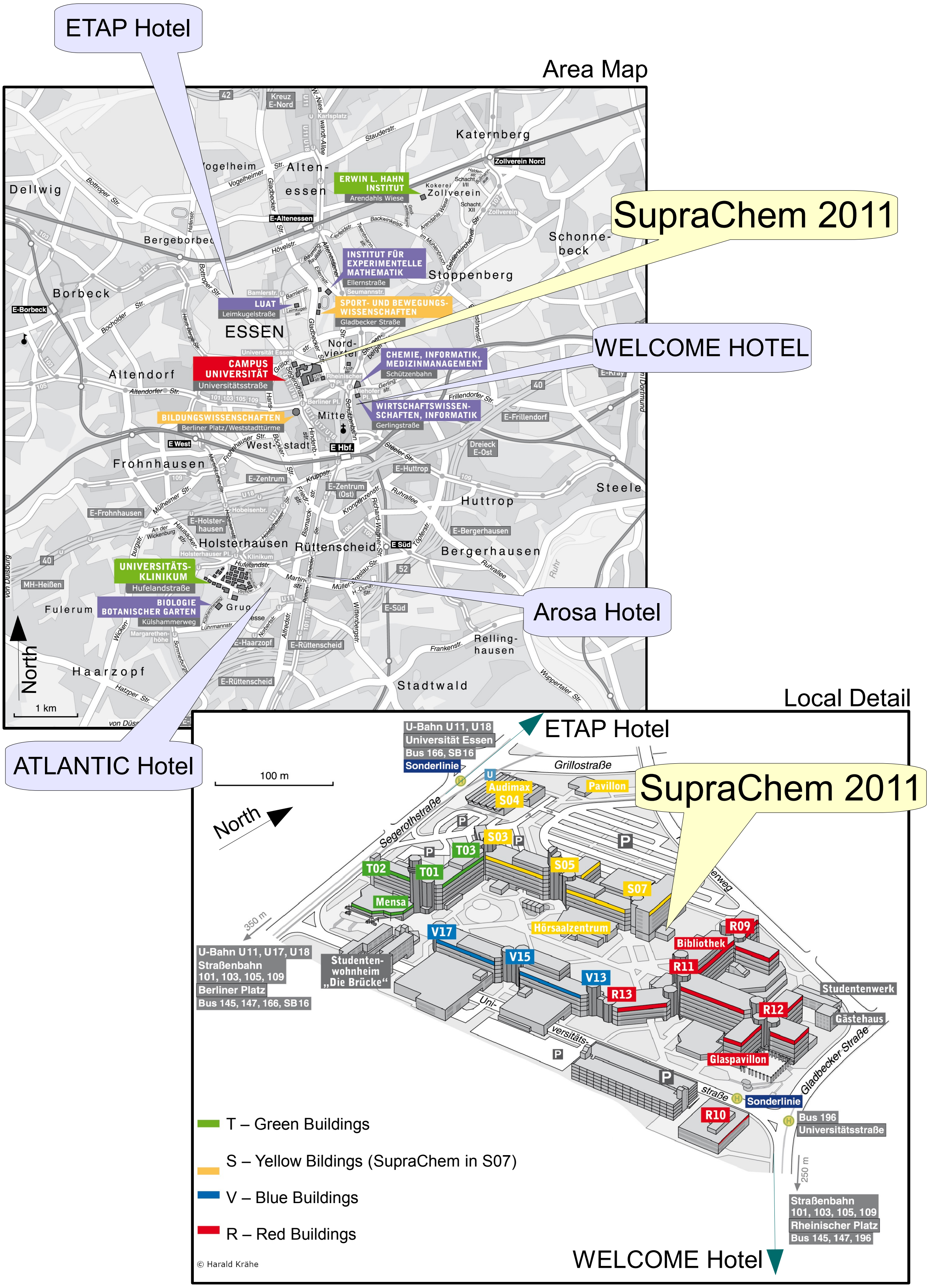

Program

Thursday, 24th

until 11:45	arrival & registration, poster setup
11:45 – 12:00	welcome address (Schmuck/Ravoo) Dr. Lotz-Ahrens, vice rector of the university Duisburg-Essen
12:00 – 12:30	Prof. Arne Lützen (Uni Bonn) *Self-assembly of molecular building blocks – from structures to functions*
12:30 – 13:00	Prof. Christoph Schalley (FU Berlin) *Gas-Phase H/D-Exchange Reactions for the Examination of Supramolecular Structure and Reactivity*
13:00 – 13:30	Prof. Werner Nau (Uni Bremen) *Strong Binding of Hydrocarbons to Cucurbiturils in Aqueous Solution Probed by Fluorescent Dye Displacement: A Supramolecular Gas-Sensing Ensemble*
13:30 – 14:15	Prof. Chris Hunter (Sheffield, UK) *High Throughput Physical Organic Chemistry of Molecular Interactions*
14:15 – 15:00	coffee break
15:00 – 15:20	Dr. Evgeny Katayev (Regensburg) *Control of Coordination and Covalent Self-assembly*
15:20 – 15:40	Tim Reimers (Uni Kiel) *Chiral Concave N-Heterocyclic Carbenes*
15:40 – 16:00	Carina Schulze (RWTH Aachen) *Rational design of heteroleptic complexes as small models for large supramolecular coordination compounds*
16:00 – 16:30	Prof. Burkhard König (Uni Regensburg) *Synthetic Receptors for Selective Molecular Recognition and Catalysis*
16:30 – 17:00	Prof. Carsten Schmuck (Uni Essen) *pH switchable zwitterion induced self-assembly*
17:00 – 19:45	poster session
20:00	conference dinner (sponsored by Evonik Goldschmidt)

Friday, 25th

8:30 – 9:00	Prof. Markus Albrecht (RWTH Aachen) *Hierarchical self-assembly of dinuclear helicates*
9:00 – 9:30	Prof. Franz Schmidtchen *Recognition requires structural constraint, requires low entropy! Right?*
9:30 – 10:15	Prof. Boris Rybtchinski (Weizmann Institute, Israel) *Adaptive Supramolecular Systems in Aqueous Medium*
10:15 – 10:45	Prof. Stefan Kubik (TU Kaiserslautern) *Cyclopeptide-Derived Anion Receptors*
10:45 – 11:15	coffee break
11:15 – 11:35	Melanie Rauschenberg (Uni Münster) *Dynamic peptides as biomimetic receptors*
11:35 – 11:55	Dr. Michael Mastalerz (Uni Ulm) *Via Dynamic Formation of Covalent Bonds to Functionalized Cage Compounds - From Molecules to Materials*
11:55 – 12:15	Dr. Pol Besenius (TU Eindhoven) *Self-assembled paramagnetic dendrimer mimics: a new class of nano-sized MRI contrast agents*
12:15 – 12:35	Jens Voskuhl (Uni Münster) *Molecular Recognition of Cyclodextrin Vesicles*
12:35 – 12:55	Hannes Kuchelmeister (Uni Essen) *recognition of DNA using artificial receptors*
13:00 – 14:00	lunch break
14:00 – 14:30	Jun-Prof. Guido Clever (Göttingen) *Switching and Reactivity inside Coordination Cages and Rings*
14:30 – 15:15	Prof. Luc Brunsveld (Eindhoven, NL) *Supramolecular Chemical Biology: Controlling Protein Assembly with Supramolecular Chemistry*
15:15 – 15:45	coffee break
15:45 – 16:15	Prof. Franziska Gröhn (Erlangen) *Supramolecular Nanostructures through Electrostatic Self-Assembly of Macroions and Organic Counterions*
16:15 – 16:45	Prof. Sigfried Waldvogel (Uni Mainz) *supramolecular sensors and explosives*
16:45 – 17:15	Prof. Luis Sanchez (Madrid) *Self-Assembly of Linear and Discotic Molecules. Mechanisms and Amplification of Chirality*
17:15	closing remarks
17:30	end of conference

Abstracts of Oral Presentations

Self-assembly of molecular building blocks – from structures to functions

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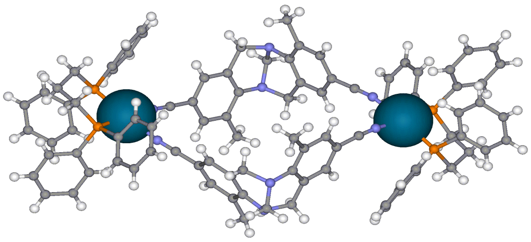
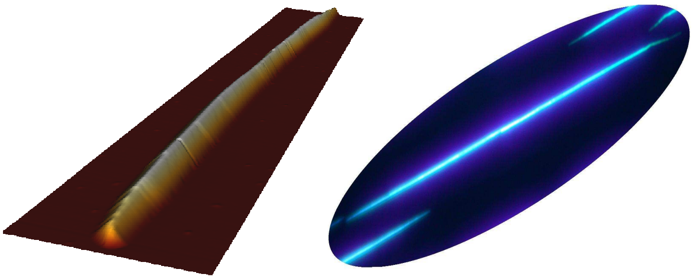
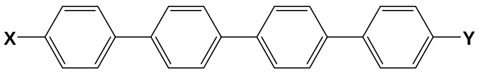
Nature uses hierarchical self-self-assembly processes of (macro-)molecular building blocks in order to generate sophisticated molecular architectures that can fulfil complex functions and so do supramolecular chemists. Interactions that have been extensively used in supramolecular chemistry are hydrogen bonds and π-π-stacking but also the coordination to metal centres and C-H-π-interactions. The use of the latter two interactions to create artificial assemblies will be the focus of this talk illustrating some examples from our work.







X,Y = OMe, Cl, CN, NH_2, NMe_2, NO_2

Starting from the formation of discrete aggregates like metallosupramolecular macrocycles and capsules from dissymmetrical ligands which have been found to have interesting stereochemical properties[1] we will make a journey all the way up to organic materials.

The latter are e.g. well defined and mutually aligned fiber-like nanoaggregates with interesting optical properties that are formed in dipole-assisted self-assembly processes upon vapour deposition of π-conjugated oligomers on muscovite mica surfaces.[2]

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[1] a) T. Weilandt, U. Kiehne, J. Bunzen, G. Schnakenburg, A. Lützen, *Chem. Eur. J.* **2010**, *16*, 2418; b) N. Dalla Favera, U. Kiehne, J. Bunzen, S. Hytteballe, A. Lützen, C. Piguet, *Angew. Chem. Int. Ed.* **2010**, *49*, 125.

[2] a) M. Schiek, F. Balzer, K. Al-Shamery, A. Lützen, H.-G. Rubahn, *Soft Matter* **2008**, *4*, 277; b) M. Schiek, F. Balzer, K. Al-Shamery, J. Brewer, A. Lützen, H.-G. Rubahn, *Small* **2008**, *4*, 176.

Gas-Phase H/D-Exchange Reactions for the Examination of Supramolecular Structure and Reactivity

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Inside ESI-FTICR mass spectrometers, bimolecular reactions with mass-selected non-covalent complex ions can be conducted. One prominent example is the exchange of labile hydrogen atoms by deuterium in reactions with exchange reagents such as ND_3, CH_3OD, or CH_3COOD.

The talk will provide two examples. The first one discusses gas-phase H/D-exchange experiments that show crown ethers to directly walk along the periphery of oligolysine peptide chains or dendrimers. The second example provides not only mechanistic information, but also structural insight: Resorcinarene dimers are closed capsules in the gas phase as long as the guest cation is small enough. In H/D-exchange experiments, they show a quite unexpected behavior, which can be explained by a concerted Grotthuss-type mechanism reminiscent of proton transport through water.

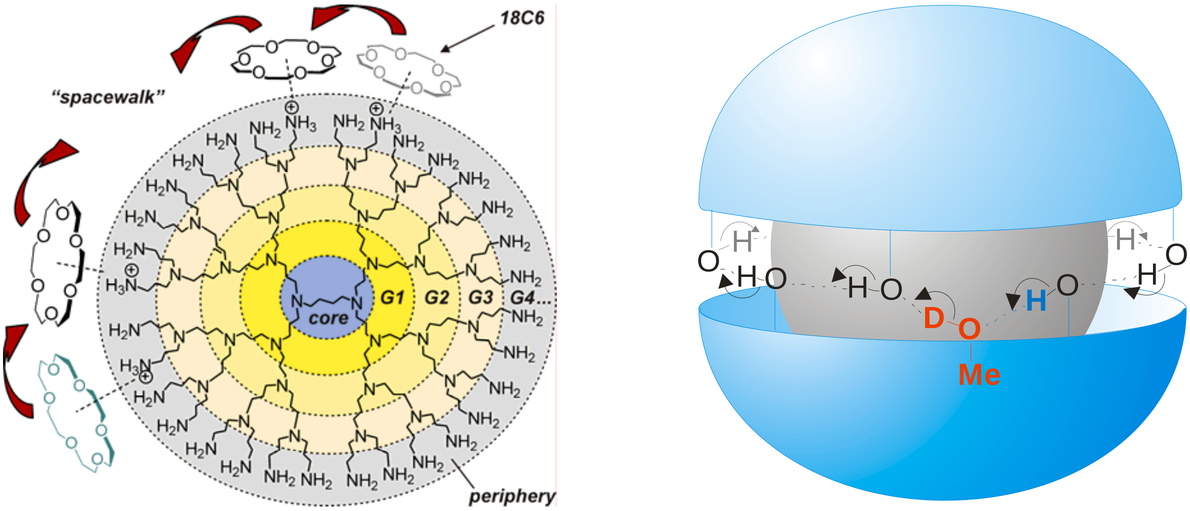

Figure 1. "Spacewalk" of 18-crown-6 on a dendrimer (left) and HDX on a resorcinarene dimer (right).

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[1] D.P. Weimann, H.D.F. Winkler, J.A. Falenski, B. Koksch, C.A. Schalley, *Nat. Chem.* **2009**, *1* 573

[2] H.D.F. Winkler, D.P. Weimann, A. Springer, C.A.S., *Angew. Chem. Int. Ed.* **2009**, *48*, 7246-7250

[3] H.D.F. Winkler, E.V. Dzyuba, J.A.W. Sklorz, N.K. Beyeh, K. Rissanen, C.A.S., *Chem. Sci.*, subm.

Strong Binding of Hydrocarbons to Cucurbiturils in Aqueous Solution Probed by Fluorescent Dye Displacement: A Supramolecular Gas-Sensing Ensemble

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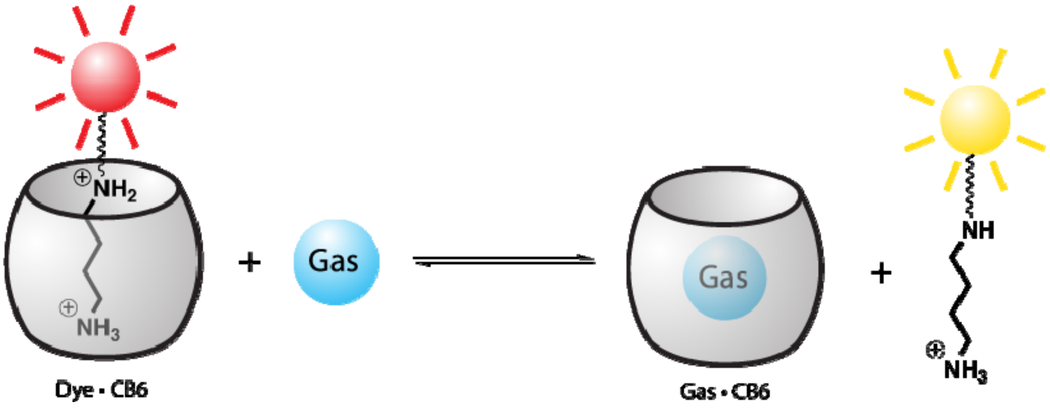
There is an increasing interest in the development of supramolecular chemistry methodologies for gas sensing. Macrocyclic molecules, such as calixarenes, cyclodextrins, and cucurbiturils can be perceived as attractive receptors for gas recognition due to their spherical cavity of well-defined size, which should result in a sizable selectivity towards the gases of interest.[1] The cucurbituril family stands out in this context due to its rigid and hydrophobic cavity.[2] The hexamer and original macrocycle, cucurbit[6]uril (CB6), is the most attractive for gas sensing due to its intermediary size, which should be capable of sensing gas molecules up to 7 heavy atoms or 110 Å^3 volume in its inner cavity. Unfortunately, CB6 displays very poor water solubility (30 μM or less), which limits the routine investigation of gas binding.[3]

We have recently developed a strategy for the design of fluorescent dyes, which bind to CB6 and generate a readily detectable fluorescence response.[4] This allows us now to monitor gas binding with high sensitivity at low (μM) CB6 concentrations in neat aqueous solution (Scheme 1). Particularly, we employed our system to investigate the complexation of low-molecular-weight hydrocarbons and inert gases with CB6. Additionally, the sensing methodology could be transferred and implemented for a systematic investigation of higher hydrocarbons with the larger analogue cucurbit[7]uril (CB7). We observe strong, highly selective binding.



Scheme 1. Gas sensing in aqueous solution using CB6 and a fluorescent dye derivative.

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[1] (a) D. M. Rudkevich, *Angew. Chem. Int. Ed.* **2004**, *43*, 558-571. (b) D. M. Rudkevich, *Eur. J. Org. Chem.* **2007**, 3255-3270. [2] (a) K. Kim, N. Selvapalam, D. H. Oh, *J. Incl. Phenom. Macro.* **2004**, *50*, 31-36. (b) J. Lagona, P. Mukhopadhyay, S. Chakrabati, L. Isaacs, *Angew. Chem. Int. Ed.* **2005**, *44*, 4844-4870. [3] C. Márquez, R. R. Hudgins, W. M. Nau, *J. Am. Chem. Soc.* **2004**, *126*, 5806-5816. [4] A. Praetorius, D. M. Bailey, T. Schwarzlose, W. M. Nau, *Org. Lett.* **2008**, *10*, 4089-4092.

Control of Coordination and Covalent Self-assembly

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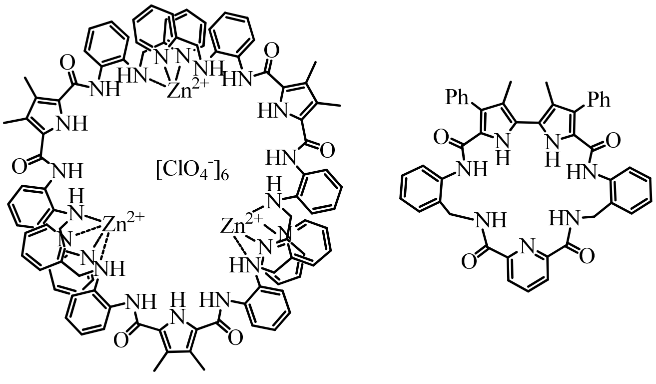
One of the biggest challenges in supramolecular chemistry is the control of self-assembly in order to obtain desired structures with desired properties.[1] Nature can easily perform this with the help of templates, it builds functional molecules in response to external stimuli or environmental factors. The self-assembly of building blocks using reversible covalent bonds under thermodynamic conditions in the presence of a template has proven to be an excellent method to generate molecules with desired structures and new properties.[2] In our work we explore the control of self-assembly using coordination and covalent bonds. The access to molecules **1** and **2** (Fig.1) were gained only using templates - amines and hydrogensulfate anion, respectively. Different analytical tools were used to evaluate major driving forces for selective formation of a product, binding properties of new molecules, and the influence of the amount of a template and sequence of addition of reagents on the reaction yields.[3]



1 *2*

Figure 1. The structures of compounds which were prepared using templated self-assembly.

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[1] G. M. Whitesides, M. Boncheva, *Proc. Nat. Acad. Sci*. **2002**, *99*, 4769..

[2] S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders, J. F. Stoddart, *Angew. Chem. Int. Ed.* **2002**, *41*, 898.

[3] E. A. Katayev, M. B. Schmid, *Dalton Trans*., **2011**, in press

Chiral Concave N-Heterocyclic Carbenes

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In the last two decades, N-heterocyclic carbenes (NHC) have gained large interest. They are widely applied in organocatalysis and also as ligands in transition metal catalyzed reactions, e.g. Grubbs' Second Generation Catalyst.[1] Due to their versatility, a control of their reactivity and selectivity is desirable.

For example, the incorporation of an NHC in a concave bimacrocycle was realized by Winkelmann (for precursor see structure **A**). The influence of the concave shape of the catalyst in respective reactions has already been shown.[2] In order to achieve enantioselectivity, axial chirality was created by exchanging a phenyl bridgehead for a naphthyl unit (structure **B**).

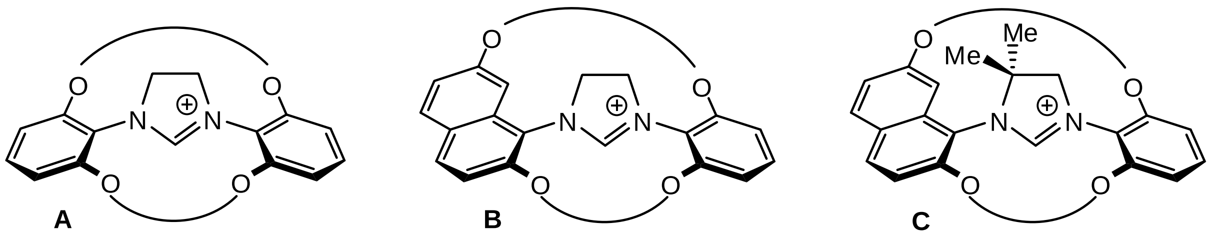

Figure 1. Three concave NHC precursors: **A** is achiral, **B** and **C** are axially chiral, but only **C** is configurationally stable.

If the backbone of the NHC precursor is not modified, a rotation of the N-heterocycle along the C_{Ar}-N bond is observed. This leads to an equilibrium of the two enantiomers at room temperature and separation is not possible.[2]

This contribution shows an approach to avoid the rotation by adequate substitution to reach configurational stability. The synthesis of a respective axially chiral bimacrocycle has been accomplished (structure **C**).[3] The stabilization of the configuration has been proven by NMR experiments and by chiral HPLC. The application of axially chiral bimacrocyclic N-heterocyclic carbenes in asymmetric supramolecular catalysis is the final goal.

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[1] M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953-956.

[2] O. Winkelmann, U. Lüning, *Supramol. Chem.* **2009**, *21*, 223-229.

[3] T. Reimers, C. Näther, U. Lüning, *Eur. J. Org. Chem.*, DOI: 10.1002/ejoc.201001367.

Rational design of heteroleptic complexes as small models for large supramolecular coordination compounds

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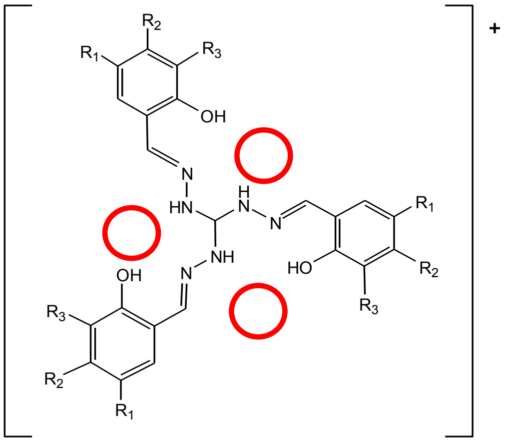
We are interested in the coordination chemistry of differently modified derivatives of the C_3 symmetric ligand Tris(2-hydroxybenzylidene) triaminoguanidinium chloride (Figure and Table), which can exist in four different conformations (*aaa*, *aas*, *ass*, *sss*). In the *aaa* conformation the ligand is able to coordinate three metal centres in tris-chelating manner forming in this way building blocks which cover nearly completely a triangular face [1, 2].
Discrete coordination cages with the outer shape of tetrahedra [3, 4], an octahedron [5], a trigonal bipyramid [6] and a double-walled tetrahedron [7] could already be formed using different metal ions as Pd^{2+}, Zn^{2+} or Cd^{2+}. In addition to these compounds, several 'unexpected' complexes with quite flexible coordination modes at the metal centres were observed during the reaction of the ligand with e.g. Ga^{3+}, Zn^{2+} or Sn^{4+} ions [8].



R_1	R_2	R_3	abbreviations
H	H	H	$[H_6\mathit{L}]^+$
Br	H	H	$[H_6\mathit{Br}_3\mathit{L}]^+$
Br	H	Br	$[H_6\mathit{Br}_6\mathit{L}]^+$
Br	OMe	Br	$[H_6(\mathit{OMe})_3\mathit{Br}_6\mathit{L}]^+$
Br	H	OMe	$[H_6(\mathit{OMe})_3\mathit{Br}_3\mathit{L}]^+$

In order to learn more about the favoured types of connectivity in these systems and to simplify the sometimes very complex results we decided to block one or two coordination sites of the ligand with MPR_3-fragments (M = Pd^{2+}, Pt^{2+}; R = Et, Ph) leaving two or only one site(s) vacant for the coordination of a different metal centre like Cd^{2+} or Zn^{2+}. The resulting complexes and their characterisation is topic of talk and the corresponding poster.

Acknowledgements: We would like to thank W. S. Sheldrick, C. Dietz and R. W. Seidel for support and helpful discussions

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[1] I. M. Müller, R. Robson, *Angew. Chem. Int. Ed.* **2000**, *39,* 4357.
[2] I. M. Müller, D. Möller; *Eur. J. Inorg. Chem*. **2005**, 257.
[3] I. M. Müller, R. Robson, F. Separovic; *Angew. Chem. Int. Ed.* **2001**, *40*, 4385.
[4] I. M. Müller, D. Möller, C. A. Schalley, *Angew. Chem. Int. Ed.* **2005**, *44*, 480.
[5] I. M. Müller, S. Spillmann, H. Franck, R. Pietschnig, *Chem. Eur. J.* **2004**, *10*, 2207.
[6] I. M. Müller, D. Möller, *Angew. Chem. Int. Ed.* **2005**, *44*, 2969.
[7] I. M. Oppel (neé Müller), K. Föcker, *Angew. Chem. Int. Ed.* **2008**, *47*, 402.
[8] I. M. Müller, D. Möller, K. Föcker, *Chem. Eur. J.* **2005**, *11*, 3318.

Synthetic Receptors for Selective Molecular Recognition and Catalysis

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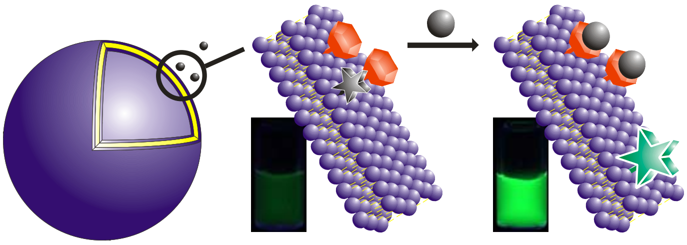
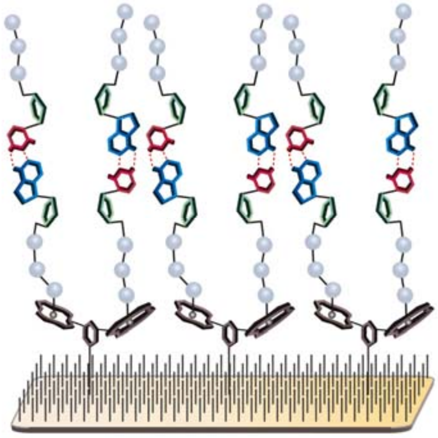
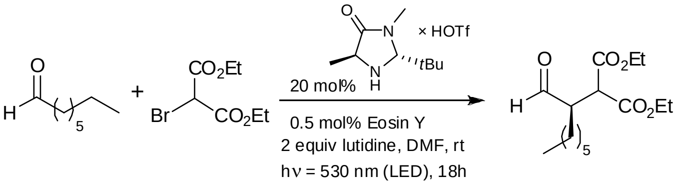
Gaining control over intermolecular interactions is essential for the development of selective chemosensors and catalysts. We use reversible coordinative bonds, hydrophobic interactions and hydrogen bonds to assemble chemosensors and sensory nanoparticles for the specific interaction with peptides, protein surfaces and nucleotides. The combination of a binding site with a reporter dye allows direct monitoring of recognition events, but conjugates of substrate binding sites and chromophores are likewise useful as chemical photocatalysts mediating selective reactions under visible light irradiation. The lecture will review some principles using coordinative bonds in molecular recognition and discuss recent results from our laboratory in protein recognition, self-assembly and chemical photocatalysis.



Functionalized liposomes as chemosensors





Asymmetric organophotocatalysis

Guided self-assembly at surfaces

D. A. Jose, B. König, *Org. Biomol. Chem*. **2010**, 655-662. *Polydiacetylene Vesicles Functionalized with N-Heterocyclic Ligands for Metal Cation Binding*

D. Amilan Jose, S. Stadlbauer, B. König, *Chem. Eur. J.,* **2009**, *15*, 7404 – 7412. *Polydiacetylene based colorimetric self assembled vesicular receptors for biological phosphate ion recognition*

D. Vomasta, C. Högner, N. R. Branda, B. König, *Angew. Chem. Int. Ed*. **2008**, *47*, 7644 - 7647. *Regulation of Human Carbonic Anhydrase I (hCAI) Activity by Using a Photochromic Inhibitor*

B. Gruber, S. Stadlbauer, A. Späth, S. Weiss, M. Kalinina, B. König, *Angew. Chem. Int. Ed*. **2010**, DOI: 10.1002/ange.201001101. *Luminescent Vesicular Chemosensors by Self-assembly of Amphiphilic Binding Sites and Reporter Dyes*

A. Riechers, F. Schmidt, S. Stadlbauer, B. König, *Bioconjugate Chem*. **2009**, *20*, 804–807.
Detection of protein phosphorylation on SDS-PAGE using probes with a phosphate-sensitive emission response

M. Neumann, S. Füldner, B. König, K. Zeitler*, Angew. Chem.* ***2010****,* in print.
Metal-Free, Visible Light Cooperative Asymmetric Organophotoredox Catalysis

I. C. Rosnizeck, T. Graf, M. Spoerner, J. Tränkle, D. Filchtinski, C. Herrmann, L. Gremer, I. Vetter, A. Wittinghofer, B. König, H. R. Kalbitzer, *Angew. Chem*. **2010**, *122*, 3918 – 3922.
Stabilizing a weak binding state for effectors in the human Ras-protein by small compounds

Switchable zwitterion induced self-assemblies

Schmuck, C. Essen/D

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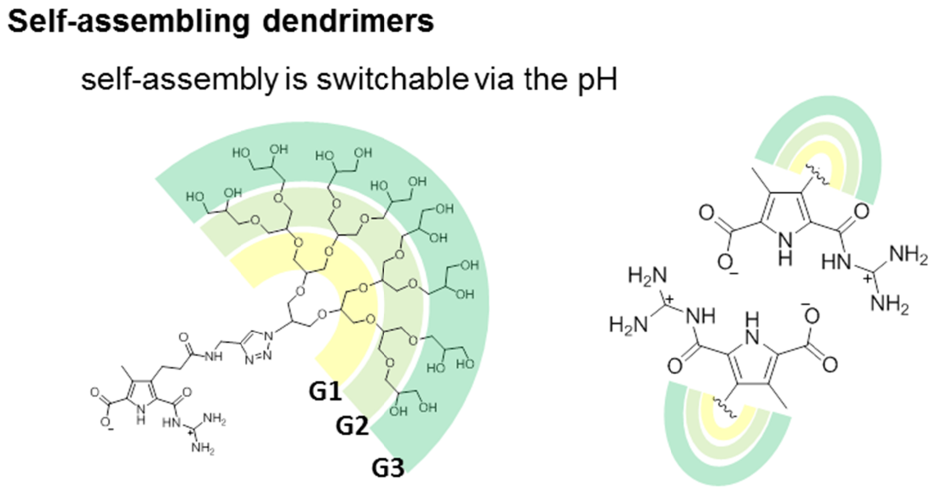
Our research focuses on the development, synthesis and evaluation of new supramolecular systems which function in polar solvents and thus might have prospect for applications. Currently our work mainly involves ionic interactions as a key non-covalent bond.[1] We have introduced guanidiniocarbonyl pyrroles as one of the most efficient oxoanion binding motifs known so far relying on H-bond assisted ion pair formation.[2] We study self-assembling zwitterions which form soft materials such as vesicles, polymers or monolayers in polar solvents and on surfaces. For example, recently we developed a supramolecular polymer based on a monomer with two orthogonal self-complementary binding sites using either metal-ligand or ionic interactions. In a hierarchical self-assembly process this molecule first forms ion paired dimers which can be polymerized by the addition of metal ions.[3] Due to the necessity of the zwitterionic protonation state for self-complementarity, self-assembly can be switched on and off by addition of acid or base. Using similar principles we have also constructed self-assembling dendrimers, based on a functionalized polyglycerol dendron which form stable and monodispers dimers in water.[4] We also found that even simple zwitterionic amino acid derivatives self-assemble in polar solution into vesicles which again respond to an external stimulus (pH).[5] The lecture will discuss the synthesis and study of such switchable zwitterionic self-assemblies.



1 C. Schmuck, Th. Rehm *Chem.Commun.* **2008**, 801-813; *Chem. Soc. Rev.* **2010**, *39*, 35997-3611.
2 C. Schmuck, W. Wienand *J. Am. Chem. Soc.* **2003**, *125*, 452-459.
3 G. Gröger, C. Schmuck et al. *Chem. Commun.* **2009**, 698-700.
4 M. Merschky, C. Schmuck et al. *Chem. Eur. J.* **2010**, *16*, 14242-14246.
5 C. Schmuck, C. Mayer et al. *Angew. Chem. Int. Ed.* **2010**, *49*, 8747-8750.

Hierarchical self-assembly of dinuclear helicates

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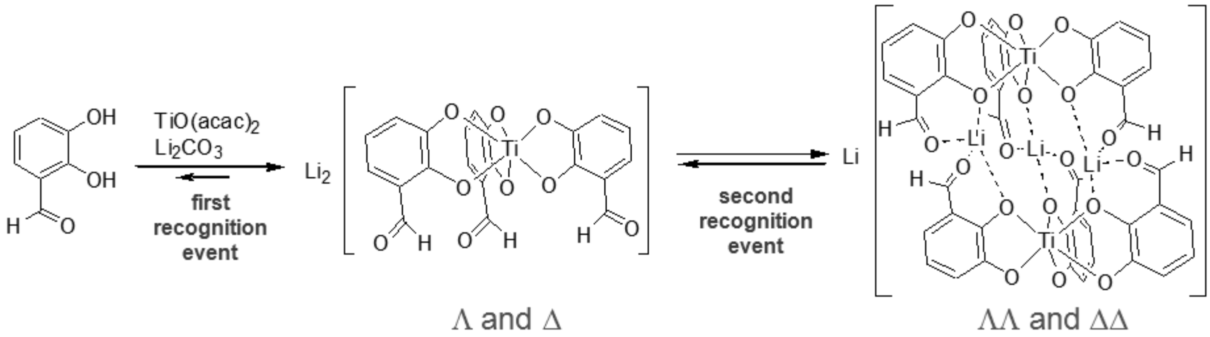
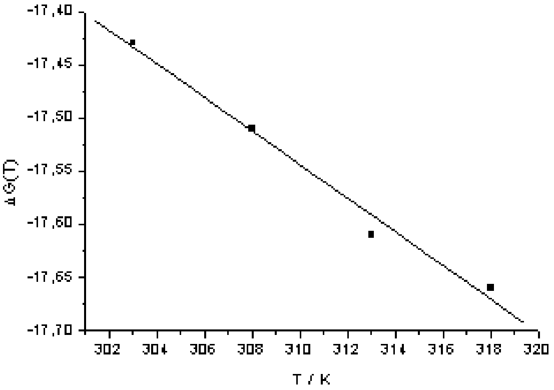
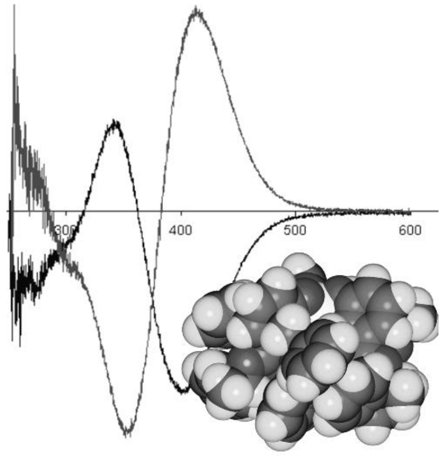
Helicate –type complexes with lithium ions as spacers are obtained in hierarchical self-assembly processes from carbonyl substituted catechol ligands and titanium(IV), gallium(III), cis-dioxomolybdenum(VI) or boron(III) in the presence of lithium ions. In solution the "dimeric" compounds are in equilibrium with the monomers. The thermodynamics of the dimerization process were investigated and the complexes were modified to introduce e.g. chiral groups or dendritic side chains.







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Recognition requires structural constraint, requires low entropy! Right?

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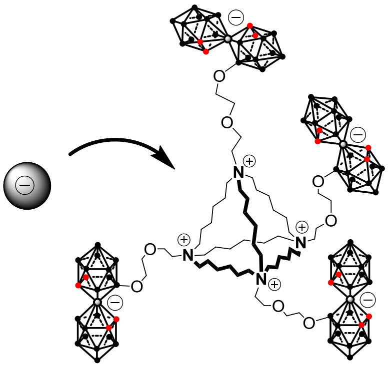
Department Chemie, Technische Universität München

Molecular associations do not necessarily furnish structurally well-defined host-guest complexes. In fact, many instrumental methods currently in use to detect and quantify intermolecular stickiness report on time- and position-averaged ensembles, thus preventing the immediate experimental assessment of the structural integrity. The distinction whether host-guest binding results in a unique and exclusively populated complex or rather represents a rapidly interconverting series of possibly quite different structures, however, is of utmost importance for the function and use of the host-guest pair and therefore plays the leading role in the design of artificial receptors. For instance, the success of supramolecular applications like self-assembly or organocatalysis depends on the unperturbed spatial arrangement of the host-guest pair, whereas two-phase extractions or carrier-mediated transport across membranes have more relaxed requirements in the positional correspondence of the binding partners.



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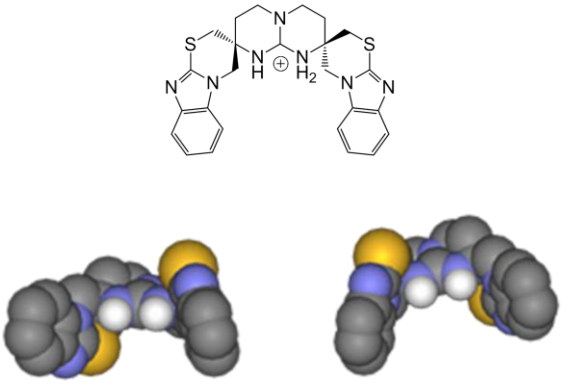

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One way to learn more about the structural fuzziness in supramolecular interactions takes the global energetics as determined by calorimetry as a guide. Modern isothermal microcalorimetry (ITC) allows the convenient and accurate, rapid and destructionless determination of thermodynamic state functions opening the door to inspect the role of entropy in host-guest complexations. Guided by cases taken from the complexation of anions by abiotic receptors, e.g. A and B, the magnitude, origin and influence of the entropy component in molecular recognition are evaluated. Special emphasis is placed on the assessment of entropy as the dominant driving force in ionic interactions, the distinction of intrinsic versus solvent contributions, and on efforts to create a singular host-guest binding mode as required in the enantio-recognition of chiral anions in a special example of ion pairing.

Adaptive Supramolecular Nanostructures in Aqueous Medium

Boris Rybtchinski

Weizmann Institute

Self-assembled systems, whose structure and function can be reversibly controlled in situ are of primary importance for creating multifunctional adaptive materials. We will present our work on design, synthesis, fundamental properties and functionality of supramolecular polymeric systems and porous nanoscale networks in aqueous media. These systems are robust, yet adaptive, showing multiple stimuli-responsiveness, accompanied by switching of optical functions and mechanical properties. We will also present our work on recyclable supramolecular membranes.

Cyclopeptide-Derived Anion Receptors

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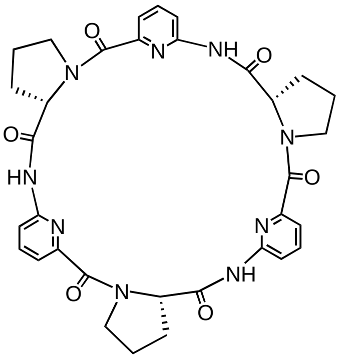
Anion recognition in aqueous solution was for a long time the domain of receptors containing multiple positive charges and/or metal ions while interactions of neutral receptors with anions were believed to be too weak to be efficient in water.[1] Independent work in several groups has shown, however, that even neutral receptors which interact with anions only by hydrogen bond formation can possess considerable anion affinity in aqueous media. One example is cyclic hexapeptide **1** containing L-proline and 6-aminopicolinic acid, which binds inorganic anions (halides, sulfate) in 80% water/methanol by sandwiching the guests between two interdigitating cyclopeptide moieties.[2]



1

To elucidate the reasons for the unusual properties of **1** we systematically varied the structure of this cyclopeptide, for example, by replacing proline with hydroxyproline subunits or amide groups with triazole rings.[3] In addition, we converted the 2:1 complexes into 1:1 complexes by covalently linking two cyclopeptide rings together.[4] Systematic variation of the linker then showed that while affinities of bis(cyclopeptides) toward a given anion are not significantly affected by linker structure, there are profound differences in the thermodynamics of anion complexation.[5] Finally, we also studied the influence of the number of linkers on anion affinity. Introduction of a second and a third linker was expected to cause a substantial increase in anion affinity. While this has indeed been observed in some cases, there are exceptions.[6] This presentation summarizes our different approaches to study and improve the anion binding properties of **1** and related derivatives.

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Dynamic peptides as biomimetic receptors

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A dynamic combinatorial library (DCL) of peptides was created using the disulfide-exchange reaction of cysteines. Three cyclic peptides were found to be selective receptors for carbohydrates in water. One of these, HisHis, formed preferentially in a DCL in the presence of the neurotransmitter NANA, while TyrTyr was identified to interact with trehalose. When adding α-Methylfucopyranoside into a library of tripeptides, the oligomer ThrThr was amplified. Upon identifying the amplification with HPLC-MS, NMR titrations and ITC titrations were done to obtain the stochiometry of the complex and the binding constants. In case of the HisHis, this oligomer forms a 2:1 complex with the NANA, while the other two oligomers form a 1:1 complex with the introduced sugars. The interaction is also highly selective because other sugars did not show any interactions with the oligomers. [1]

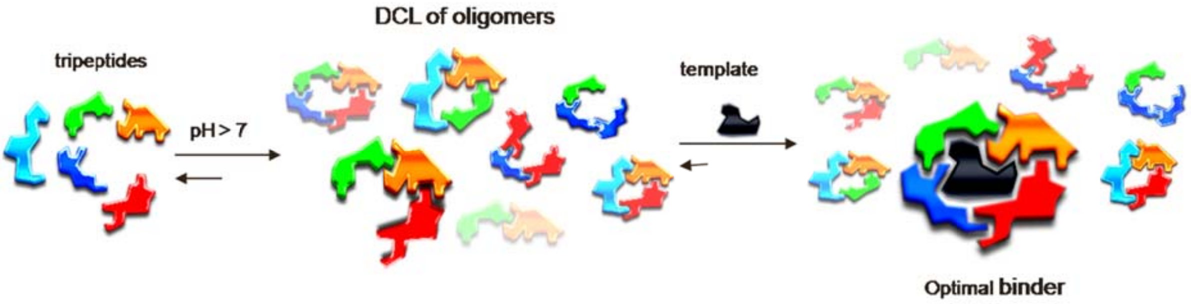

Figure 1. Schematic overview of the DCL-concept.

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Via Dynamic Formation of Covalent Bonds to Functionalized Cage Compounds - From Molecules to Materials

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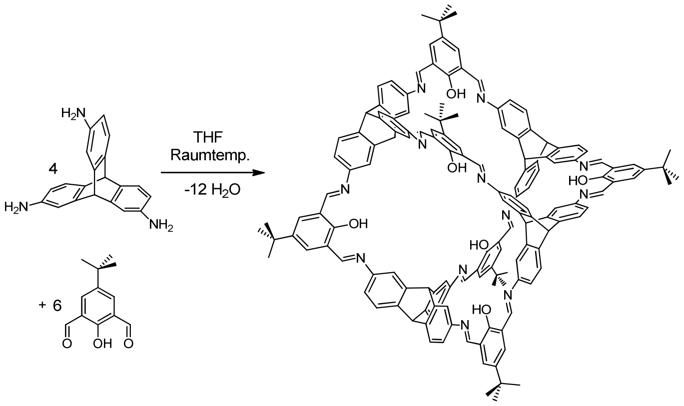
In comparison to extended polymeric structures, porous organic materials deriving from self-assembling discrete organic molecules are quite rare.[1] This can usually be attributed to two major facts: 1st: it is still difficult to predict the self-assembling process just by the structural information molecules are giving and therefore it is not easy to create crystalline porous compounds by the self-assembling of small molecules.[2] 2nd: those porous organic assemblies often collapse, when solvent is removed in vacuo and no accessible pores are remaining after the evacuating process.[1] Those obstacles can be circumvented by synthesizing shape-persistent cage compounds with cavites that remain even after removing inclathrated solvent molecules in vacuo.[3]



Recently we introduced the synthesis of a rigid shape-persistent cage compound by dynamic covalent bond formation.[4] These cage compounds show extraordinary high specific surface areas (BET: 1375 m^2/g) and good selectivities for gas adsorption (CO_2: 9.4 wt%, CH_4: 0.98 wt%).[5] Here, the synthesis and material properties of various functional organic porous cages based on Schiff base condensations are presented.

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Self-assembled paramagnetic dendrimer mimics:
a new class of nano-sized MRI contrast agents

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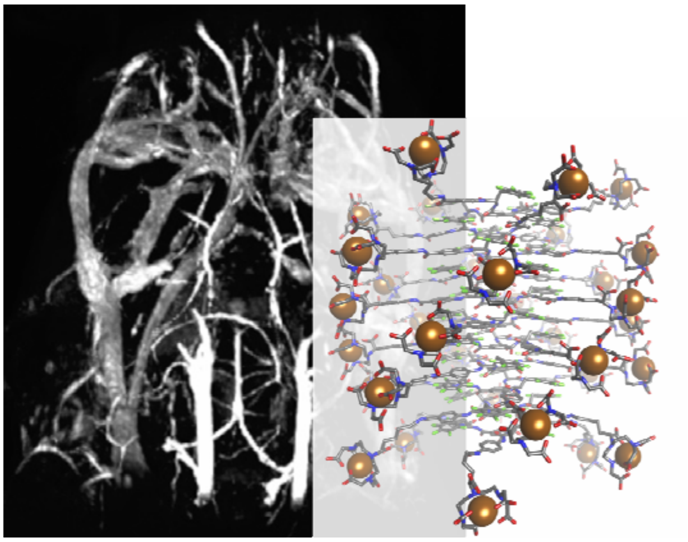
A challenging target in the non-covalent synthesis of nanostructured functional materials is the formation of uniform features that exhibit well-defined properties, *e.g.* precise control over the size, spatial resolution and the degree of functionalisation.

We have developed a strategy based on self-assembling discotic amphiphiles that leads to the control over stack length and shape of ordered, chiral columnar aggregates in water. By balancing out attractive non covalent forces with electrostatic repulsive interactions, we are able to switch from elongated, rod-like assemblies to small and discrete objects. [1, 2] Analogous to many systems found in biology, mechanistic details of the self-assembly pathways emphasise the importance of cooperativity as a key feature that dictates the physical properties of the produced supramolecular polymers.

By controlling the size of one dimensional columnar assemblies with diameters in the range of 6 nm, we obtained the supramolecular equivalent of a dendritic polymer. Applications of these scaffolds as contrast agents in magnetic resonance imaging (MRI) have revealed superior properties compared to traditional covalent macromolecules. Some recent developments and in vivo experiments will be discussed.



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Molecular Recognition of Cyclodextrin Vesicles

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Cyclodextrin vesicles are dynamic chemical systems that respond to multivalent molecular recognition [1]. We report here the formation of an artificial glycocalix based on unilamellar bilayer vesicles of amphiphilic β-cyclodextrins which were decorated with maltose and lactose at their surface via host-guest interactions. To this end, maltose and lactose were conjugated with adamantane [2]. The carbohydrate – adamantane conjugates strongly bind to β-cyclodextrin ($K_a \sim 4 \times 10^4$ M^{-1}). The maltose decorated vesicles agglutinate in the presence of the lectin Conacavalin A, whereas the lactose decorated vesicles agglutinate in the presence of Peanut Agglutinin. The agglutination depends on the surface density of guest carbohydrates. The orthogonal multivalent interaction in the ternary system of host vesicles, guest carbohydrates and lectins was investigated by using isothermal titration calorimetry (ITC), dynamic light scattering (DLS), UV-Vis spectroscopy and cryo-transmission electron microscopy (cryo-TEM). It was shown that the agglutination is reversible and the non-covalent interaction can be broken by the addition of competitive inhibitors such as glucose or β-cyclodextrin.

Furthermore we investigated the interaction of cyclodextrin vesicles with DNA. It was observed, that cyclodextrin vesicles decorated with spermine aggregate in the presence of DNA. The aggregates were investigated with cryo-TEM, UV-Vis and DLS measurements.

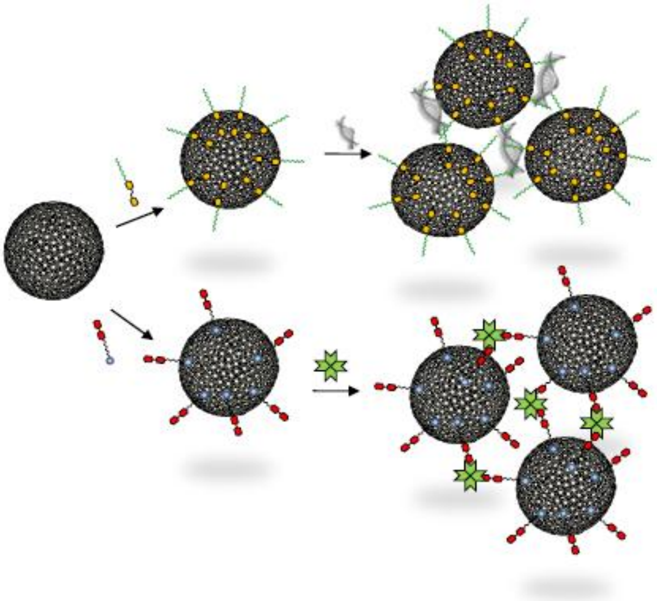

Fig.1: Schematic representation of the DNA induced aggregation of CD vesicles in the presence of a spermine guest molecule (top) and Concanavalin A induced aggregation of CD vesicles in the presence of a maltose guest molecule.(bottom)

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Molecular Recognition of Nucleotides and Nucleic Acids

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Many physiological functions of life, are controlled by the interplay between natural or synthetic agents with their corresponding receptors in the human body.[1] This process of molecular recognition is achieved by the combination of many weak non-covalent interactions.[2] Our work concentrates on the recognition of mononucleotides as well as RNA and DNA in aqueous solution. Nucleotides are ubiquitously present in biological systems and exercise key roles in many cellular functions like the transport across membranes, energy and electron transfer processes, DNA synthesis and cell signaling.[3] Since these complex events are not entirely understood to this date, the synthesis of artificial nucleotide receptors as model systems is worthwhile. Furthermore, current challenges in diagnostics and emerging therapies for the treatment of genetic diseases call for new and improved technologies for the targeting of nucleic acids. Although it is essential for e.g. replication, transcription or regulation processes, RNA has only recently come to focus as an attractive target for therapeutic uses.[4] Therefore, small artificial molecules that are able to specifically interact with DNA or RNA are of great interest as they open new pathways for the development of diagnostic probes, drug design and delivery.[5]

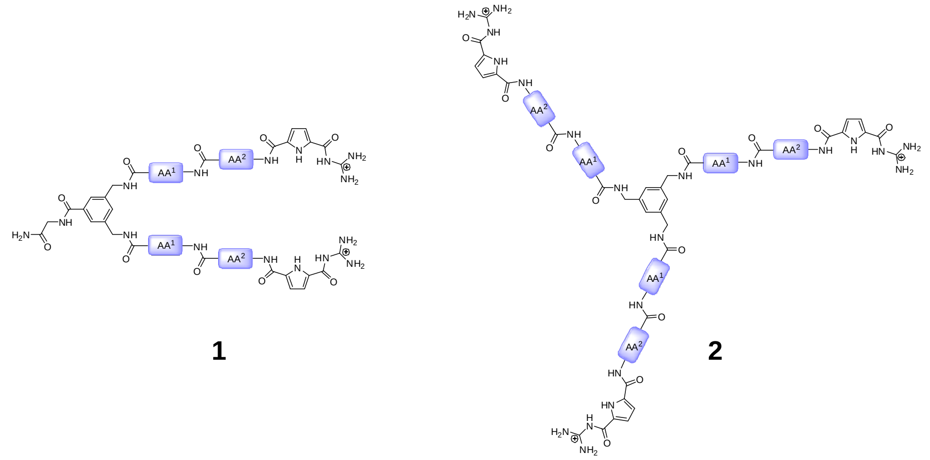

Figure 1: Illustration of the dipodal (**1**) and tripodal receptor (**2**)

By means of microwave assisted SPPS we developed receptors **1** and **2**, which are able to effectively bind their substrates at physiological conditions. They consist of two or three peptidic arms that include the guanidinium carbonyl pyrrole moiety as efficient binding motif for oxoanions.[6] The positions AA^1 and AA^2 are variable, allowing for the introduction of structural and functional diversity by integrating different amino acids into the two arms. The binding studies we conducted show that **1** selectively binds to nucleotides. Both molecules bind very strongly to DNA with binding constants up to 10^7 M^{-1} and show promising abilities for the transfection of cells with plasmid DNA.

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Switching and Reactivity inside Coordination Cages and Rings

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Supramolecular coordination cages are promising systems for the application as tailor-made cavities for the rate-enhancement and selective control of chemical reactions in their interior.[1] We recently prepared the new cages **1** - **3** quantitatively in solution (as characterized by NMR, DOSY, ESI-MS, X-Ray and AFM methods).[2] The two Pd(II) or Pt(II) centers are surrounded by four rigid and concave bis-monodentate pyridyl-donor ligands. Due to their position and charge, the metals can act as anchors for the quantitative binding of bis-anionic guests of appropriate size. Based on these findings, we managed to develop a new method for making rotaxanes[3] and a system capable of light-initiated crystallization.[4] Towards the immobilization of potentially catalytic centers in the center of molecular cage **3**, we were able to incorporate a variety of metal complexes and clusters inside the cavity. So far, we succeeded in the encapsulation of *one* Fe(II) (ferrocene-bis-sulfonate), *three* Pt(II) (Magnus' Salt: $\{[PtR_4][PtX_4]_2\}^{2-}$, R = NH_2Bu, Py; X = Cl, Br) and *six* Mo(VI) (hexamolybdate) inside cage **3**. Furthermore, we synthesized cage **2** which displays four trityl groups pointing inside the cavity that can be used as acid cleavable tethers or Lewis acidic reagents.

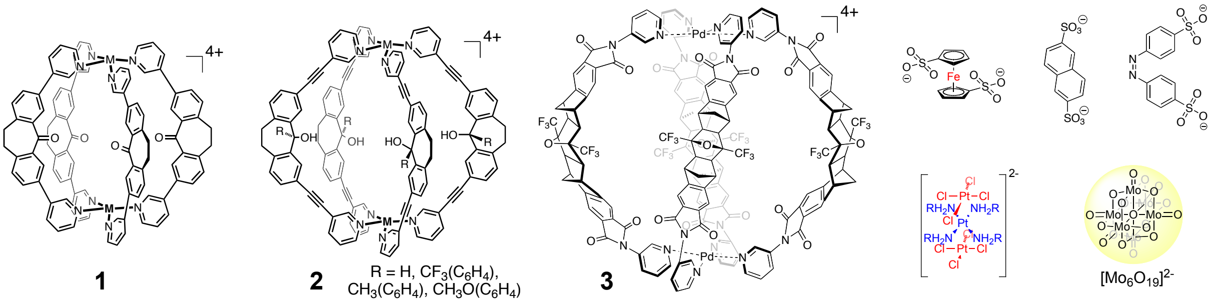

Figure 1. Coordination cages **1** – **3** and a selection of our most welcome guests

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Supramolecular Chemical Biology:

Controlling Protein Assembly with Supramolecular Chemistry

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Supramolecular chemistry has primarily found its inspiration in biological molecules, such as proteins and lipids, and their interactions. Currently the supramolecular assembly of designed compounds can be controlled to great extent. This provides the opportunity to combine these synthetic supramolecular elements with biomolecules for the study of biological phenomena. Supramolecular elements can for example be ideal platforms for the recognition and modulation of proteins and cells. This lecture will focus on two concepts in this respect.

Synthetic host-guest systems can be applied for the controlled and reversible dimerization of proteins. Host-guest elements can for example be appended to proteins to induce or stabilize weak protein heterodimerization. Other supramolecular host molecules can be used to recognize specific protein elements and applied as supramolecular inducers of protein homodimerization. As an example, caspase homodimerization is a key step in the activation of their enzymatic activity. Control over this protein homodimerization allows investigating the molecular processes underlying the activation mechanism. We have generated a so-called supramolecular inducer of dimerization that can act as an allosteric modulator of caspase-9 dimerization and allows highly efficient and reversible activation of caspase activity.

Self-assembling supramolecular architectures provide attractive scaffolds for the organized display of biological ligands. Their dynamic nature allows for simple non-covalent synthesis of multivalent structures and for the introduction of multiple different functionalities. As an example, columnar supramolecular polymers can be decorated with biological ligands such as sugars and peptides for the recognition of cells or for the assembly of proteins along the supramolecular framework.

Supramolecular Nanostructures through Electrostatic Self-Assembly of Macroions and Organic Counterions

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The design of supramolecular nanostructures holds high promise, as self-assembly allows the production of a variety of structures for applications for example as carrier systems or sensors. Particular potential lies in assemblies that can respond to external triggers while a macromolecular component can provide stability and processability of the supramolecular objects. In this talk the recently developed concept to “electrostatic self-assembly” for the formation of supramolecular structures in solution will be presented. In this approach, polyelectrolytes and multivalent organic ions build well-defined and stable nanoassemblies. Aggregates with narrow size distribution and varying shape such as spheres, cylinders, vesicles and networks can result.[1-7] For assemblies of weak polyelectrolytes, aggregation can be repeatedly switched “on” and “off” through pH.[2,5] A particular challenge in this area is the formation of “nano-objects” with a controllable size. Recently we were able to build supramolecular particles the size of which can be triggered by light.[8] Detailed characterization by static and dynamic light scattering, AFM and small-angle neutron scattering as well as zeta-potential measurements and centrifugation experiments yield insight into driving forces and structural control in the self-assembly process. In addition, quantitative measurements of thermodynamic parameters will be considered.

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Detection of Explosives by Supramolecular Interaction

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Inexpensive and mass producible sensors represent one of the keys to affordable security applications. We develop and apply high fundamental frequency quartz microbalances (HFF-QMB) as technology platform. The high frequency combined with appropriate supramolecular affinity coatings on these QMBs allow a fast and direct determination of airborne analytes. In particular, the tracing of home-made peroxides like TATP and HMTD is usually challenging but can be performed with our HFF-QMB system. The advantages are an on-line measurement of the desired analytes. Identification of the peroxides explosives is achieved by an array of at least three micro balances equipped with orthogonal affinities. Most remarkably, the system operates not only in a closed laboratory system but can be exploited for an application close scenario as an open system. With appropriate supramolecular affinity coatings on the QMBs the scope of the method can be expanded to the continuous and direct detection of 2,4,6-trintrotoluene (TNT).

In addition, a novel way for the safe handling of authentic material of peroxide explosives will be demonstrated representing the key for the evaluation of novel detection systems such peroxide explosives.

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Self-Assembly of Linear and Discotic Molecules. Mechanisms and Amplification of Chirality

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In this communication, we present the investigations carried out in our research group to elucidate the mechanisms, isodesmic or cooperative,[1] followed by a number of linear and discotic molecules to self-assemble. In addition, we will also present the amplification of chirality observed in the studied molecules.[2,3]

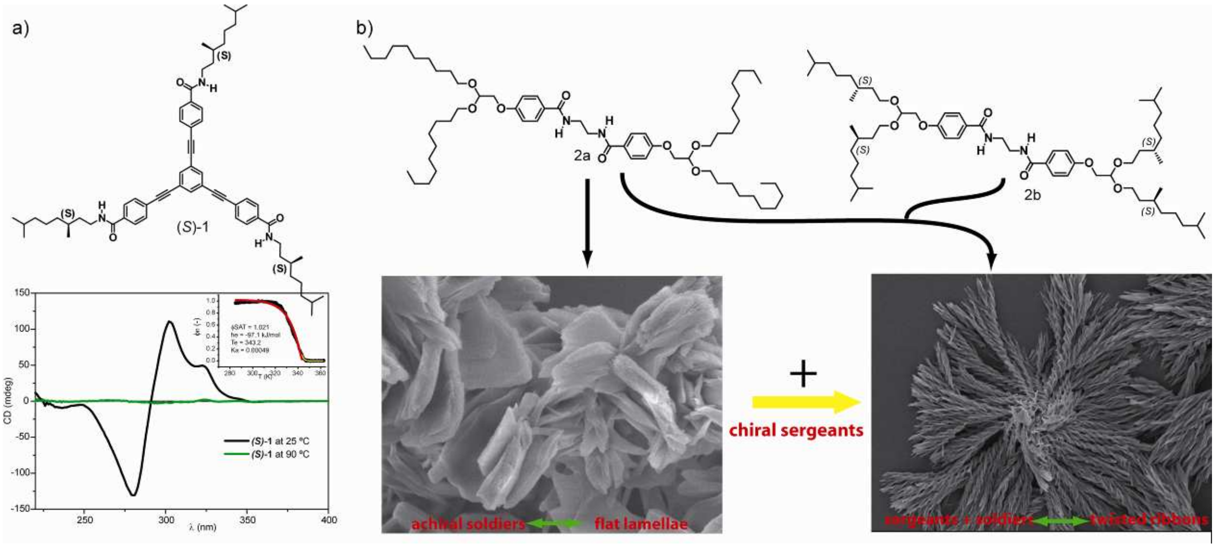

Figure 1. (a) Chemical structure, circular dichroism and melting curve of the π-extended trisamide **(*S*)-1**; (b) Chemical structure of bisamides **2a** and **2b** and SEM images of the pristine **2a** and the mixture of **2a** with 5% of **2b**.

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Abstracts of Posters

Triple-stranded Dinuclear Complexes of Rare Earth Metals

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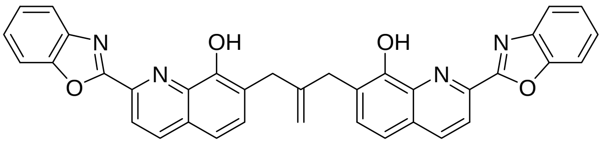
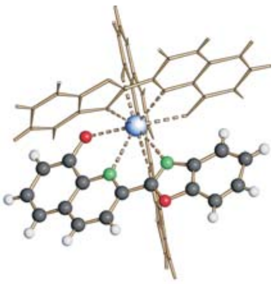
Helicates are of particular interest in supramolecular chemistry and can be obtained by coordination of two or more ligands to at least two metal centres. Helicates with trivalent lanthanides possess unique properties. Highly efficient near-infrared emission is observed due to indirect excitation by the ligands and energy transfer processes to the metal centre. Among other things NIR-emitters of that kind are attractive to optical devices.



(a)



(b)

A new hexadentate ligand based on 8-quinolinol is prepared (a). The building block as well as the hexadentate ligand were applied to complexation studies with lanthanide ions, resulting in the expected 3 : 1 and 3 : 2 complexes, respectively. A crystal structure of the Nd(III)-complex shows that the ligand may form helical structures in the corresponding triple-stranded dinuclear complexes (b).

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Synthesis of porphyrin based coordination cages

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The supramolecular chemistry can be divided by the products formed into two domains: coordination polymers and discrete molecules. Both of them can be used for host guest chemistry. Our research group mainly focuses on discrete molecules, which are less investigated up to now. The symmetry and the geometry of the building blocks define the topology and shape of the coordination cages formed. Various modified derivatives of a C_3-symmetric ligand combined with diverse metal ions such as Pd^{2+}, Zn^{2+} or Cd^{2+} have been successfully implemented [1, 2]. In the supramolecular coordination chemistry of porphyrin-based ligands, the formation of polymers is the dominant topic in the literature. The focus of interest of our research group is again on the formation of coordination cages with C_4-symmetric porphyrin derivatives (Fig.1). The combination of square-planar palladium-complexes and porphyrin derivatives results in coordination cages. One of these completely analyzed compounds is shown in Fig. 2. The host-guest chemistry behavior of such a trigonal prism is an important part of our research [3, 4]. Single crystal structure analysis and a large variety of NMR spectroscopic experiments give insight into changes of symmetry, dynamic processes and host guest interactions.

The poster presents coordination cages based on *meso*-tetrapyridyl porphyrin and their host-guest chemistry.

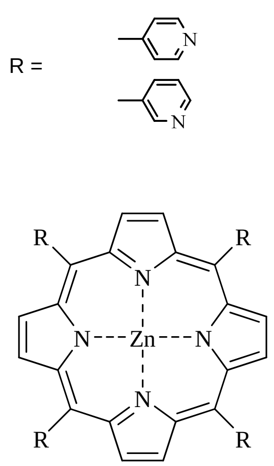

Figure 1: C_4-symmetric *meso*-tetrapyridylporphyrin ligand

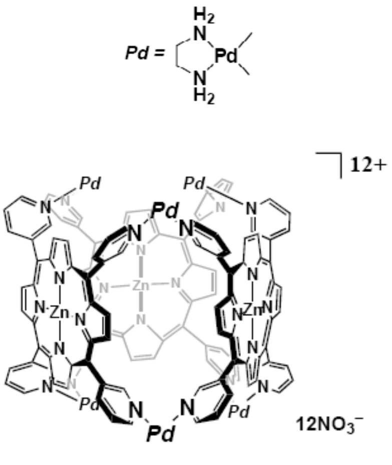

Figure 2: Trigonal prism [4].

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FRET based distance measurements on vesicle surfaces - Towards the dynamic recognition of multivalent target molecules

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Mimicking recognition processes at natural cell membranes we recently reported synthetic vesicles with multi-receptor surfaces as chemosensors for small biomolecules.[1] Based on these results we want to develop a simple model system for the dynamic recognition of multivalent target molecules by multiple membrane-embedded receptors equipped with FRET labels.

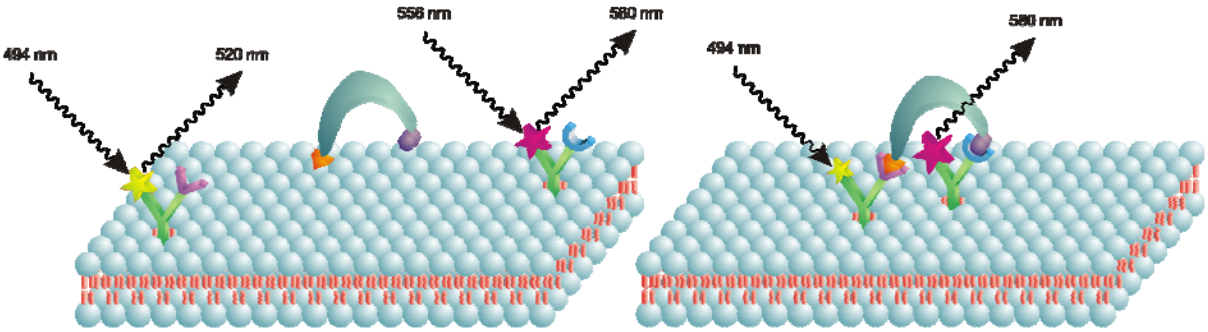

Figure 1. A multivalent biomolecule with two different ligands binding to two fluorescent labeled receptor molecules, embedded in a membrane and detected via FRET.

For preliminary studies the metal complex coupled donor-dye was combined with an acceptor-dye that was not tethered with a second charged metal complex. The influence of analyte binding towards the FRET distances was investigated by emission titrations. Increasing amounts of analyte (PP_i) cause separation of receptor bound dyes and their FRET partners due to sterical enhancement of the metal-complex binding sites and interruption of attractive interactions between receptors and dyes. As a result dye displacement is shown by a lower value of energy transfer.

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Synthesis of Highly Fluorinated Cyclodextrins and their Host-Guest Interactions with Fluorinated and Non-Fluorinated Guests

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Cyclodextrins are one of the most investigated host molecules in supramolecular chemistry. Besides the hydrophobic effect, various non covalent bonds (hydrogen bonding, electrostatic interaction, van der Waals forces) between host and guest molecules can contribute to the formation of an inclusion complex. So far, the role of fluorine-fluorine interactions in host-guest binding of cyclodextrins has not been investigated because of the difficulty to make fluorinated cyclodextrins watersoluble.[1, 2, 3] Here we report the synthesis of water-soluble trifluoroethanethiol substituted cyclodextrins.[4] The primary side of α-, β- and γ-cyclodextrin was chlorinated at the C-6 position and substituted with trifluoroethanethiol. To make the cyclodextrins water-soluble, the secondary side was functionalized with triethyleneglycol. The cyclodextrins were obtained in good yields and purity. The host-guest interactions were investigated by ITC and NMR-titration. The log K_a values show a stronger host-guest interaction between fluorinated cyclodextrins and fluorinated guests than with non-fluorinated guests.

In addition, we intend to inverstigate host-guest interactions in fluorinated phases. For this aim highly fluorinated cyclodextrins where synthesized by thiol-ene click chemistry, which should be soluble in fluorinated phase.

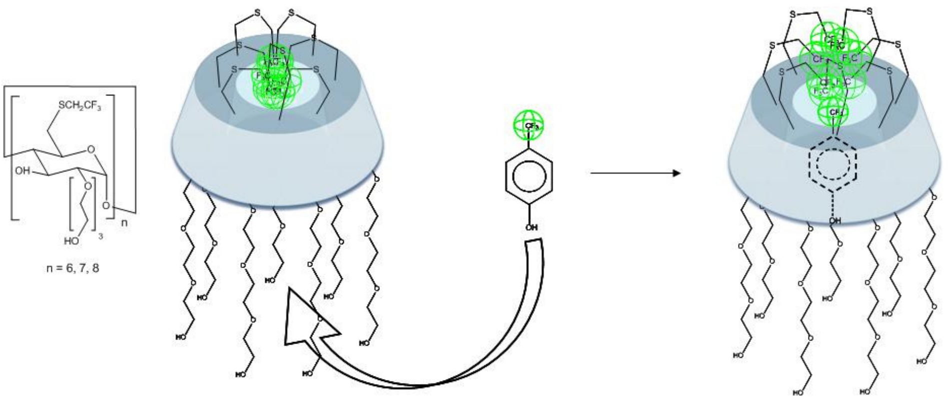

Figure 1. Enhanced host-guest interaction between fluorinated guest and fluorinated cyclodextrin.

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Membrane bound amphiphilic peptides as Carbohydrate receptors

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Carbohydrates play a crucial role in various recognition processes in nature and are present in form of the glycocalix on all mammalian cells. They are, for example, involved in the inflammatory process, they determine the blood type, mediate cell-cell adhesion and recognition and are involved in cell-cell communication. Furthermore the glycocalix is subject to various dynamic processes due to cell growth and function and different infections or malign transformation of cells lead to a change in its structure.[1]

Thus artificial carbohydrate receptors are of great interest. In a previous work it could be shown that dimers of cyclic tripeptides are able to specifically bind different carbohydrates.[2] In this project amphiphilic peptides are utilized to introduce carbohydrate binding peptides to the surface of Lecithin vesicles. These are able to specifically interact with different carbohydrates and could be used as drug delivery systems or model systems for biology.

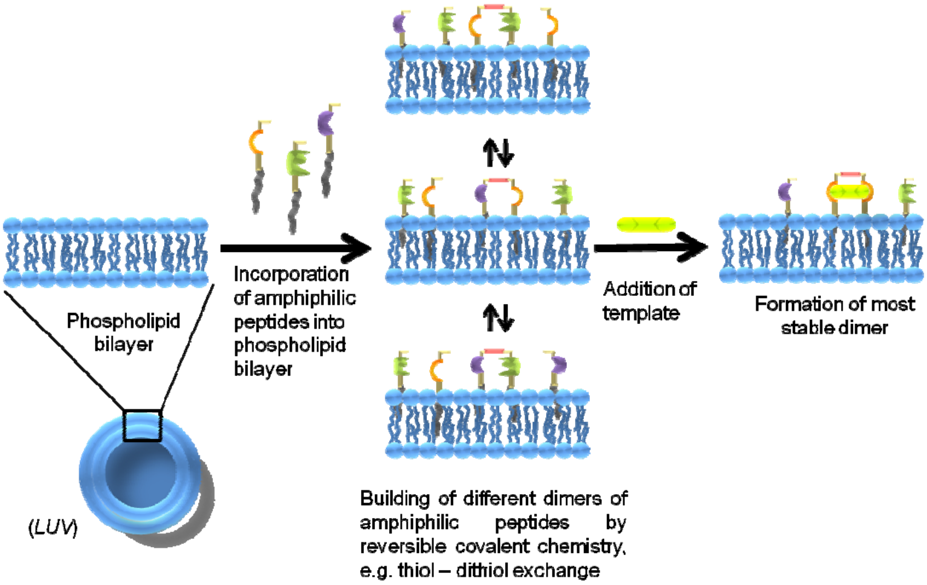

Figure 1. Scheme for the incorporation of amphiphilic peptides into liposomes and the interaction with carbohydrates.

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Entirely Artificial Signal Transduction with a Primary Messenger

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An artificial system has been devised for messenger-induced transmembrane signaling. External addition of a primary messenger molecule (DET, Figure 1a) thus leads to formation of a heterodimeric complex of two transmembrane units bearing tryptophan–dansyl (Trp–Dan) donor–acceptor pairs, which, in turn, stimulates a strong FRET effect on the opposite intracellular side of the membrane. The readout can be enhanced and transferred into the visible range by external eosin addition, thus producing a multi-FRET system. Spectral changes on DET addition demonstrate intracellular FRET with unaltered eosin emission intensity (Figure 1b), which is an experimental evidence for true signal transduction. Signaling can thus be visible to the naked eye (Figure 2c).[1]

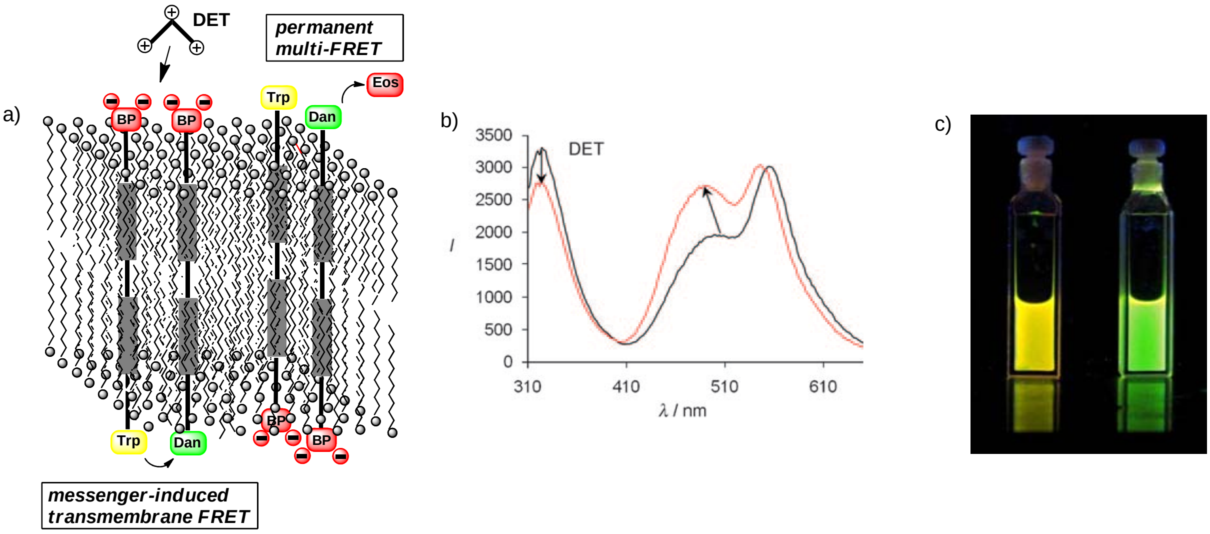

Figure 1. a) Induced FRET signal (inside) and permanent multi-FRET (outside); b) Fluorescence emission spectra before and after addition of DET; c) Cuvettes before and after addition of DET

The intention in our current work is the exchange of the signaling sites, in order to synthesize transmembrane units, which are able to trigger a chemical reaction with the release of a second messenger. A further challenge is the pre-orientation of the transmembrane units for inherent unidirectionality.

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Coupling of self-assembly and metabolism to protocells

Ralph Bosmans, Prof. L. Brunsveld

Getting a better understanding of the structural and functional complexity of the cellular environment is one of the key interests of molecular researchers. In the field of chemical biology researchers try to mimic parts of these cells. In particular, because the development of a synthetic cell gives inside in its functioning but also directly relates to the crucial questions regarding to the definition and the origin of life.

The building of synthetic cells is still in its conceptual stage and the focus of this research is on the cellular membranes. The permanent nature of the supramolecular membranes developed so far do not compare well to the extensive dynamic compartmentalization seen in natural systems. Natural self-assembled structures such as the phospholipids membranes are continuously formed and disassembled. Crucial in natural systems is the existence of feedback loops controlling the self-assembly of these supramolecular membranes, which are essential in self-healing and self-replication. So far, it remains a challenge to integrate feedback to the self-assembly process.

The introduction of such a feedback mechanism requires the regulation of chemical reactivity, controlled by the formation of self-assembled structures. In this research we try to develop a self-organizing system that shows how feedback loops triggered by molecular assembly can lead to macroscopic self-organization. The way we want to introduce feedback mechanisms upon molecular assembly is by using protein dimerization on the membrane surface. This controlled dimerization could lead to the activation of an enzymatic pathway, which in turn has either a positive or negative influence on the initial membrane formation.

In initial experiments we are working on the enzyme caspase-9. This protease is able to cleave a specific peptide motif, which could be incorporated in a membrane building block. So far, we successfully expressed and purified caspase-9 containing an N-terminal cysteine. For incorporation of the caspase-9 into the membrane, we are currently working on the coupling of the caspase-9 to a hydrophobic tail using the N-terminal cysteine.

Cucurbit[8]uril mediated supramolecular protein dimerization

D. T. Dang, H. D. Nguyen, and L. Brunsveld

Protein-protein interactions control nearly all biological process. Most proteins have multiple interaction partners and external control over these interactions is only possible in very limited cases. For most protein-protein interactions a molecular understanding is missing and concomitantly the molecular tools to control them are not available. Selective induction and control over protein dimerization is therefore an important goal in the field of chemical biology, but the number of successful small molecule approaches is however highly limited. Supramolecular approaches and molecules, could provide strong entries to fill this gap. The supramolecular host cucurbit[8]uril (Q8) is known to selectively recognize and dimerize the aromatic tripeptide Phe-Gly-Gly in aqueous solution[1]. In this study, we designed proteins with N-terminal phenylalanine-glycine-glycine motifs whose induced dimerization is under control by cucurbit[8]uril (Figure 1).

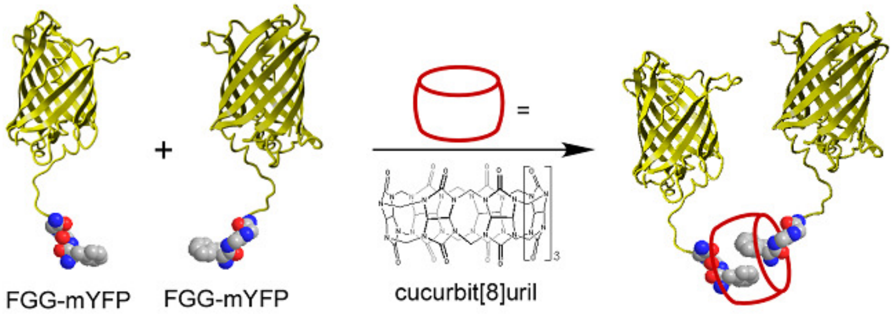

Figure 1. *Dimerization of proteins mediated by cucurbit[8]uril (Q8).*

Reference

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Orthogonal Recognition Domains for Supramolecular Structures

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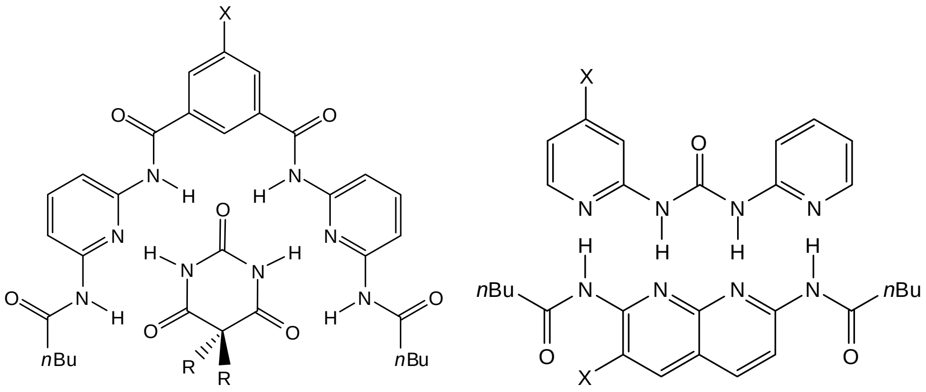
Supramolecular chemistry allows molecular recognition by non-covalent binding. To design supramolecular structures via multiple hydrogen bonds it is necessary to use complementary acceptor and donor patterns. Well defined structures should be obtained if these binding motifs are orthogonal to each other. An example for a molecular receptor was developed by Hamilton which is able to bind barbituric acid by forming six hydrogen bonds in a well defined sequence of acceptors and donors.[1]

Here different Hamilton receptors have been synthesized and used for binding studies with derivatives of barbituric and cyanuric acid. In addition to this angulate molecule also linear orthogonal receptors and donors with four hydrogen bonds have been synthesized and their association constants investigated.[2-4] Several different functional groups X have been attached to the recognition domains to allow a supramolecular assembly.



A comparison of association constants determined by ^{1}H NMR titrations, ^{1}H NMR diffusion experiments, isothermal titration calorimetry (ITC) and osmometry will be presented and discussed. By mixing non complementary recognition domains, the concept of orthogonality was tested, which is fundamental to use these buildings blocks in more complex supramolecular architectures.

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Kinetic studies of the host-guest chemistry of a supramolecular container molecule

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We present the synthesis of a supramolecular container molecule, built up by a triarylphophinoxide spanning over a planar molecular scaffold.[1] The enclosed cavity provides sufficient space for the inclusion of molecules, like e.g. chloroform.[2]

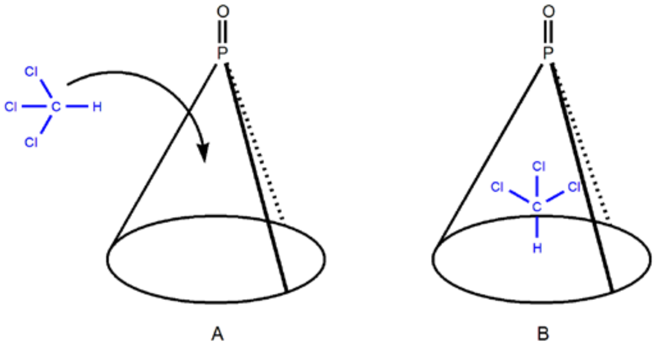

Figure 1. Scheme of the $CHCl_3$ inclusion in the container molecule.

The kinetics of the inclusion and exclusion of chloroform were analyzed by the acquisition of ^{1}H-NMR spectra at different temperatures. A specific NMR signal was used as indicator for the reaction progress, as it is shifted during the reaction.[3]

For further characterization the rate constants and half-lives for the inclusion and exclusion reaction were calculated. Furthermore the thermodynamic quantities $\Delta G^{\neq}$, $\Delta H^{\neq}$ and $\Delta S^{\neq}$ were calculated and analyzed.

The results suggest that reaction entropy is the driving force for this reaction.

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The self-assembly of calcium phosphate hollow spheres as an indication for the supramolecular assembly of amino acids

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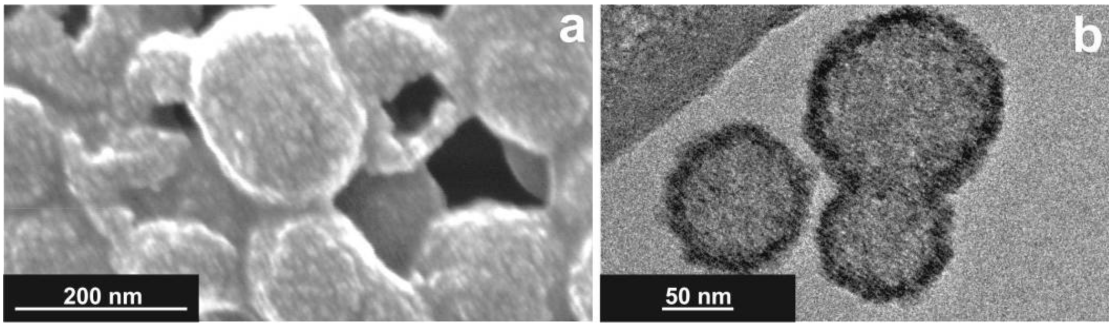
Calcium phosphate is the inorganic mineral of bone and teeth. Hollow calcium phosphate microspheres and nanospheres can be prepared by hard-templating synthesis[1,2] or template-free-synthesis.[3] We have discovered a self-assembly of primary nanoparticles of calcium phosphate into hollow by precipitation of calcium phosphate in water in the presence of amino acids or dipeptides. Then the nanoparticles were mixed immediately with an aqueous solution of the amino acids or dipeptides. The dispersions of the calcium phosphate hollow spheres were analyzed with dynamic light scattering (DLS), nanoparticle tracking analysis (NTA), scanning electron microscopy (SEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM). The size of the hollow capsules was of the order of of 100 to 250 nm.



a) SEM and b) cryo-TEM image of the calcium phosphate hollow spheres (Recorded by N.A.J.M. Sommerdijk and A. Dey, Eindhoven).

We propose that the formation of the hollow spheres involves a template of the amino acids or dipeptides around which the calcium phosphate nanoparticles assemble. Such supramolecular aggregates were detected by NTA, and atomic force microscopy with a diameter of 100 to 150 nm.

We thank Dr. K. Ganesan, Prof. Dr. N.A.J.M. Sommerdijk, Dr. A. Day, Dr. D. Schunk, Prof. Dr. C. Mayer, T. Fenske, Prof. Dr. C. Schmuck, and PD Dr. W. Schrader for experimental assistance.

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Metal Ion-Driven Molecular Hinges with Adjustable Amplitude

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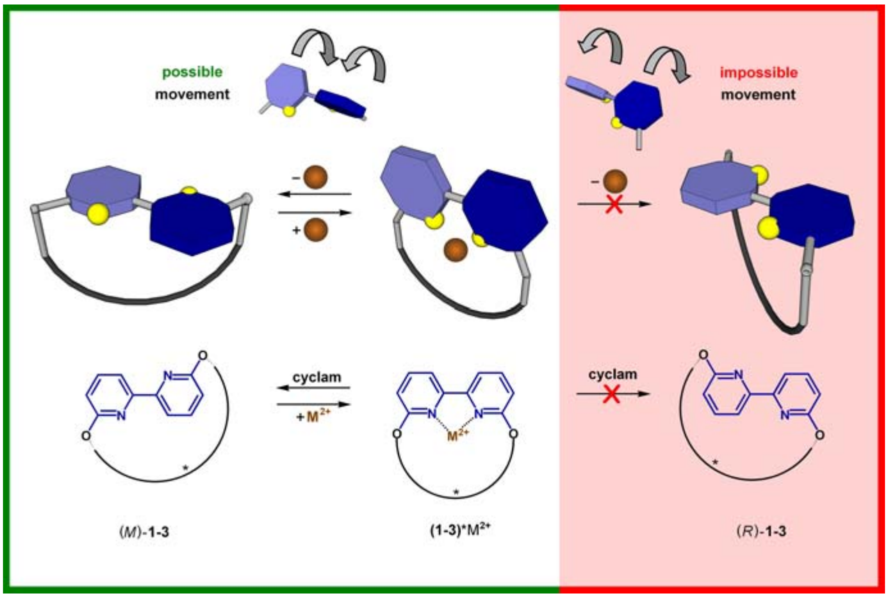
A basic requirement for each molecular system which is supposed to perform work is a synchronized and unidirectional movement which can be achieved by a change of configuration or conformation which is controllable by external stimluation.[1] Molecular hinges based on a bipyridine unit work unidirectionally and are able to reach an amplitude of motion which amounts to about 180°.[2] To analyze if it is possible to adjust the height of the unidirectional amplitude of motion, several molecular hinge systems with a 2,2'-bipyridine unit as functional element were designed and stimulated with various divalent metal ions in different solvents.[3] The configurations of the hinges were determined by DFT calculations using B3LYP and the 6-31G* basis set and experimentally verified by 2D NMR NOESY. The stimulation processes were monitored by CD and UV spectra.



Scheme 1: Illustration of a chiral hinge with unidirectional open-close motion.

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Supramolecular rod formation based on guanidiniocarbonyl pyrrole carboxylate zwitterions

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Rods are one – dimensional structures that are widely used in nature like for example in collagen fibrils, connective tissues or actin filaments in muscles. In the last few decades it has become increasingly clear that nature often forms complex structures by self – assembly of smaller components. Inspired by nature many artificial self complementary rod like structures have been investigated.[1] We developed a self – complementary binding motive based on guanidiniocarbonyl pyrrole carboxylate zwitterions. Zwitterion **1 • 1** associates with a dimerization constant of *ca*. $10^{10} – 10^{12}$ M^{-1} in DMSO and is able to form stable dimers even in water.[2] Additional amide bonds at the 3 position of the pyrrole lead to the formation of rod like structures that bundle together on surface.

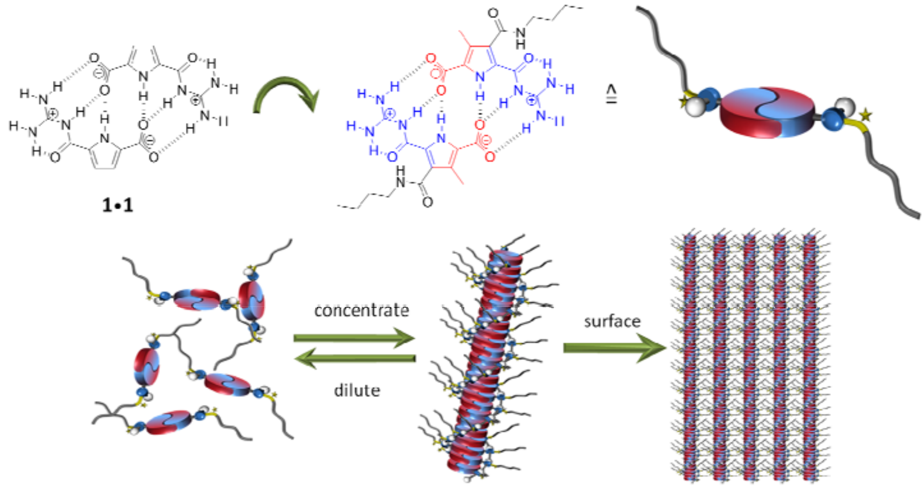

Figure 1. Configuration of zwitterion **1** and schematic formation of rod like structures.

NMR – and UV – dilution studies revealed that the formed aggregates are stable in a concentration range between 40 and 0.1 mM. Below that concentration the aggregates start to dissociate into the zwitterionic dimers. Further studies with AFM and SEM proved the existence of the rod like structures that bundles together to even bigger aggregates on surface.

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Supramolecular metal complexes: anion encapsulation and DNA binding

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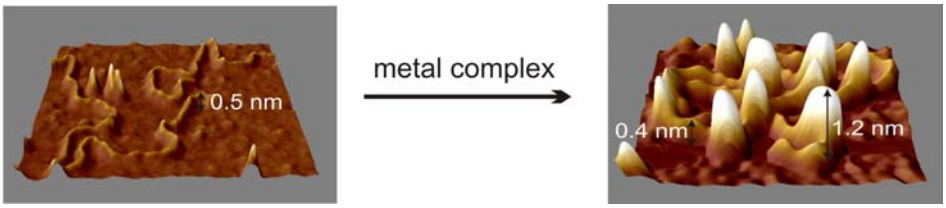
Positively charged discrete supramolecular structures, which are constructed by using organic ligands and metals centres, have recently attracted curiosity in view of their potential to interact non-covalently with DNA [1]. This class of compounds are good alternative to classical DNA binders, since in some cases these interactions are very selective [2].

A series of Pt, Pd and mixed-metal complexes of the N-heterocyclic ligand 2,2'-bipyrazine have been prepared and characterised in our group [3]. Based on our previous work, size and shape of the molecules have been modified by combining different structural units. Two aspects of such complexes were of specific interest: anion binding properties and interactions with double-stranded DNA. Both the high positive charges of complexes and the presence of the π-electron deficient 2,2′-bpz heterocyclic rings facilitate anion binding [4]. Non-covalent binding interactions of metal complexes with linearized plasmid DNA 3.1 (5428 bp) were studied using the AFM technique. It was found that upon interaction dsDNA starts to bend and coil and the long fibres of free DNA are no longer visible.



The synthesis, crystal structures, solution studies concerning the interactions of anions with cyclic homo- and heterometallic complexes and non-covalent interactions with dsDNA of the new self-assembled compounds will be described.

References:

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Acknowledgement: Financial support by the International Max-Plank Research School, COST, DFG and TU Dortmund gratefully acknowledged.

8-Hydroxyquinoline as a Building Block for Artificial Receptors: Binding Preferences in the Recognition of Glycopyranosides

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Artificial carbohydrate receptors using noncovalent interactions for sugar binding[1,2] provide valuable model systems to study the underlying principles of carbohydrate-based molecular recognition processes. Although effective receptor systems have been developed, the exact prediction of the binding preferences of the artificial receptors is still further away and it is hoped that systematic studies towards effective recognition motifs for carbohydrates will contribute significantly to the solution of this problem. Our previous studies showed that acyclic receptors,[2] such as compounds containing a trisubstituted trialkylbenzene core, represent particularly interesting objects for such systematic studies. Depending on the nature of the recognition units and connecting bridges used as the building blocks, a variety of receptors with different binding properties could be obtained.

The aim of the present study was to evaluate the potential of 8-hydroxyquinoline-based receptors (see for example Figure 1) in the complexation of carbohydrates.[3] 8-Hydroxyquinoline unit has been extensively used for the construction of metal ion ligands. In the area of sugar recognition by receptors employing noncovalent interactions the potential of this unit has not been evaluated.

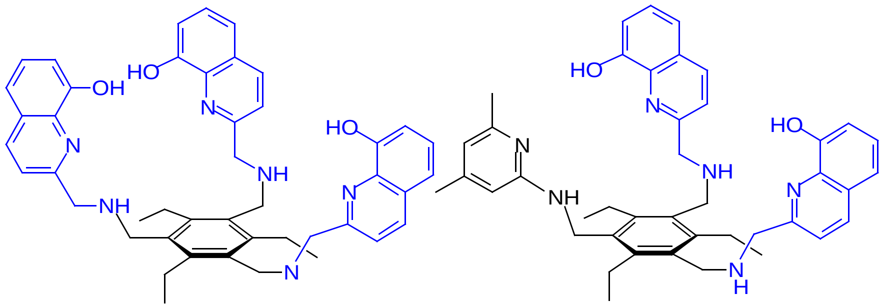

Figure 2. Examples of 8-hydroxyquinoline-based receptors.

The recognition properties of the new compounds were compared with those of the previously studied receptors. In addition, the properties of the 8-hydroxyquinoline-based receptors were compared with those of the quinoline-based compounds. Binding studies in competitive and non-competitive media showed both effective recognition of carbohydrates and interesting binding peferences of 8-hydroxyquinoline-based receptors.

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Design and Synthesis of Biomimetic Carbohydrate Receptors

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Artificial carbohydrate receptors provide valuable model systems to study the basic molecular features of carbohydrate recognition and to find interesting applications e. g. as sensors or drug candidates in the future. Understanding how carbohydrates interact with their protein receptors is of particular importance due to the key roles that sugar molecules play in a variety of biological processes starting from fertilization, embryogenesis, cell-cell communication, extending to such pathological processes as tumor metastasis and infection of cells through bacteria and viruses.

There are a multitude of examples for carbohydrate recognition in apolar solvents, while only a few examples of carbohydrate receptors able to bind their substrates in water are published.[1] Natural carbohydrate binding proteins use complex array of H-bonds to bind the carbohydrate guest. Additionally hydrophobic surfaces are desolvated and undergo apolar interactions (C-H→π) with neighboring aromatic amino acid side chains.

Taking these intermolecular interactions into account led us to design artificial carbohydrate receptors which mimic the binding strategies used in natural carbohydrate recognition domains and which should bind carbohydrates in aqueous media.

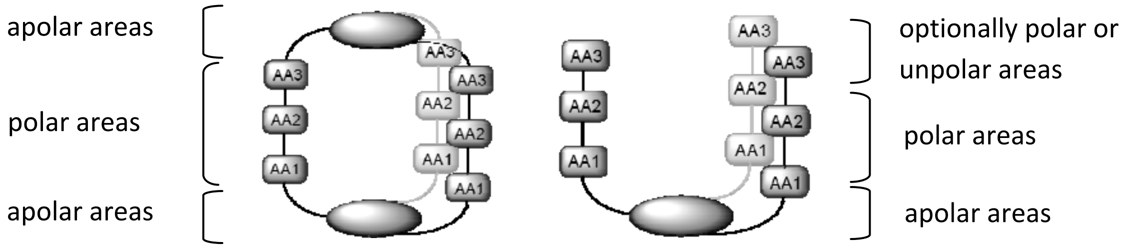

Figure 1. General receptor design.

The artificial receptors consist of three peptidic arms attached to a preorganized aromatic scaffold which can form a cavity shaped like a binding pocket. The receptors are either closed (left) or open (right). First binding studies of a prototype showed the principal usefulness of the receptor design.[2]

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Surface Modification of Gold Nanoparticles Using Template Controlled Ligand Exchange Reactions

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Monolayer protected gold nanoparticle (MPC) have attracted interest in many fields of research because of the easily tunable properties.[1] Another attractive feature is that surface-bound alkanethiols can be exchanged with functionalized thiols allowing the preparation of nanoparticles with characteristic surface functionalities, so-called mixed-monolayer protected gold nanoparticles (MMPC). Decorating MPC with suitable binding sites gives rise to synthetic receptors, for instance, whose properties are characteristically influenced by the gold core.[2] Exchange of the thiols on the surface of a gold cluster is a reversible reaction which proceeds under thermodynamic control. Equilibrium is thus controlled by parameters such as concentration of free thiols in solution, temperature, as well as steric and electronic effects of substituents in the functionalized thiols stabilizing a certain MMPC surface distribution.[3] We speculate that distribution of functional groups on the surface of an MMPC could also be controlled by a suitable template molecule present during the ligand exchange reaction that binds to the substituents of the functionalized thiols. This concept relates to the *molding* strategy in dynamic combinatorial chemistry used for the identification of synthetic receptors.[4] If successful, this approach would extent the repertoire of reversible reactions in dynamic combinatorial chemistry and introduces a new route for the synthesis or optimization of nano-sized receptors. To evaluate the concept we chose the flavine binding MMPC described by Rotello as a model system.[5] A octadecanethiol passivated gold nanoparticle was equilibrated with pyrene and diaminopyridine functionalized thiols. Ligand exchange reactions were carried out in the absence and presence template, and the resulting nanoparticles compared. Results of these investigations are presented in the poster.

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Computational Study of Single Stranded Ln(III) Metallorotamers

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As the effective coordinating nature on rare earth metal ions have been demonstrated in earlier studies[1,2], other ligands containing phenanthroline with hexadentate coordinating nature have been synthesized. They are shown in Figure 1.

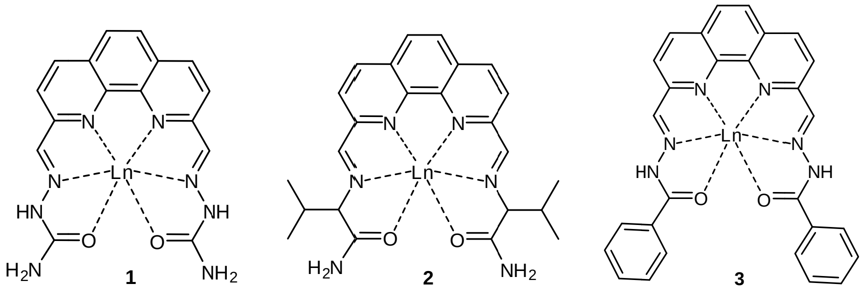

Figure 1. Synthesized Ln(III) complexes with phenantroline and different semicarbazones.

To study the structure and the capacity as a sensor for anions and cations of these complexes, a computational study has been carried out. Spartan with the MMFF force field was used for the conformational search. The obtained structures have been energetically optimized with Gaussian`09 on the PBE1PBE/TZVP level of theory. For the metal ions, the combination of SDD/MWB28 was used. One of the computational analyzed complexes is shown in Figure 2.

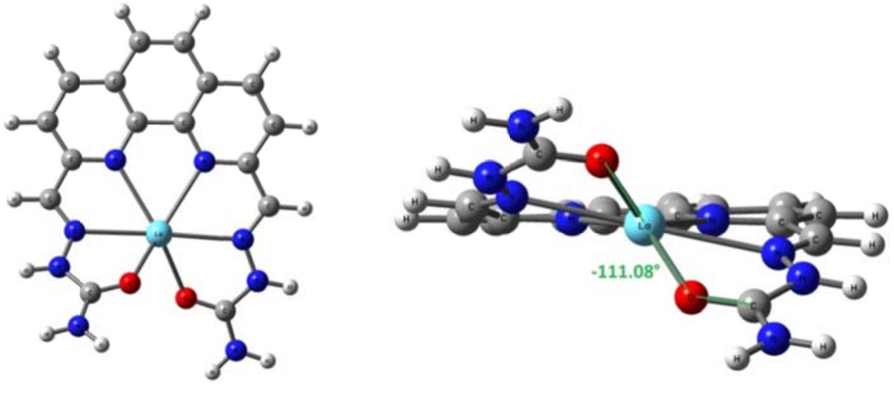

Figure 2. With PBE1PBE/TZVP and SDD/MWB28 for La(III) energetically optimized structure of complex **1**, dihedral angle (O,La,O,C): $\alpha = -11.08°$.

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Hydrolytic Reactions at the Interface - Self-assembled Multi-site Catalysts for Efficient Phosphodiester Cleavage

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Phosphate esters are ubiquitous in nature and their specific hydrolysis plays an important role in metabolic processes. As hydrolytic enzymes often contain coordinated metal ions in their active sites various synthetic catalysts based on transition metal ions like Zn(II) have been reported. The design of efficient catalysts for the cleavage of stable phosphodiester bonds, as in DNA, usually involves the connection of two or more metal centers by a variety of spacers or by immobilization on different supports.[1]

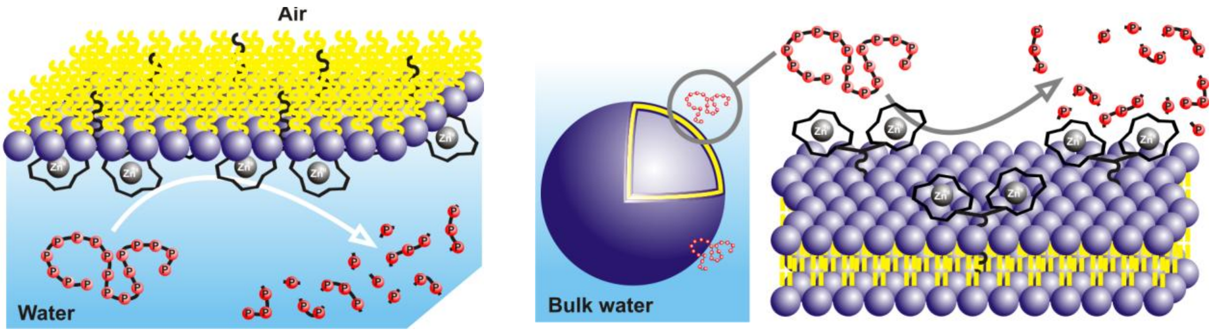

Figure 1. Schematic hydrolysis of phosphate ester substrates by self-assembled LB monolayers (left) and vesicular bilayers (right) containing embedded transition metal catalysts.

Based on previously reported Zn(II)-cyclen complexes that promote phosphate ester cleavage,[2] we have developed amphiphilic catalyst derivatives, which were embedded in Langmuir-Blodgett lipid monolayers and vesicular lipid bilayers. Their hydrolytic activity against substrates like BNPP, plasmid DNA and oligonucleotides is reported.

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Surface-bound peptides as biomimetic carbohydrate receptors

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Cell surface lectin–carbohydrate interactions are involved in diverse biological processes such as inflammation, adhesion of infectious agents to host cells, cell-cell communication and immune responses.[1] In order to mimic these processes membrane-fixed peptide receptors are synthesized and their interaction with carbohydrates is explored. Bilayer vesicles of amphiphilic cyclodextrins are used as surface for anchoring the peptide molecules as these vesicles consist of a membrane with a high density of embedded host molecules that bind hydrophobic guests.[2] Moreover cyclic hexapeptides were identified by a dynamical approach as strong biomimetic carbohydrate receptors recently.[3] Based on these results the peptide receptor is composed of an adamantyl anchor which is connected to an oligopeptide acting as recognition unit and a cysteine terminus. This enables the peptide receptor to bind to the surface of the cyclodextrin vesicle and to form disulfide bonds with another receptor molecule. The so formed cyclic cavity should act as binding side for carbohydrates (see figure 1). The interaction of the peptide-decorated vesicles with different carbohydrates is analyzed by fluorescence spectroscopy and surface plasmon resonance measurements.

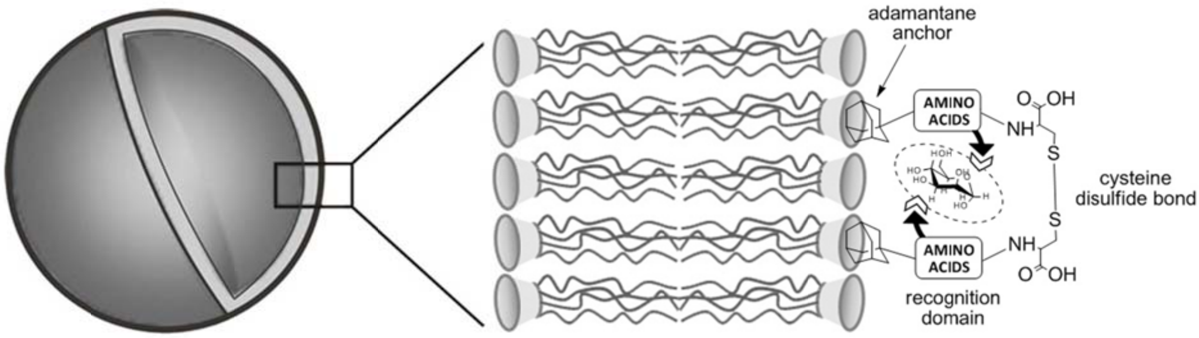

Figure 1: Diagram of bilayer vesicle of amphiphilic cyclodextrins with surface-bound peptides and interacting carbohydrate.

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A Reversible, Light-induced Chirality Switch of a Bridged Azobenzene Derivative

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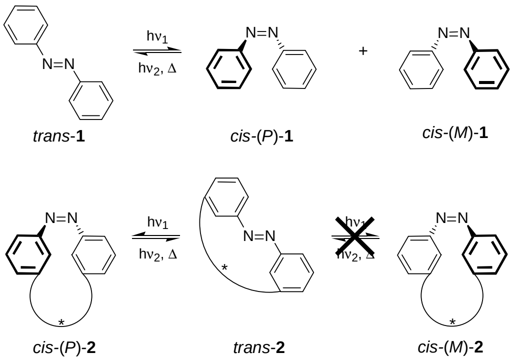
For the development of molecular motors and machines; photochromic molecules are of high interest.[1] The trans→cis isomerization of azobenzene and its derivatives is a prominent example for a light-induced switching process (Scheme 1). In the past azobenzene derivatives have been used for several switching processes in which chirality is eminent, but unidirectional switching of the azobenzene unit has not been possible so far.[2] Our working group had already succeeded in accomplishing a unidirectional switching of bipyridine derivatives by means of chiral cyclic imidazole peptides.[3] Thus we decided to use the chiral clamp also for the synthesis of the azobenzene derivative **2** (Scheme 1) to switch the azobenzene unit unidirectionally via light-induction.



Scheme 1. Light-induced switching of azobenzene **1** (bidirectional) and derivative **2** (unidirectional).

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Isopropylamino and Isobutylamino Groups as Recognition Sites for Carbohydrates

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38106 Braunschweig

Isopropyl and isobutyl groups were incorporated into acyclic receptor structures to mimic the interactions of valine/leucine side chains, which were shown to participate in the formation of van der Waals contacts in protein-sugar-complexes (Figure 1a). The artificial receptors, containing either a trisubstituted triethylbenzene[2] or dimesitylmethane core, were expected to recognize sugar molecules through a combination of $NH\cdots O$ and $OH\cdots N$ hydrogen bonds, $CH\cdots\pi$ interactions and numerous van der Waals contacts (Figure 1b).

^{1}H NMR spectroscopic titrations in competitive and non-competitive media, as well as binding studies in two-phase systems, such as dissolution of solid carbohydrates in apolar media and phase transfer of sugars from aqueous into organic solvents, revealed effective recognition of neutral carbohydrates and interesting binding preferences in comparison with the previously described receptors.[3-5] The isopropylamino-based receptors were shown to be more effective carbohydrate receptors than the isobutylamino-based compounds.

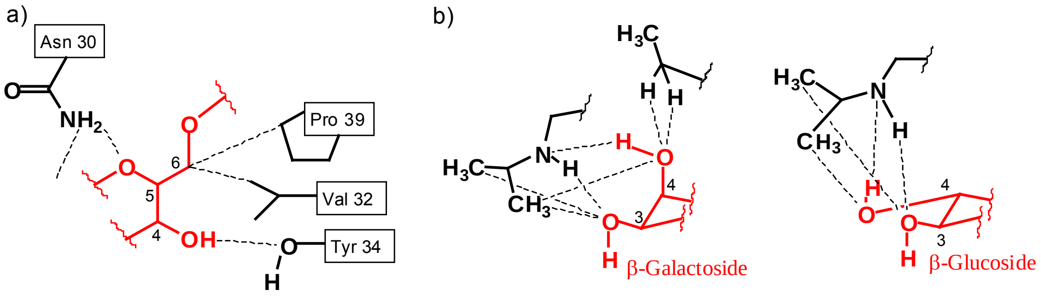

Figure 1. (a) Examples of hydrogen bonds and van der Waals contacts in the complex of *Galanthus Nivalis Agglutinin* with Manα3(Manα6)Man.[1] (b) Examples of noncovalent interactions (hydrogen-bonding and van der Waals contacts) indicated by molecular modeling calculations in 1:1 complexes of the isopropylamino-based receptor with β-galactoside and β-glucoside.

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Tetrazole-Containing Anion-Binding Cyclic Pseudopeptides

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The recently described cyclic hexapeptide **1** has, for a neutral compound, the unusual ability to strongly bind to inorganic anions in highly competitive aqueous solvent mixtures.[1] A decisive factor responsible for the unique properties is its relatively rigid conformation whose characteristic features are three converging NH groups and *cis*-conformations at the tertiary amides. We wondered whether other macrocycles possessing similar structural features would also act as anion receptors. A promising candidate is cyclic pseudopetide **2**, in which the tertiary amide groups of **1** are replaced by 1,5-disubstituted triazole units (Figure 1).[2]

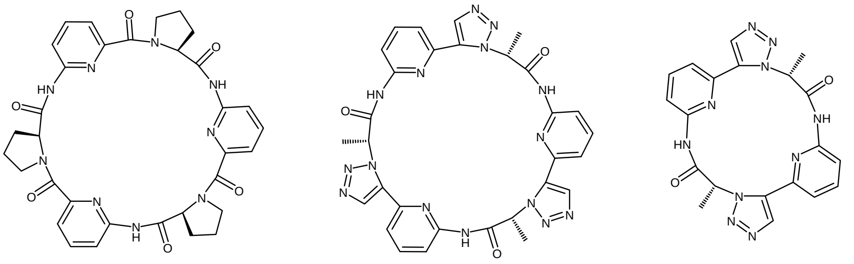

Figure 1. Structures of cyclic hexapeptide **1**, its triazole containing analogue **2** and compound **3**.

Studies on compound **3** (Figure 1), a structurally related smaller analogue of **2**, demonstrated the general applicability of this concept.[3] Moreover, preliminary ^{1}H-NMR experiments indicated that **2** is a promising receptor for chloride ions in competitive aqueous media. This poster summarizes our first results in this project.

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Zwitterion-chromophore modules for white light emitting supramolecular polymers

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With our poster we intend to show the synthesis of chromophore-zwitterion modules for supramolecular white light emitting polymers. These polymers would be formed via the self-assembly of the zwitterions subunits. Therefore we use the self-complementary guanidiniocarbonylpyrrole-zwitterion developed by our group which has already been successfully used to obtain water stable supramolecular polymers and other nanostructured materials such as vesicles.[1,2] By combining this zwitterion with different fluorescent chromophores, light emitting supramolecular polymers should be accessible.

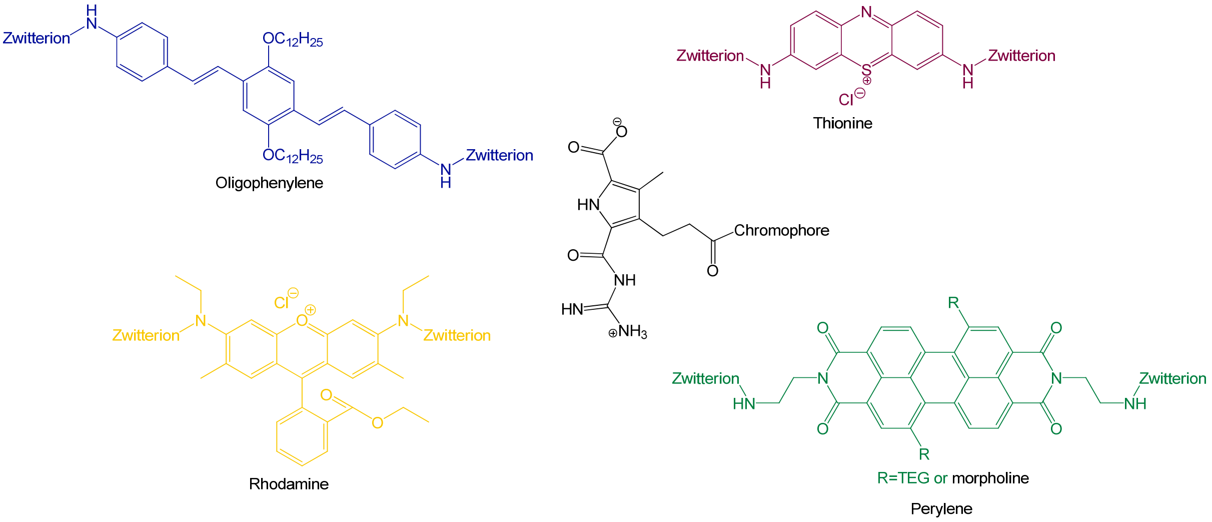

Figure 1: Synthesized molecules.

As known from the theory behind different color spaces, white light emission is obtained by mixing different colored dyes e.g. red, green and blue dyes. With the right mixing ratio of different colored zwitterions-chromophore units it should be possible to get a white light emitting solution. The main advantage of this zwitterion driven supramolecular aggregation, besides its stability in aqueous solutions, is that the self-aggregation can be reversibly switched on and off e.g. by pH adjustments.

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New possible allosteric systems based on β-cyclodextrins

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Functionalized bipyridines fulfill all needs for acting as switches in artificial allosteric receptor-systems due to their ability to change from *anti* to *syn* by coordination of transition metal ions[1]. In the past, we were able to synthesize many receptor-systems based on 2,2'-bipyridins and resorcinarenes[2]. However, the latter came out to be a little small for our purposes. Searching for alternatives, we came across β-cyclodextrins and found them to be very useful with regard to their ability to take up larger nonpolar molecules and their adjustable solubility properties which might open up new possibilities for later applications.

We were able to synthesize an allosteric system based on a 4,4'-functionalized 2,2'-bipyridin and two peracetylated β-cyclodextrins linked by thiourea-groups which were built up by using 4,4'-isothiocyanato-2,2'-bipyridine[3] and peracetylated 6^A-amino-β-cyclodextrins. Currently, we are investigating the coordination and guest-binding behavior of this system while we are also working on new variations of this system like the use of 2,2'-bipyridins with different substitution patterns.

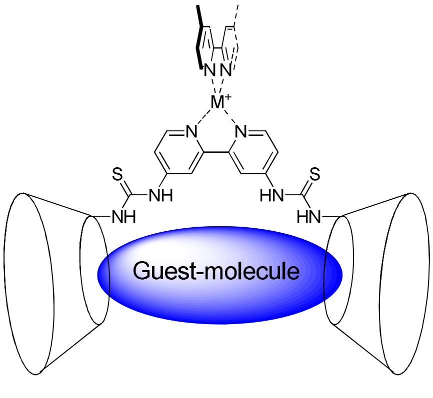

Figure 1. Allosteric system based on 4,4'-disubstituted bipyridine and β-cyclodextrins ("on-state" with coordination of a metal ion and a guest-molecule).

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RECYCLABLE SUPRAMOLECULAR MEMBRANE FOR SIZE-SELECTIVE SEPARATION OF NANOPARTICLES

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Noncovalent materials are highly advantageous in terms of fabrication, processing, and recyclability. However, lack of robustness resulting from insufficient strength of noncovalent interactions has prevented the utilization of noncovalent materials as a viable replacement for the covalent ones. We have synthesized an amphiphilic molecule based on perylene diimide (PDI) decorated with polyethylene glycol (PEG) groups. This amphiphile self-assembles in water into an extensive and exceptionally robust three-dimensional fibrous network that is suitable for fabrication of supramolecular ultrafiltration membranes. Structure and function of the prepared membranes were investigated using cryogenic scanning electron microscopy (cryo-SEM), transmission electron microscopy (TEM), and steady state absorption and luminescence spectroscopy. The membranes were used to separate metal and semiconductor nanoparticles according to size: a thin (~12 μm) membrane retains nanoparticles larger than ~5 nm, whereas a thicker (~45 μm) membrane allows for size-selective chromatography in the size range of 2 to 5 nm. Importantly, the supramolecular membrane is rapidly disassembled by organic solvent, allowing for facile recycling and multiple uses. Our findings indicate that functional noncovalent materials can serve as a versatile, economical, and environmentally friendly alternative for conventional (polymer-based) materials in real-life applications.

Synthesis of bis(acetylacetonate) ligands for the formation of oligonuclear metallosupramolecular assemblies

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The formation of metallosupramolecular assemblies is a common strategy for building up cavities of different sizes und functionalities.[1] Highly interesting is the selective formation of cages of well defined stereochemistry that can be applied in stereoselective processes such as chiral resolution or asymmetric synthesis. These aggregates can be obtained through diastereoselective self-assembly of chiral ligands. BINOL (2,2′-dihydroxy-1,1′-binaphthyl) is an extraordinary useful building block for those purposes, as its chiral resolution is well described and its 3- and 3’-position is quiet easily functionalized via ortho-lithiation. Recently we were able to report on several BINOL-based ligands that undergo stereoselective self-assembly to charged, enantiomerically pure aggregates.[2]

In our current work we investigate the formation of neutral complexes. Therefore, we chose acetylacetonate groups as chelating units in 3- and 3’-position of the BINOL-backbone to form a ligand that is able to built tetranuclear complexes of tetrahedral shape with trivalent metal ions like Fe^{3+} and Ga^{3}.

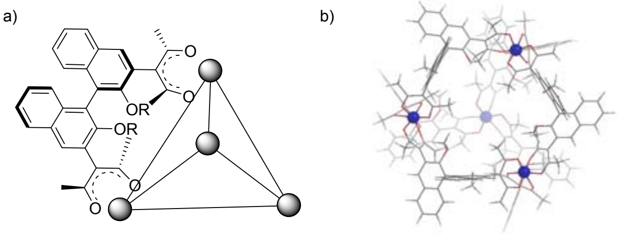

Figure 1. a) Scheme of the cage M_4L_6; b) *PM3-TM*-minized structure of (Λ,Λ,Λ,Λ)- $[\mathrm{Ga}_4((R_a)\text{-L})_6]$.

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Physico-chemical Studies on multi-Receptor Synthetic Membranes – Towards Imprinted Surfaces

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Non-covalent interactions of receptors and ligands at liposomal surfaces are very similar to recognition processes at biological membranes which are responsible for cell recognition, adhesion and fusion. Molecular recognition on such membranes is often governed by dynamic multivalent interactions.[1] Based on previously reported vesicular chemosensors for the recognition of small biomolecules,[2] we currently focus on the structuring of such multi-receptor surfaces and the dynamic recognition of multivalent target molecules.

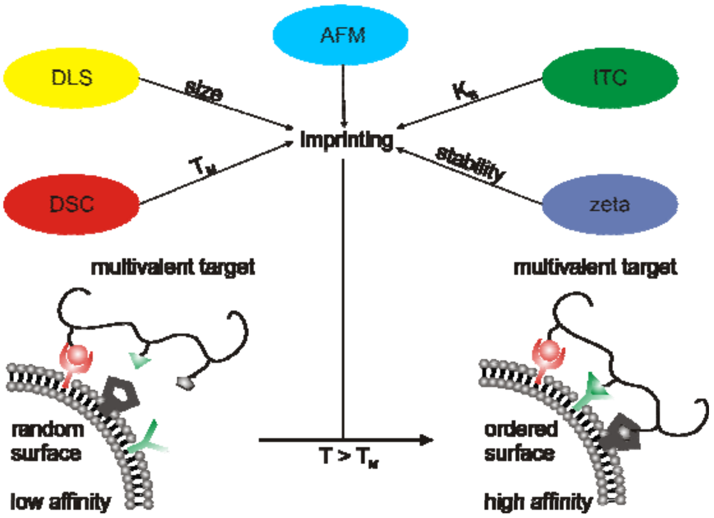

Figure 1. Schematic drawing of an imprinting approach of a receptor embedded vesicular surface to improve the binding affinity towards a multivalent ligand.

Approaches for the ordering of surface-exposed binding sites include heating above the main phase transition temperature in the presence of multivalent template molecules and subsequent cooling and removal of the templates.

Here we present preliminary physico-chemical studies of membranes doped with synthetic receptors in the gel and liquid crystalline state and their reversible phase transitions.

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Biomimetic and Dynamic Receptors by Non-covalent Interactions

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The response of dynamic combinatorial libraries (DCL) of various tripeptides to templates, especially carbohydrates, using covalent exchange reactions was published recently.[1] Additional degrees of library diversification can be achieved in a DCL using reversible non-covalent interactions such as metal-ligand-coordination to build up peptide-dimers as biomimetic receptors, which are likely to interact with templates (**figure 1**). Therefore peptides are synthesized containing a recognition unit between a pyridine based metal-ligand at the *N*-terminus and an allyl-functionalized *C*-terminus as an inert end of the peptide-chain. The dynamics of the DCL can be controlled using redox active transition metal ions (e.g. Co^{2+}/Co^{3+}). As a result oxidation of the octahedral complexes allows analysis of the resulting library composition.[2]

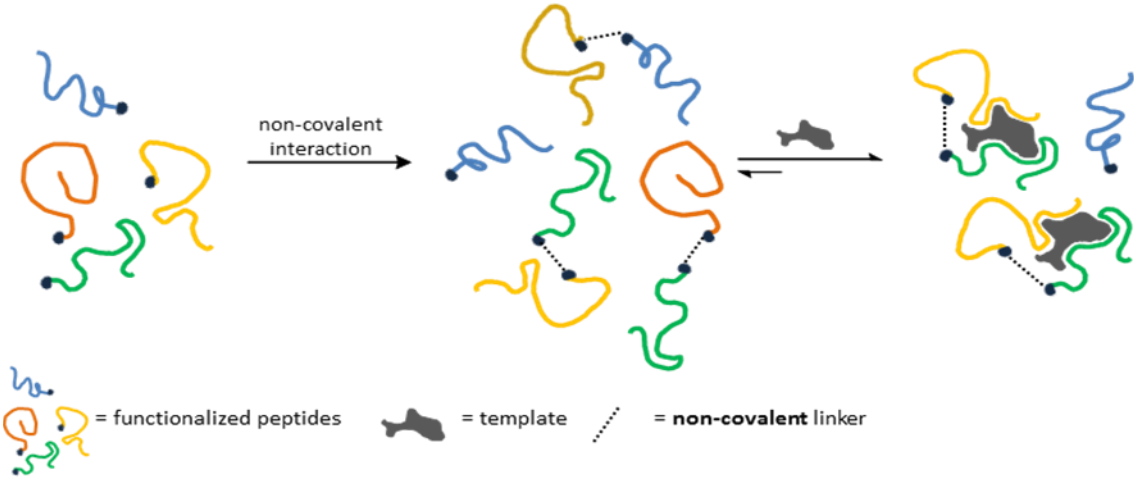

Figure 1. : Schematic overview of a dynamic combinatorial library using non-covalent interactions to build up peptide dimers as biomimetic receptors.

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Aminoacid functionalized heterodinuclear metallohelicates

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After having successfully synthesized different triple stranded helicates with a variety of geometries and metals [1, 2] we began to functionalize these helicates with different rests, as for example phenyl groups.

The possibility of being able to imitate nature by introducing peptides in our structures goaded us to start off with the introduction of aminoacids in our helicates. The first derivative was the phenylalanine functionalized ligand **1** which was complexed with La (III) and Ga (III) ions giving as a result the first chiral helicate with catecholate-acylhydrazone based ligands.

Circular dichroism measurements of complex **1a** in DMSO 10^{-3}M gave the spectrum which is shown in Figure 2.

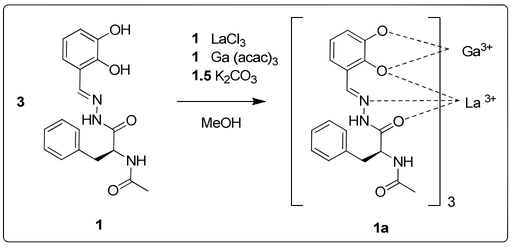

Figure 1. Synthesis of complex **1a**

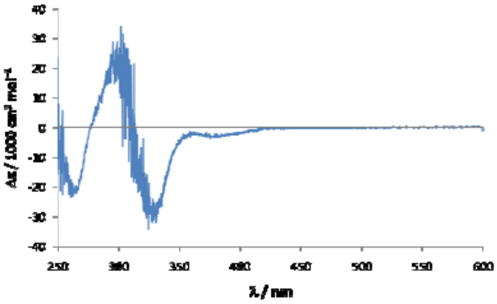

Figure 2. CD Spectrum of complex **1a** in DMSO (10^{-3} M)

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Synthesis and recognition properties of non-covalently assembled receptors for the recognition of monosaccharides

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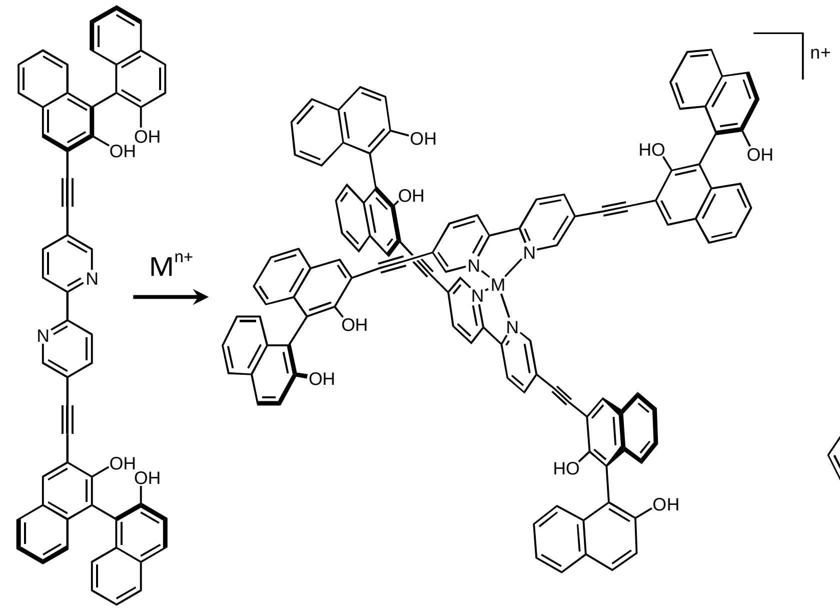
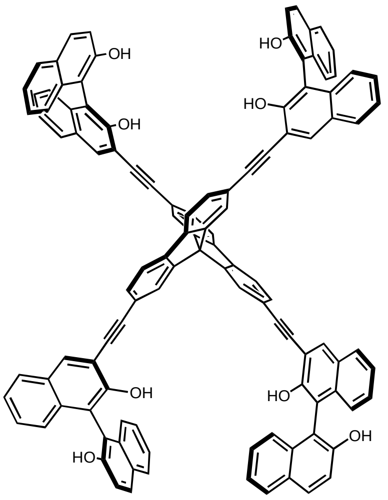
Carbohydrate recognition plays a very important role in biological processes. Thus, many efforts have been made in supramolecular chemistry to develop artificial receptors to understand the underlying principles.[1] Recently, we were able to synthesize a 2,2'-bipyridine (**1**) carrying two BINOL groups.[2] This ligand forms mononuclear complexes with suitable transition metal ions that were found to bind monosaccharide derivatives in a remarkably strong manner, much better than a structurally very similar covalently assembled analogue **2**[3] in which a 9,9'-spirobifluorene substitutes the central bis(2,2'-bipyridyl) complex.



(*all-S*)



($all\text{-}S_a$)-**1** [M{($all\text{-}S_a$)-**1**}$_2$]$^{n+}$ ($all\text{-}S_a$)-**2**

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Synthesis of potential receptors for the recognition of ammonium ions

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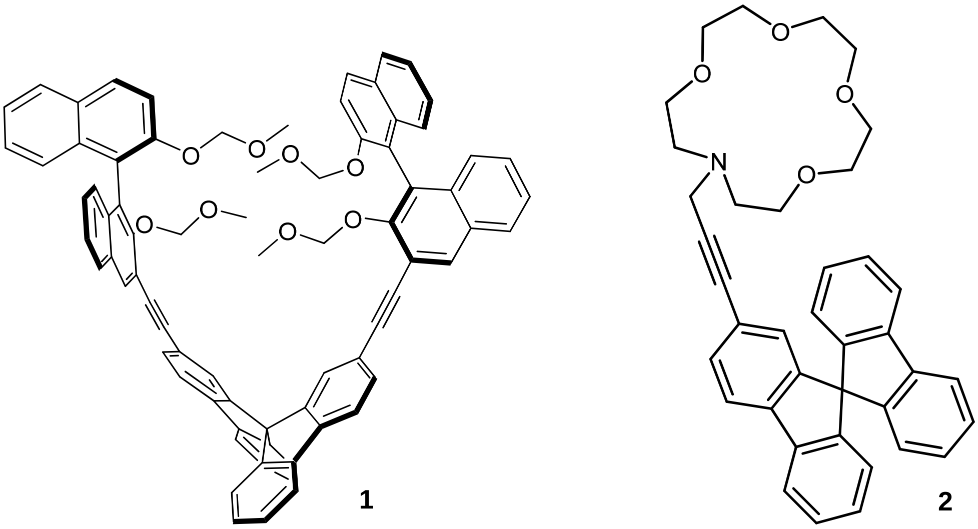
The development of stereoselective receptors and effective resolution of enantiomers is of great importance in chemical research and industrial synthesis. *F. Thiemann* from our group demonstrated that receptor **1** has a strong affinity to bind ammonium ions[1]. This work lead to the synthesis of new potential receptors. One approach aims at the use of monofunctional spirobifluorens as basic components which are functionalized by ethynyl or phenyl groups as linkers and crownethers or aza-crownethers as binding sites for ammonium ions.



1

2

Figure 1. *F. Thiemanns* receptor **1** and a possible monofunctional spirobifluoren receptor **2**.

The synthesis of some of these new potential receptors will be presented.

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Perfluoro modified affinity molecules for application on quartz crystal microbalances

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Abstract:

Supramolecular receptors based on a triphenylene ketale backbone show a high affinity towards aromatic C_3 and *pseudo* C_3 symmetric molecules (figure 1).[1,2]

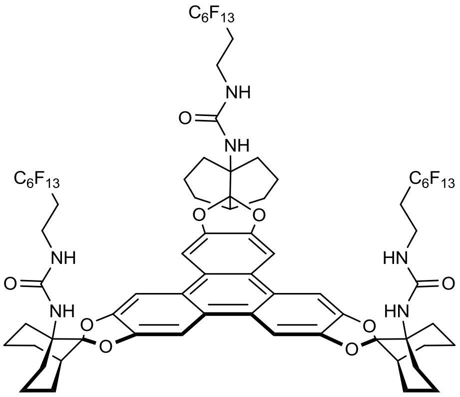

Figure 1: Perfluoroalkylated receptor

For example, these compounds are useful for detection of TNT or caffeine. The receptor material is deposited on quartz crystal microbalance using an established electrospray protocol.[3] However, the adsorption of water on the hydrophilic surface of the quartz electrode causes wrong readings, which should be reduced by perfluoroalkylation of the surface. After equipment of the receptor with perfluoro groups, dip coating could become an alternative coating procedure. The implementation of these groups is carried out by a well-known protocol in which the triamine precursor of the receptor reacts with the corresponding isocyanates.[1] First results of the synthesis will be presented. Furthermore we show the behaviour of the modified quartz crystals in our measurement setup.

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8-Hydroxyquinoline as a Building Block for Artificial Receptors: Binding Preferences in the Recognition of Glycopyranosides

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Artificial carbohydrate receptors using noncovalent interactions for sugar binding[1,2] provide valuable model systems to study the underlying principles of carbohydrate-based molecular recognition processes. Although effective receptor systems have been developed, the exact prediction of the binding preferences of the artificial receptors is still further away and it is hoped that systematic studies towards effective recognition motifs for carbohydrates will contribute significantly to the solution of this problem. Our previous studies showed that acyclic receptors,[2] such as compounds containing a trisubstituted trialkylbenzene core, represent particularly interesting objects for such systematic studies. Depending on the nature of the recognition units and connecting bridges used as the building blocks, a variety of receptors with different binding properties could be obtained.

The aim of the present study was to evaluate the potential of 8-hydroxyquinoline-based receptors (see for example Figure 1) in the complexation of carbohydrates.[3] 8-Hydroxyquinoline unit has been extensively used for the construction of metal ion ligands. In the area of sugar recognition by receptors employing noncovalent interactions the potential of this unit has not been evaluated.

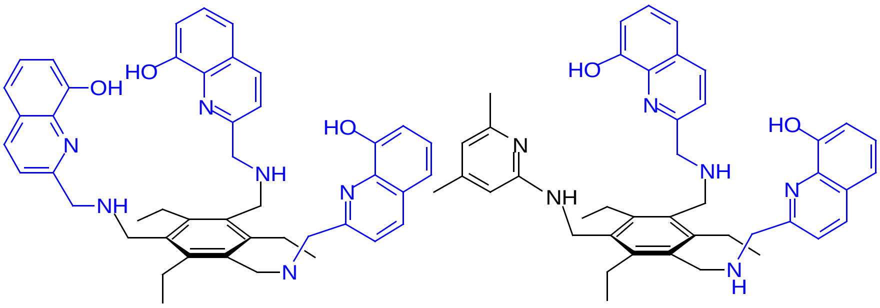

Figure 2. Examples of 8-hydroxyquinoline-based receptors.

The recognition properties of the new compounds were compared with those of the previously studied receptors. In addition, the properties of the 8-hydroxyquinoline-based receptors were compared with those of the quinoline-based compounds. Binding studies in competitive and non-competitive media showed both effective recognition of carbohydrates and interesting binding peferences of 8-hydroxyquinoline-based receptors.

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Supramolecular chemistry and molecular recognition.

From multiple hydrogen bonds to dynamic combinatorial chemistry.

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Otto Diels-Institut für Organische Chemie der Christian-Albrechts-Universität Kiel

Molecular recognition of a guest by a host needs attractive supramolecular interactions. The hydrogen bond is of special importance as it is directional, and the combination of several hydrogen bonds produces patterns which contain the information, only to bind the complementary hydrogen bond acceptor/donor pattern. Orthogonal multiple hydrogen bond systems will be presented and their binding properties will be discussed.

A second important feature for host guest chemistry is the complementarity of convex and concave shapes. Most molecules are "potato shaped", i.e. they are mostly convex. Thus a receptor must possess a concave structure which can either be guaranteed by a stiff U-shape of the molecule or by using macrocycles. The syntheses of the latter are not straightforward because the desired macrocyclization always competes with oligo- and polymerization. While in the past, this difficulty has mainly been overcome by using the high-dilution principle, dynamic combinatorial approaches which exploit the template effect are increasingly used these days. Macrocycle syntheses with the help of inorganic and organic templates will be presented. Furthermore, the direct use of a dynamic combinatorial library for a function will be presented:

A dynamic combinatorial library consisting of amines and aldehydes can directly be used for ion transport across different membranes.

Chiral 4,12- and 4,15-disubstituted [2.2]paracyclophanes

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Besides a certain size and chemical nature chirality is one of the most important features of (supra-)molecules. Thus, one of the major subjects in our group is the development of stereoselective self-assembly processes of e.g. metallosupramolecular aggregates. Usually we use a dissymmetric chiral unit as the key-element that controls these processes like e.g. BINOL, Tröger's base, or 9,9'-spirobifluorene derivatives. These compounds all have in common that they contain rather unusual stereogenic elements like chiral axes, spiro-carbon atoms or stereogenic N-atoms. Another interesting element in this context are chirality planes. These can be found e.g. in 4,12- and 4,15- disubstituted [2.2]paracyclophanes. Due to their special electronic properties they are also interesting for the synthesis of π-conjugated oligomers. Yet we have been able to synthesize some disubstituted [2.2]paracyclophanes carrying e.g. two hydroxy, aldehyde, or carboxyl groups which can be transformed in a number of further functional groups. Although many of these functionalized [2.2]paracyclophanes are known from the literature[1] we were able to greatly improve some of the synthesis to achieve higher yields and develop new resolution procedures via HPLC.

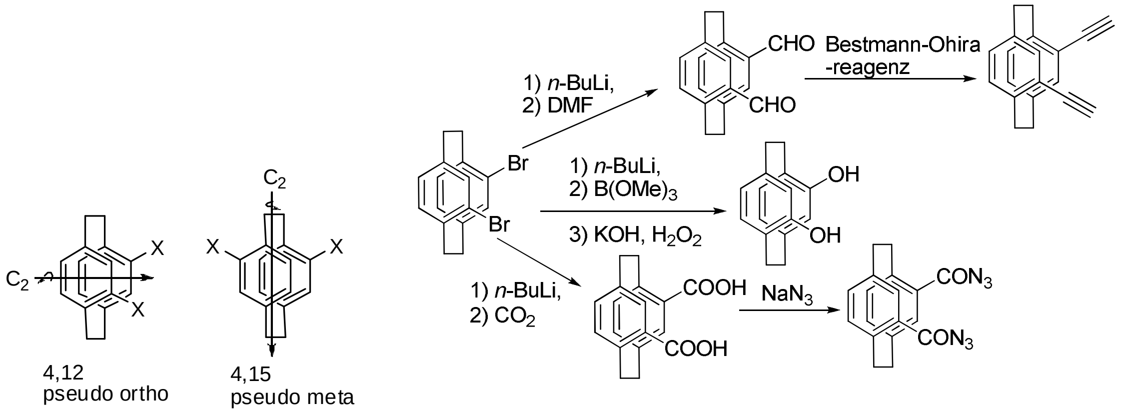

Figure 1. 4,12- and 4,15- disubstituted [2.2]paracyclophanes and the their synthesis.

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HIERARCHICAL PROTEIN ASSEMBLY DIRECTED BY SUPRAMOLECULAR ELEMENTS

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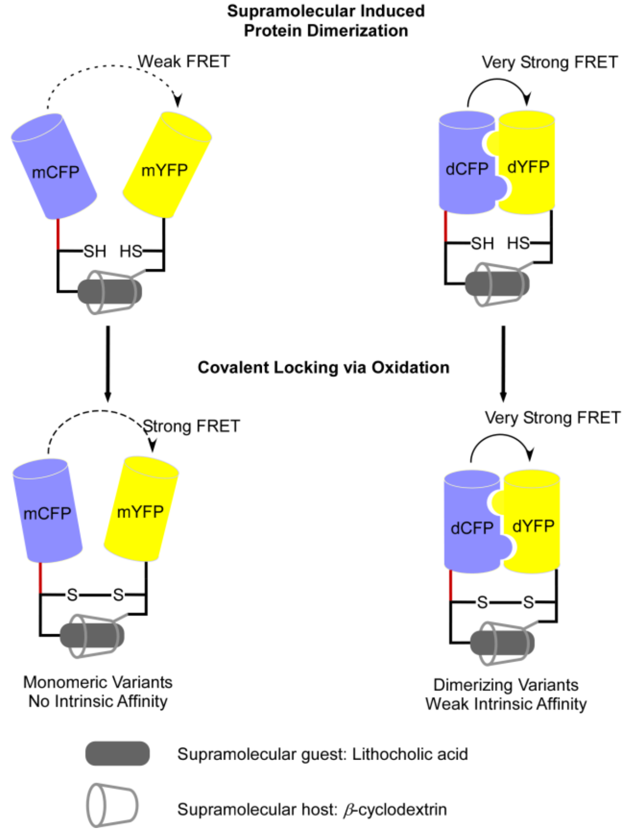
Supramolecular chemistry utilizes reversible non-covalent interactions to assemble molecules into multi-molecular complexes. These can be modulated by external elements such as light, temperature, pH or ligands. Supramolecular systems promise to be powerful tools for the study of biological phenomena. For example, host-guest chemistry has been used to immobilize proteins on surfaces[1] in order to control the assembly of two protein fragments,[2] and to dimerize two proteins in the cell.[3] We have shown that protein interactions can be controlled using the host-guest complex formed between lithocholic acid (**LA**) and β-cyclodextrin (**CD**).[4] This poster illustrates the design and synthesis of supramolecular host-guest elements, their conjugation to fluorescent proteins and subsequent in vitro biochemical studies.



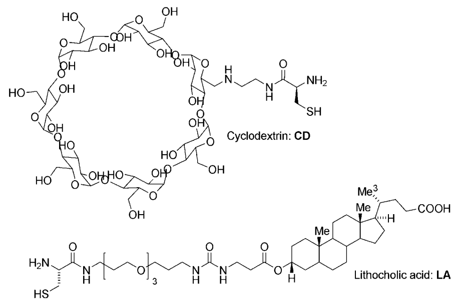


Figure 1. Schematic model for the hierarchical assembly / disassembly process of monomeric (mCFP and mYFP) and the dimerizing (dCFP and dYFP) protein pairs. Depending on the dimerization characteristics of the protein, the supramolecular host-guest pair either induces selective assembly of a protein dimer via the supramolecular elements alone, or induces the formation of a more stable protein heterodimer by virtue of the its interplay with the protein dimerization surface. By switching the redox conditions, the protein heterodimers can be covalently locked via the assisted formation of a disulfide bridge between a CFP and a YFP protein.

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Leaving the cosy cradle –
Dependence of anion-π interactions on fluorination degree of the arene

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Supramolecular Chemistry is the chemistry of noncovalent interactions.[1] In the last 20 years theoretical studies and experimental evidence have revealed a new kind of non-covalent interaction **– the anion-π interaction**.[2] Previous studies of our group showed that the pentafluorophenyl unit is an appropriate system for anion-π interactions.[3]

The dependence of the fluorination degree of the arene on anion-π interactions is investigated in the current work. A rising distance between the anion and the phenyl unit with increasing degree of fluorination (**1a-d**) of the arene was obtained.

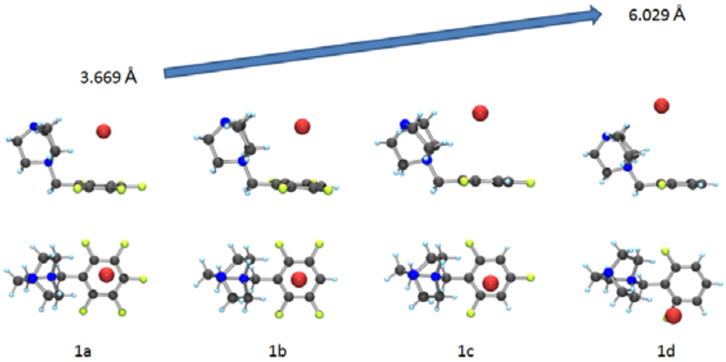

Figure 1. Comparison of the crystal structures of **1a-d** showing the rising distance between the centromer of the arene and the anion.

In DABCO-derivatives with ortho hydrogens the anion is surrounded by CH-units. No anion-π interaction can be observed. The arenes are antiparallel π-stacking with an offset.

In conclusion our recent results show that at least three to four fluorine atoms on the arene are required for an effective anion-π interaction.

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Stimuli-Responsive Supramolecular Interactions of Vesicles

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Cyclodextrins (CDs) are a group of cyclic oligosaccharides composed of six (α-CD), seven (β-CD) or eight (γ-CD) α(1,4)-linked glucopyranose units with hydrophobic internal cavities. Amphiphilic CDs form bilayer vesicles in aqueous medium [1]. The surface of CD vesicles displays hydrophobic cavities in a liquid crystalline array. These vesicles are able to recognize and bind hydrophobic guest molecules and it was possible to achieve intravesicular and intervesicular interaction by orthogonal host-guest and metal-ligand complexation [2].

The inclusion of azobenzene as a guest into a CD host is light-responsive: the rod-like *trans*-isomer forms a stable inclusion complex with α-CD as well as with β-CD, while the bent *cis*-isomer does not fit in either CD. In this contribution we show that the photo-isomerization of a bifunctional azobenzene non-covalent linker molecule can be used as a trigger to induce and reverse the molecular recognition and adhesion of vesicles [3]. In a similar way, we also show a competitive photo-responsive system in which a monofunctional photo-responsive azobenzene molecule can be used as a competitor to inhibit and induce the adhesion of vesicles accompanied by a weak non-covalent linker molecule. Further, we investigate a system in which a metal ion is used as a stimulus to control the aggregation and dispersion of vesicles by the reversible change in the conformation of guest molecule.

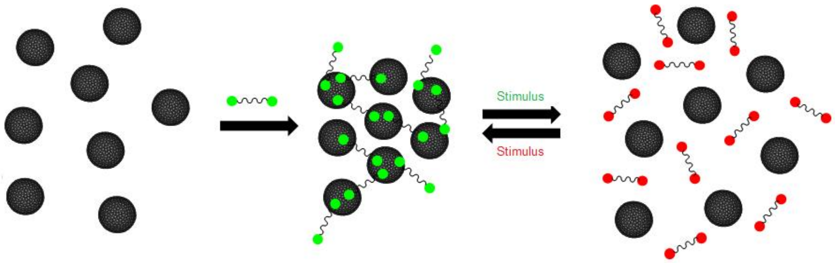

Figure 1. Stimuli-responsive supramolecular interactions of vesicles.

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Supramolecular Induced Dimerization and Activation of Caspase-8

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Caspase-8 is a protease and plays a key role in the apoptosis pathway, cleaving proteins at specific aspartate residues. Naturally, the function of caspase-8 is as initiator to generate and activate caspase-3 by proteolysis, resulting in apoptosis. Caspase-8 is primarily present in its inactive monomeric form under normal physiological conditions, but becomes active upon induced dimerization. In our work, the human caspase-8 was generated with an N-terminal FGG motif by using the N-terminal intein technology from plasmid pTWIN1. In our study the FGG-caspase-8 has to be induced into its dimeric form using the host-guest molecule, cucurbit[8]uil (Q8), resulting in enhancement of its activity.

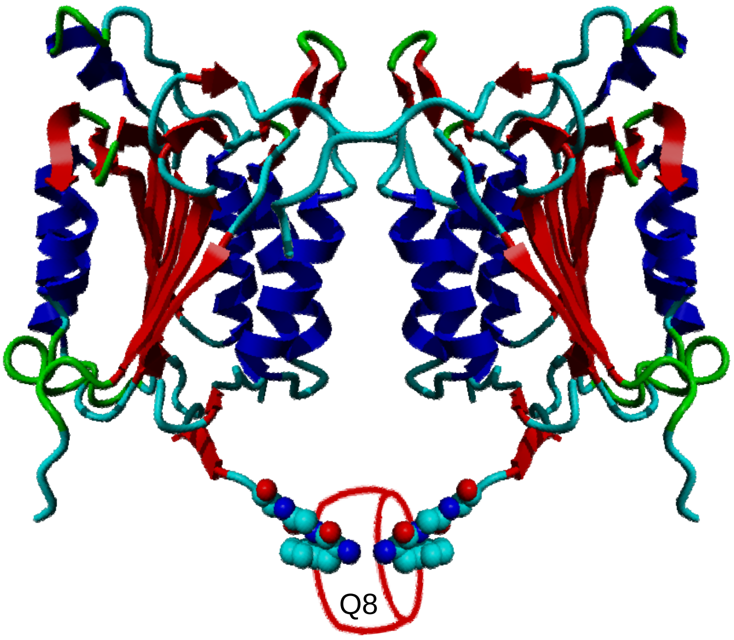

Figure 1. The process of protein dimerizing using FGG motifs and Q8

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[1] H.D. Nguyen, T.D. Dang, J.L.J. Dongen, L. Brunsveld, *Angewandte Chemie* **2010**, *122*, 907-910

Self-Assembling Multivalent Columns

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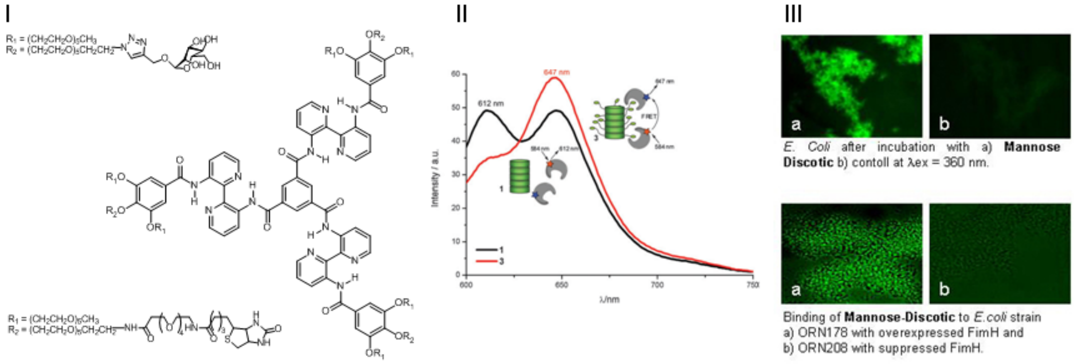
Binding events in nature, like those between cells, are typically based on relatively weak and non-covalent interactions. To stabilize and enhance these interactions nature uses the advantages of multivalent binding. To interfere in these multivalent processes, multivalent binders are investigated. Multivalent synthetic (co)polymers with a precise placement of functional groups and well-defined fold are not accessible. Supramolecular assemblies promise to provide an ideal platform to display multiple ligands on a self-assembled polymeric backbone. A multivalent system that can adapt its structure and the position of functional groups upon the environment will enable an optimal binding to a cell surface.

In this work we show that supramolecular discotics (Figure 1) can successfully self-assemble to a dynamic multivalent architecture in water, displaying ligands at will at the periphery. The intrinsic fluorescence of the discotics enables investigation with optical techniques such as fluorescence microscopy or FRET. These molecules have been functionalized with several bioactive ligands. The discotics with mannose-moieties for example bind strongly to FimH receptors of *E. coli* in a specific, selective and multivalent manner. [1] After functionalization with biotin these columnar assemblies can act as platforms for directed protein assembly. [2]



E. Coli after incubation with a) **Mannose Discotic** b) contoll at λex = 360 nm.

Binding of **Mannose-Discotic** to *E.coli* strain
a) ORN178 with overexpressed FimH and
b) ORN208 with suppressed FimH.

Figure 1. I) Chemical structure of mannose and biotin fuctionalized discotic; II) The biotin–streptavidin interaction mediates the assembly of streptavidins on the supramolecular wire and facilitates approximation of the FRET pair; III) The discotics with mannose moieties bind strongly to FimH receptors of *E. coli* in a specific, selective and multivalent manner.

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[1] M. Müller, L. Brunsveld, *Angew. Chem. Int. Ed*. **2009**, *48*, 2921.

[2] M. Müller, K. Petkau, L. Brunsveld, *Chem. Commun*., **2010**, DOI: 10.1039/C0CC02084B

A Cyclopeptide-Derived Molecular Container For Inorganic Anions

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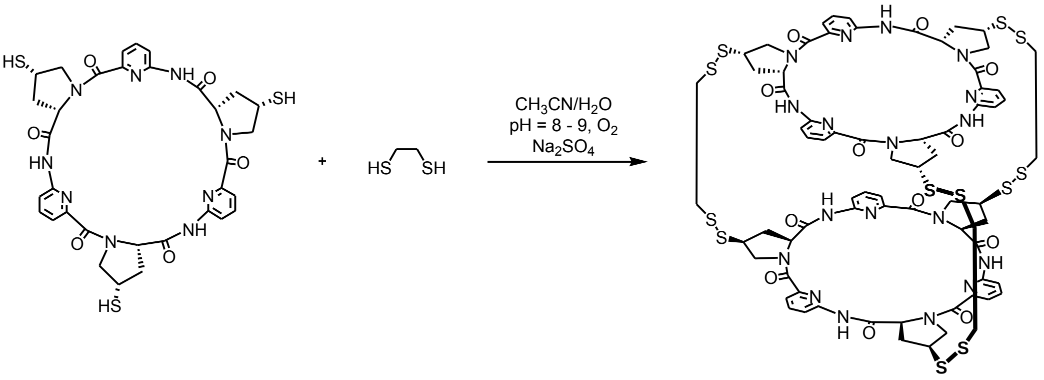
Neutral anion receptors have recently been developed in our group, derived from two cyclic hexapeptide subunits covalently linked via one linker, which form highly stable complexes with inorganic anions in competitive aqueous solvent mixtures.[1] Subsequently, the idea emerged to try to permanently entrap inorganic anions inside the cavity of such bis(cyclopeptides) by introducing three linkers between the cyclopeptide. The synthesis of the corresponding triply-linked bis(cyclopeptide) was achieved by using dynamic chemistry under thermodynamic control and disulfide exchange as the reversible reaction. Specifically, cyclopeptide trithiol **1** was equilibrated in the presence of sodium sulfate as an anionic template and three equivalents of a 1,2-ethanedithiol. Under these conditions the formation of of a compound was observed as the major product that turned out to be the desired capsule **2** with the anion entrapped between the two cyclopeptide rings.



1

2

Figure 1. Synthesis of the triply-linked bis(cyclopeptide) **2**

Detailed NMR spectroscopic experiments demonstrated that the bound sulfate ion can be exchanged with other anions. Experimental evidence about the thermodynamic stabilities of the anion complexes of **2** and the mechanism of anion exchange will be presented in this poster.

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[1] S. Kubik, R. Kirchner, D. Nolting, J. Seidel, *J. Am. Chem. Soc.* **2002**, *124*, 12752-12760.

Phenanthroline- and Naphthyridine-Based Receptors: Syntheses, Crystal Structures and Binding Properties

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As part of our program aimed at the development of effective and selective carbohydrate receptors,[1] we have analyzed the binding properties of acyclic receptors consisting of phenanthroline-[2-4] and naphthyridine-based[5,6] recognition groups. The interactions of these receptors and saccharides were investigated in homogenous media by ^{1}H-NMR and fluorescence titrations and in two-phase systems by extraction experiments. Both hydrogen bonding (see Figure 1) and interactions of the sugar CH's with the aromatic rings of the receptors were shown to contribute to the stabilization of the receptor-sugar complexes.

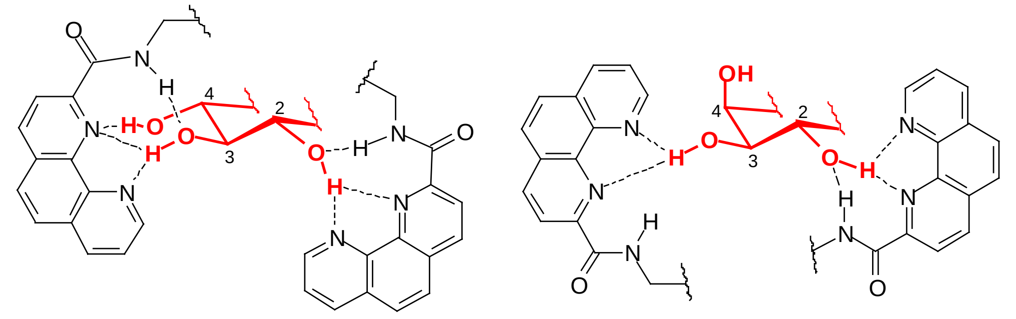

Figure 1. Examples of hydrogen bonds in the complexes of a phenanthroline-based receptor and β-glucoside (left) or β-galactoside (right).

Compared to the previously described acyclic receptors, the new phenanthroline- and naphthyridine-based receptors show significantly higher binding affinities as well as selectivities, which are quite different from those of the earlier systems. Both recognition units have been established as valuable building blocks for the construction of artificial carbohydrate receptors. The syntheses, crystal structures and recognition properties of the receptors towards mono- and disaccharides will be presented in this poster.

[1] M. Mazik, *Chem. Soc. Rev.* **2009**, *38*, 935-956. [2] M. Mazik, A. Hartmann, P. G. Jones, *Chem. Eur. J.,* **2009**, *15*, 9147-9159. [3] M. Mazik, A. Hartmann, *J. Org. Chem.* **2008,** *73*, 7444-7450. [4] J.-R. Rosien, M. Mazik, unpublished results. [5] M. Mazik, H. Cavga, *Eur. J. Org. Chem.* **2007,** 3633-3638. [6] U. Schmidt, M. Mazik, unpublished results.

Supramolecular M_4L_4 Tetrahedra with triangular Acylhydrazone Ligands

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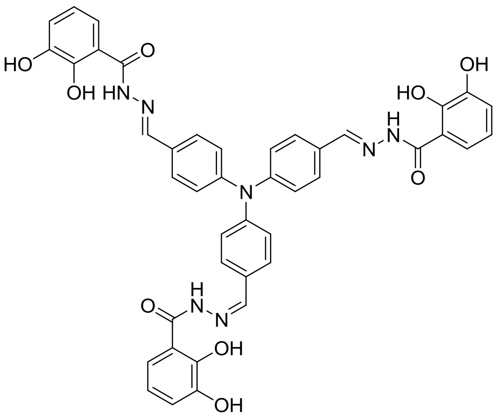
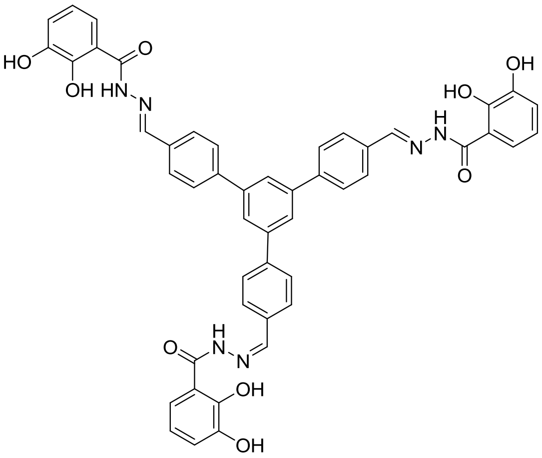
An easy way to obtain metallo-supramolecular tetrahedra $M_8[L_4Ti_4]$ is self-assembly from the triangular ligands L-H_6 and titanoyl bis(acetylacetonate) in the presence of alkali metal carbonates as base. We report two similar ligands, **L^1-H_6** and **L^2-H_6**, which are prepared by condensation of the corresponding aldehyde and 2,3-dihydroxybenzhydrazide. All the complexes can be well characterized by ^{1}H NMR in combination with ESI FT-ICR MS.



L^1-H_6



L^2-H_6

Enantioselective coiling of chiral alkanes inside supramolecular capsules

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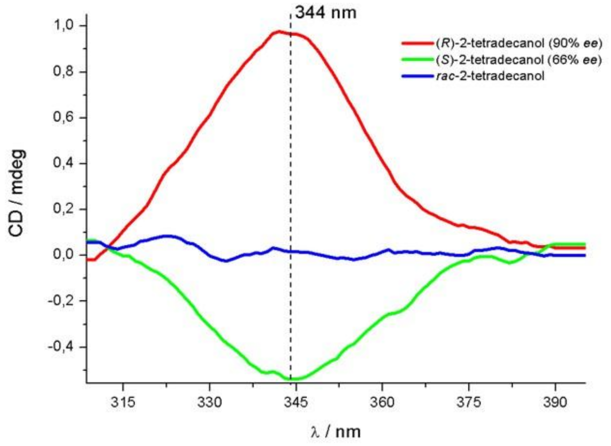
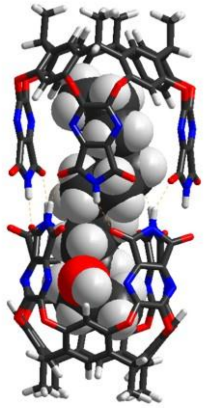
Self-assembled capsules have been a prominent playground for supramolecular chemists for decades. Especially those capsules developed by Rebek and coworkers have been most inspiring for generations of chemists. Besides building new architectures, he also discovered new effects of encapsulation. Most surprisingly, he found a helical, “compressed” conformation of linear alkanes inside the capsules. However, there was no report on the induction of preferential helicity of these alkanes.

Therefore, a chirally modified alkane (2-tetradecanol) was intitially synthesized and enantiomerically enriched. After encapsulation extensive NMR and CD investigations revealed a significant preference of helicity for a given chirality at the carbon chain. Theoretical treatment of the whole system allowed to assign the obtained CD signals to the absolute helicity of the chain. To our surprise, the CD signal is predominantly determined by the helicity but not the chiral center.





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[1] C. Siering, J. Toräng, H. Kruse, S. Grimme, S. R. Waldvogel, *Chem. Commun.* **2010**, *46*, 1625-1627.

Redox Controlled Conformation In Biphenyl-Systems

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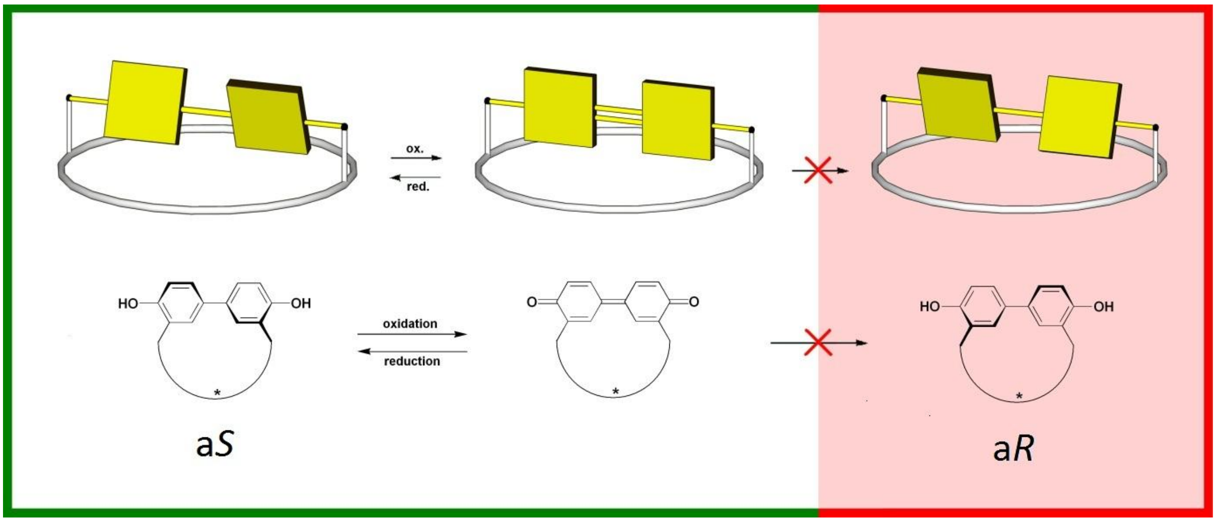
A remarkable challenge for the design of molecular machines[1] is the realization of a unidirectional and synchronized rotation caused by an external stimulus. Such a rotation can be achieved by a unidirectionally controlled change of the conformation or the configuration.[2,3] Biphenol derivatives are one possibility to realize a redox controlled unidirectional molecular switch. For this reason a 4,4'-biphenol derivative was fixed to a chiral cyclopeptidic scaffold. Several oxidation agents and various conditions were tested, among which DAIB in methanol proved to be the best. In this way it was possible to synthesize a redox stimulated molecular switch with a rotation around a biaryl binding axis.



Scheme 1: Principle of redox processed unidirectional switching.

[1] a) V. Balzani, M. Venturi, A. Credi, *Molecular Devices and Machines*, Wiley-VCH, Weinheim, **2003**; b) E. R. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem. Int. Ed.* **2007**, *46*, 72-191

[2] a) S. Ernst, G. Haberhauer, *Chem. Eur. J.* **2009**, *15*, 13406-13416; b) G. Haberhauer, C. Kallweit *Angew. Chem. Int. Ed.* **2010**, *49*, 2418-2421; c) G. Haberhauer, *Angew. Chem. Int. Ed.* **2010**, *49*, 9286-9289.

[3] a) S. P. Fletcher, F. Dumur, M. M. Pollard, B. L. Feringa, *Science* **2005**, *310*, 80-82; b) N. Koumura, R. W. J. Zijlstra, R. A. van Delden, N. Harada, B. L. Feringa, *Nature* **1999**, *401*, 152-155.

Enantio-recognition of oxoanions by guanidinium host

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Among the various applications of supramolecular interactions, the discrimination of enantiomers occupies a prominent position because of the exclusive dependence on geometrical factors, but not at all on the differences in the chemical nature or solvation of the competing partners. As indicated in the biological systems, the embedding of a guanidinium anchor group in an open chain or macrocyclic chiral framework opens an access to dedicated enantioselective recognition of chiral carboxylates. To avail this, open chain hosts containing the chiral C2-symmetric bicyclic guanidinium unit as the primary binding site for the anionic guest appended to mono allylated bisphenol A and estradiol moieties were synthesized. Hydrophobic substituents attached to the guanidinium core act as walls to restrict the accessibility of the binding site and thus aid in generating stucturedness of the supramolecular complexes formed with the guests. Isothermal calorimetric titrations of enantiomers of the rigid trolox anion, with the open chain host, however, do not show any significant difference in the interaction energy of two enantiomers with the host.

Molecular modelling studies carried out in explicit solvent on open chain and macrocyclic hosts with enantiomers of binaphthyl phosphate anion show a geometrical preference for the S-enantiomer of the guest anion for binding to the macrocyclic hosts whilst no differentiation while interaction with open-chain hosts. Following the guideline from modelling, Ring-Closing-Metathesis was employed in order to obtain a macrocyclic guanidinium host. The RCM reaction was carried out under classical thermodynamic conditions as well as in the presence of a templating agent. In both cases, polymerization was dominant though better cyclization yields were observed in the presence of the template. Microwave-assisted RCM gave even better results in terms of highly reduced reaction time as well as higher yields of the desired macrocyclic compounds.

“Anion Cryptates”: Entropy-driven guest encapsulation in organic solvents without H-bonds assistance

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The development of molecular cages offers numerous concepts on how to construct confined spaces, capable of sequestering charged or electroneutral species. Whereas non-covalently connected cages assembled via weak interactions are well explored, examples of hosts featuring the occlusion of a cavity by means of a covalent framework are scarce in the literature. Our research is focused on developing electroneutral anion receptors containing a inner preorganized cavity, that is based on the [6^6]adamanzane covalent scaffold. We report herein the synthesis, characterization and some anion binding studies in polar organic media of a new class of electroneutral receptors using a zwitterionic construction principle. Appending four weakly coordinating bis-cobaltdicarbollide anions onto the [6^6]adz framework via an ethylene glycol spacer generates a highly symmetric electroneutral receptor designated T_4.

The very simple ^{1}H- and ^{13}C-NMR spectra of the T_4 receptor reveal its high symmetry in organic media such as MeCN and DMSO. Binding studies were performed in gaseous and condensed phases as well. The MALDI analyses recorded in negative mode revealed association complexes between the T_4 receptor and various anions such as Cl^-, Br^-, I^-, NO_3^-, HCO_3^-, BF_4^-, ClO_4^-. NMR titration studies in acetonitrile evidenced strong binding of Br^- and NO_3^- (K_{assoc} 10^4-10^5 mol/L), whereas F^-, Cl^-, I^-, HCO_3^- exhibited low association constants in the range of 10^2-10^3 mol/L. Moreover, ITC titrations revealed the energetic signature that characterizes the anion complexation process. The ITC analysis shows that the major contribution to the anion encapsulation arises from the entropy generated by the anion desolvation process, which occurs on complexation.

In conclusion, we report a novel family of electroneutral receptors containing a covalently connected cage, capable to accommodate anions with various geometries and sizes. Due to their similarity with the cationic counterparts, these novel receptors can be regarded as “anion cryptands”.

Synthesis of Hydrolase Mimics Derived From Functionalized Cyclodextrins

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Cyclodextrins (CDx), cyclic oligosaccharides composed of 1,4-α-linked glucose subunits, are an excellent basis for the design of enzyme mimics.[1] Due to their hydrophobic cavity and their hydrophilic outside they are good hosts for non-polar guests in aqueous media. Even native cyclodextrins mediate certain reactions, in particular ester hydrolyses, but arranging suitable functional groups around the cavity generally yields more efficient catalysts. We are interested in new CDx derivatives that accelerate the hydrolysis of esters, especially ones deriving from phosphonic acid. Synthetic access to these compounds is achieved by regioselectively introducing one or more leaving groups along the α- or β-cyclodextrin ring. Substitution of these groups with residues, which can potentially mediate ester hydrolysis, then leads to the desired products (Figure 1). As active groups N- and O-nucleophiles as well as α-effect-nucleophiles are investigated. Activity of the cyclodextrin derivatives thus prepared is evaluated by using an enzyme essay.[2]

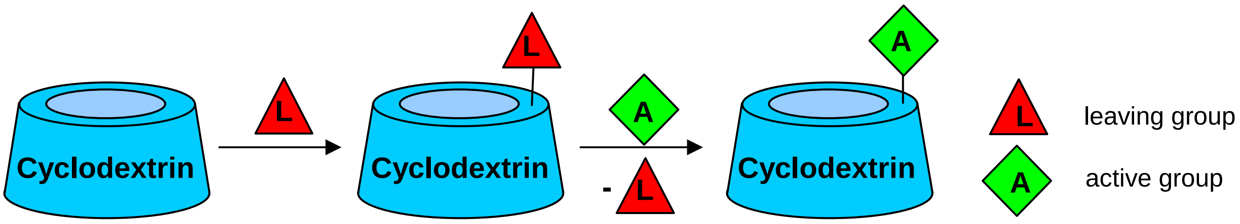

Figure 1. Schematic representation of the cyclodextrin functionalisation.

This poster introduces our concept and shows first results of the investigations.

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[1] R. Breslow, D. S. Dong, *Chem. Rev.* **1998**, *98*, 1997-2012.

[2] T. Wille, H. Thiermann, F. Worek, *Toxicol. in Vitro* **2010**, *24*, 1026-1031.

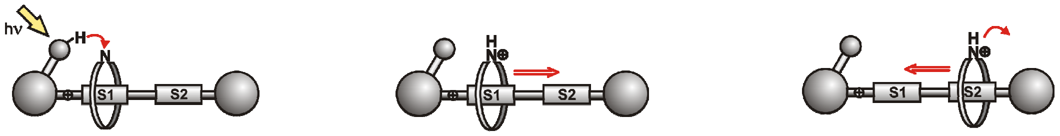
Towards a light driven proton pump

Zindler, M., Kiel/ GER, Frej, A., Kiel/ GER, Lüning, U., Kiel/ GER, Herges, R., Kiel/ Ger

Melanie Zindler, Adrian Frej, Christian-Albrechts-Universität, Otto Diels-Institut für Organische Chemie, Otto-Hahn-Platz 4, D-24098

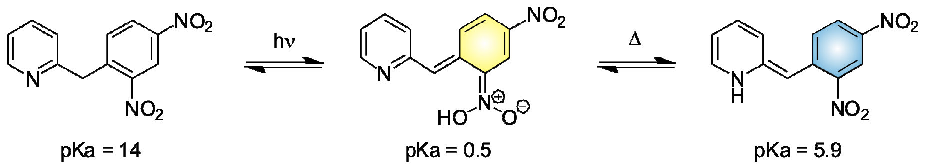
Light driven proton uphill transport is an essential process in nature. In the photosynthetic apparatus, light energy is used to pump protons across a cell membrane.

Scheme 1 depicts our model system. The proton transfer is realized by a photo-switchable acid, like 2-(2,4-dinitronbenzyl)pyridine (DNBP), attached to a rotaxane.



Scheme 1: Uphill proton transfer by a rotaxane. Due to electrostatic interactions the macrocycle moves along the axle.

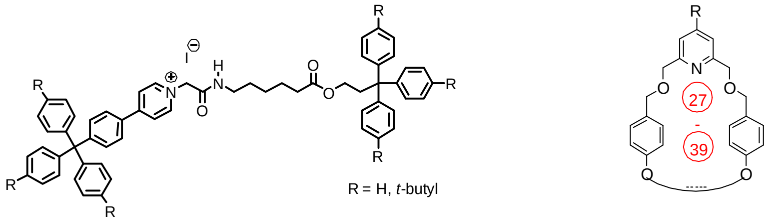
Upon irridation the photo-switchable acid tautomerizes to a more acidic form and switches back in a thermal reaction (scheme 2).



Scheme 2: Tautomeres of the DNBP with different acidity.

Several novel DNBP derivates were successfully synthesized and determined.[1] In this connection a new method to obtain di- and trinitrobenzyl substituted pyridine derivates was found.

Furthermore several axles and macrocycles were synthesized to build a [2]rotaxane via a slipping-process (scheme 3).



Scheme 3: Synthesized axles and macrocycles for the rotaxane formation.

[1] C. Goeschen, R. Herges, J. Richter, B. Tokarczyk, J. Wirz, *Helv. Chim. Acta* **2009,** *92,* 1909.

Speakers in Alphabetically Order

Poster Presenters in Alphabetically Order