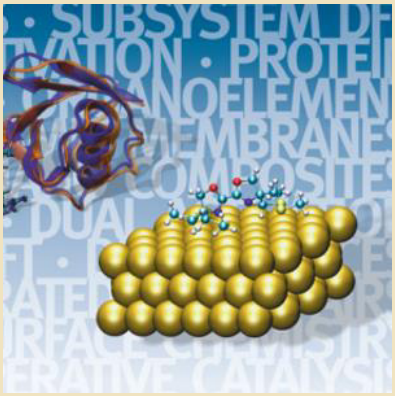
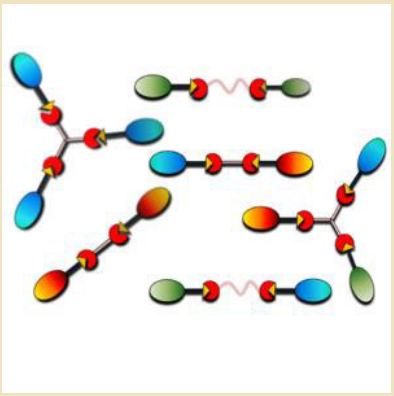
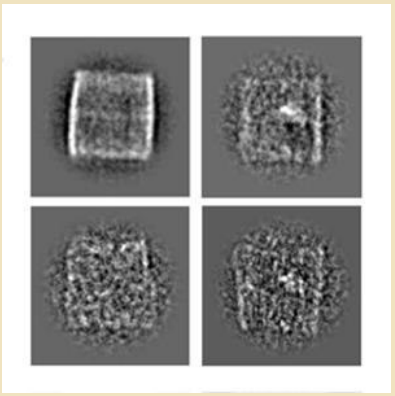
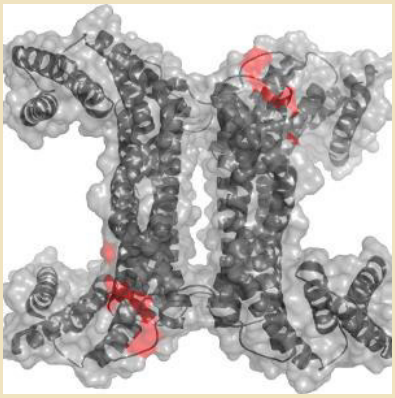
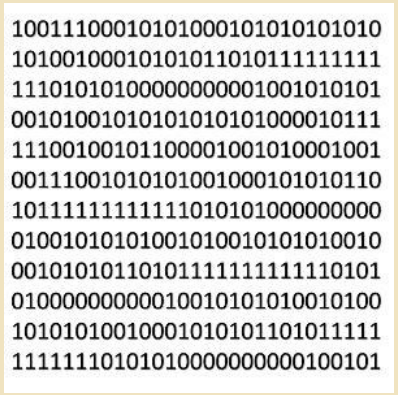
UNIVERSITÄT DUISBURG ESSEN

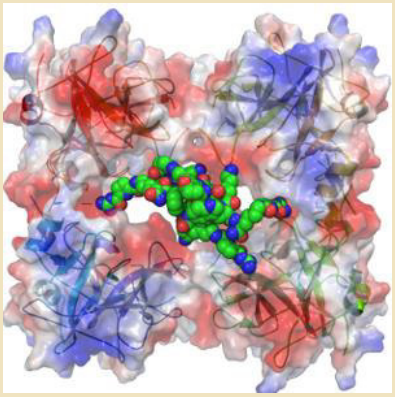
Offen im Denken

WWU MÜNSTER

CRC 1093 and CRC 858 Graduate Student Symposium

Synergistic and Supramolecular Aspects of Chemistry and Biology



29th – 31st of August 2018; Hotel Weissenburg, Billerbeck

CRC 1093

SFB 858

Supported by:

DFG Deutsche Forschungsgemeinschaft

TABLE OF CONTENTS

SCIENTIFIC PROGRAMM

Symposim Schedule

August 29th 2018 – August 31th 2018 Hotel Weissenburg Billerbeck

Wednesday, August 29th	
11:30	Arrival at Hotel Weissenburg
12:00	Lunch
13:30	**Session I – chair:**
	Welcome note
	Henning Klaasen (CRC 858)
	Matthias Hayduk (CRC 1093)
	Isabell Schönrath (CRC 858)
14:45	**Poster session A – Ma** + coffee break with cake
16:30	**Sebastian Kollenda (CRC 1093)**
	Lena Roling (CRC 858)
	Cecila Vallet (CRC 1093)
18:00	Dinner (three-course menue)
19:00	Covered wagon ride

SCIENTIFIC PROGRAMM

Thursday, August 30th	
8:00 am	Breakfast buffet
9:00	**Session II – chair:** **Anja Massolle (CRC 858)** **Florian Schulz (CRC 1093)** **Paul Mehlmann (CRC 858)** **Kyra Kujawski (CRC 1093)**
10:20	**Poster session Me – Z** + coffee break with cookies, yoghurt and fruits
12:30	Lunch
14:00	**Session III – chair:** **Beatriz Matarranz (CRC 858)** **Matthias Kracht (CRC 1093)** **Maximilian Koy (CRC 858)**
15:00	Coffee break with cake
16:00-17:00	**Christian Richter**
18:30	Dinner (three-course menü)
20:00	Games, swimming, etc.

SCIENTIFIC PROGRAMM

Friday, August 31th	
8:00 am	Breakfast buffet, clear rooms
9:00	**Session IV – chair:** **Robert Knitsch (CRC 858)** **Tatjana Ruks (CRC 1093)** **Wilke de Vries (CRC 858)**
10:00	Coffee break with cookies, yoghurt and fruits
10:30	**Session V – chair:** **Matthias Freitag (CRC 858)** **Selina van der Meer (CRC 1093)** **Constantin Stuckhardt (CRC 858)**
12:00	Lunch
13:00	Departure

TALK ABSTRACTS

Reaction Selectivity in On-Surface Chemistry: Alkyne Dimerization vs. Trimerization

H. Klaasen, L. Liu, X. Meng, P. A. Held, H.-Y. Gao, D. Barton, C. Mück-Lichtenfeld, J. Neugebauer, H. Fuchs, A. Studer

Prof. Dr. Armido Studer, Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149, Münster (Germany); studer@wwu.de.

h_klaa01@uni-muenster.de

The readily growing field of on-surface chemistry faces new challenges. Besides the development of new (clean) reactions, selectivity has to be addressed. Herein we report a new method that achieves reaction selectivity between alkyne dimerization[1] (Glaser coupling, yielding diacid **2**, and hydroalkynylation, products **3**-**5**) and alkyne trimerization[2] (benzene core formation, product **6**) of 6-ethinyl-2-naphthoic acid (ENA) **1** at the Ag(111) surface (Figure 1).[3]

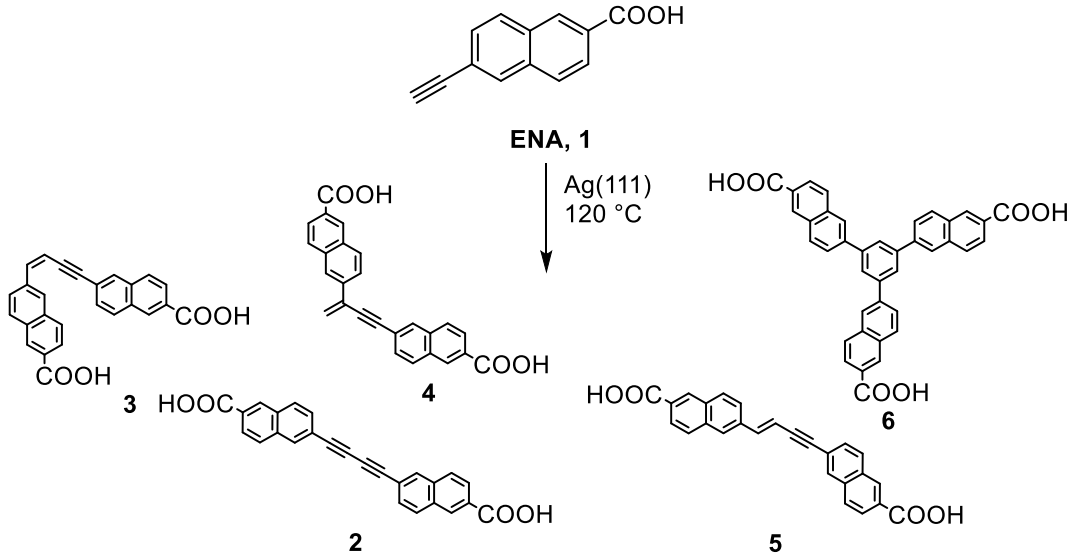


Figure 1: The main products that can be observed after thermal annealing of ENA on Ag(111).

Both reactions are well-known and understood in 2D-polymerization. Unfortunately, in most cases all of the aforementioned products will be observed. In this study we were able to show that synergistic effects play an important role and that eventually the surface coverage controls the reaction outcome. Further, we shed light on the mechanism of the cyclotrimerization by systematically investigating possible intermediates of a stepwise benzene core formation in cross cyclization with the ENA monomer. The results of this study open new pathways for the selective and sequential synthesis of well-defined nanoscaled π-conjugated materials.

References:

1. H. Y. Gao, H. Wagner, D. Zhong, J.-H. Franke, A. Studer, H. Fuchs, *Angew. Chem. Int. Ed.* **2013**, *52*, 4024–4028.
2. H. Zhou, J. Liu, S. Du, L. Zhang, G. Li, Y. Zhang, B. Z. Tang, H. J. Gao, *J. Am. Chem. Soc.* **2014**, *136*, 5567–5570.
3. H. Klaasen, L. Liu, X. Meng, P. A. Held, H.-Y. Gao, D. Barton, C. Mück-Lichtenfeld, J. Neugebauer, H. Fuchs, A. Studer, *submitted*.

TALK NOTES

Novel Luminophores with Aggregation-Induced Emission Properties for Bioamine and Protein Recognition

Matthias Hayduk and Jens Voskuhl

University of Duisburg-Essen, Institute of Organic Chemistry, Universitätsstr. 5, 45141 Essen
E-mail: matthias.haydukduk@uni-due.de

Since the discovery of the fluorescence phenomenon called aggregation-induced emission (AIE)[1], it has become a versatile tool in different disciplines in modern bio-chemistry[2]. The main advantage of AIE luminophores is their ability to light up when their motion is restricted. Only few examples are known from literature using this fluorophore class for binding to proteins, so that the influence of the binding event is largely unknown. This fluorescence "on" behavior enables the direct read-out of binding processes or morphological changes such as gelation, crystallization, binding or polymerization, which gives the AIE important applications for bio-chemistry in future. Therefore, our aim is the development of novel luminophores with AIE properties as small ligands for recognition of protein surfaces, binding pockets and specific bioamines. For this purposes, we use our AIE basic structure functionalized with short amino acid sequences and charged substituents. First molecules show selective binding towards specific bioamines, which gives us further information about the structural constitution of our luminophores which is needed to interact with the target structures.

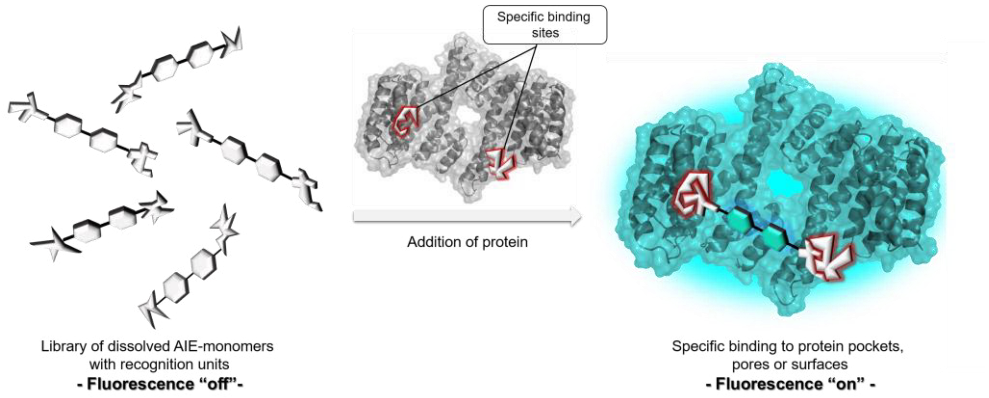


Figure 1: Schematic presentation of the fluorescence "on" behaviour upon protein binding.

References:

1. a) Luo, J.; Xie, Z.; Lam, J. W. Y.; Cheng, L.; Chen, H.; Qiu, C.; Kwok, H. S.; Zhan, X.; Liu, Y.; Zhu, D.; Tang, B. Z. *Chem. Commun.* **2001**, 1740-1741. b) Tang, B. Z.; Zhan, X.; Yu, G.; Sze Lee, P. P.; Liu, Y.; Zhu, D. *J. Mater. Chem.* **2001**, *11*, 2974-2978. c) Chen, J.; Law, C. C. W.; Lam, J. W. Y.; Dong, Y.; Lo, S. M. F.; Williams, I. D.; Zhu, D.; Tang, B. Z. *Chem. Mater.* **2003**, *15*, 1535-1546. d) Tong, H.; Dong, Y.; Häußler, M.; Lam, J. W. Y.; Sung, H. H. Y.; Williams, I. D.; Sun, J.; Tang, B. Z. *Chem. Commun.* **2006**, 1133-1135. e) Hong, Y.; Lam, J. W. Y.; Tang, B. Z. *Chem. Commun.* **2009**, 4332-4353.

2. a) Zhang, Y.; Li, D.; Li, Y.; Yu, J. *Chem Sci.* **2014**, *5*, 2710-2716. b) Wang, E.; Zhao, E.; Hong, Y.; Lam, J. W. Y.; Tang, B. Z. *J. Mater. Chem.* **2014**, *2*, 2013-2019. c) Kwok, R. T. K.; Leung, C. W. T.; Lam, J. W. Y.; Tang, B. Z. *Chem. Soc. Rev.* **2015**, *44*, 4228-4238.

TALK NOTES

1,N^6-Ethenoadenine as a nucleobase for metal-mediated base pairing

Isabell Schönrath, Soham Mandal, Jens Müller

Westfälische Wilhelms-Universität Münster, Institut für Anorganische und Analytische Chemie, 48149 Münster, Germany

isabell@muellerlab.org

To extend the field of functionalisation of DNA duplexes with dinuclear base pairs, 1,N^6-ethenoadenine (εA) was introduced as a bis(monodentate) ligand exhibiting the possibility to bind two metal ions with almost parallel N→M-bonds (Figure 1 (a)). Indeed, two Ag^+ ions are bound by an εA-εA base pair in antiparallel-stranded DNA.[1] In addition, εA can form hetero base pairs, for example with thymine (T).[2] Moreover, the εA-T pair has been established as the first base pair to bind two divalent metal ions in a DNA duplex (Figure 1(b)).[3]

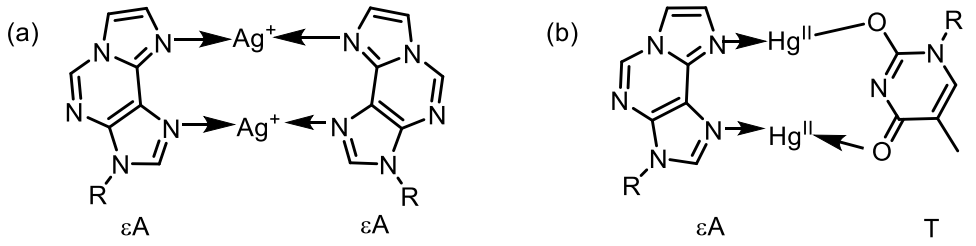


Figure 1: Proposed structure of the εA-Ag^+_2-εA homo basepair (a) and εA-Hg^{2+}-T hetero basepair (b).

The latter base pair was so far observed in a parallel-stranded duplex with *reversed* Watson-Crick base pairs only. Hence, different strategies to form such a duplex were applied, e.g. using alpha-anomeric nucleotides. We are reporting here the influence of the relative orientation of the DNA strands (parallel *vs*. antiparallel) and the glycosidic bonds (cisoid *vs.* transoid) on the Hg^{2+}-binding affinity of the DNA duplexes.

References:

1. Mandal, S.; Hepp, A.; Müller, J., *Dalton Trans.* **2015**, *44*, 3540-3543.

2. Mandal, S.; Hebenbrock, M.; Müller, J., *Inorg. Chim. Acta* **2018**, *472*, 229-233.

3. Mandal, S.; Hebenbrock, M.; Müller, J., *Angew. Chem. Int. Ed.* ***2016***, *55*, 15520-15523.

TALK NOTES

Live cell imaging of fluorescent nanoprobes to envision their cellular fate

Sebastian Kollenda, Mathis Kopp, Jasmin Wens, Nina Schulze, Robert Pöhler, Hemmo Meyer, Matthias Epple

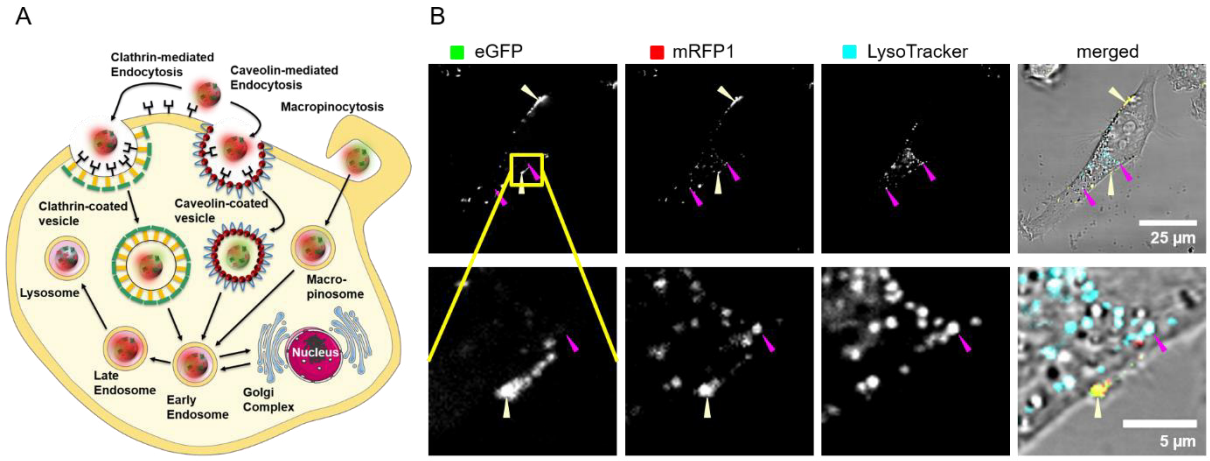
Inorganic Chemistry and Centre for Nanointegration Duisburg-Essen (CeNIDE), University of Duisburg-Essen, Essen, Germany

Corresponding Author: University of Duisburg-Essen, Universitaetsstr. 7, 45141 Essen, sebastian.kollenda@uni-due.de

Calcium phosphate naturally occurs in bone tissue and teeth and is considered to have a good biocompatibility and biodegradability in biological applications.[1] Hence nanoparticles based on this material have become a potent delivery system of a vast range of cargo molecules for *in vitro* and *in vivo* experiments.

The nanoparticles were synthesized and loaded with a fusion protein consisting of two fluorescent units mRFP1-eGFP.[2] HeLa cells were incubated with these nanoparticles (1 µg of protein per well) for 6 h, washed and then stained with 75 nM LysoTracker™ Deep Red for 1 h. Live-cell confocal laser scanning microscopy (CLSM) was performed on a TCS SP8 system (Leica Microsystems) using a 63x/1.2 water immersion objective.

The nanoparticles were taken up by the cells by endocytosis and directed into lysosomes. At a pH of 7.4, the fluorescence of both proteins (red: mRFP1 and green: eGFP) is detectable. Under acidic conditions (lysosomes) (Fig. 1), the green fluorescence will disappear[3] due to the protonation of the chromophore. Thus, only the fluorescence of mRFP1 will remain detectable.



The CLSM images showed the successful transport of protein-loaded nanoparticles, with some mRFP1 fluorescence co-localizing with lysosomes. However, eGFP fluorescence is only detectable outside of lysosomes, inside of recently build endosomes or at the cell membrane coming in from the periphery.

References:

1. V. Sokolova, M. Epple, Inorganic Nanoparticles as Carriers of Nucleic Acids into Cells. *Angewandte Chemie International Edition,* **2008**, *47*, 1382-1395.

2. D. J. Klionsky et al., Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy*, **2016**, *12*, 1-222.

3. S. Kimura, T. Noda, T. Yoshimori, Dissection of the Autophagosome Maturation Process by a Novel Reporter Protein, Tandem Fluorescent-Tagged LC3. *Autophagy,* **2007**, *3*, 452-460.

TALK NOTES

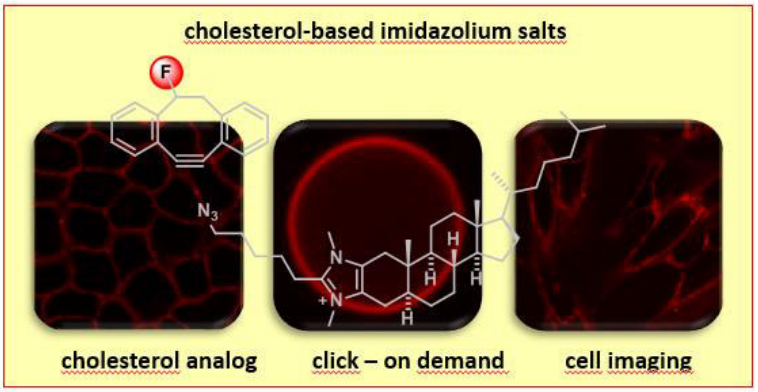
Novel addressable cholesterol analogs for live imaging of cellular membranes

Lena Roling[a], David Grill[b], Anna L. L. Matos[b], Stephanie Wulff[c], Da Wang[c], Jonas Börgel[a], Martin Körsgen[d], Heinrich F. Arlinghaus[d], Hans-Joachim Galla[c], Volker Gerke[b], Frank Glorius[a]

Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut

lena.roling@uni-muenster.de

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



References:

1. Ikonen, E., *Nat. Rev. Mol. Cell. Biol.* **2008**, *9*, 125; Brown, D. A., London, E., *J. Biol. Chem.* **2000**, *275*, 17221; Simons, K., Ikonen, E., *Science* **2000**, *290*, 1721.

2. Gimpl, G., Gehrig-Burger, K., *Biosci. Rep.* **2007**, *27*, 335; Maxfield, F. R., Wüstner, D., *Methods Cell Biol.* **2012**, *108*, 367.

3. Rakers, L., Grill, D., Matos, A. L. L., Wulff, S., Wang, D., Börgel, J., Körsgen, M., Arlinghaus, H. F., Galla, H.-J., Gerke, V., Glorius, F., *Cell Chemical Biology* **2018**, https://doi.org/10.1016/j.chembiol.2018.04.15.

TALK NOTES

Molecular characterization and modulation of Survivin´s cellular functions with supramolecular ligands

Cecilia Vallet*, Dennis Aschmann, Marcel Mertel**, Martin Ehlers**, Sandra Bäcker*, Annika Meiners*, Jana Reich*, Christine Beuck***, Peter Bayer***, Carsten Schmuck**, Shirley K. Knauer***

** Department of Molecular Biology II, Centre for Medical Biotechnology (ZMB)*
cecilia.vallet@uni-due.de, sandra.baecker@uni-due.de, annika.meiners@uni-due.de, jana.reich@stud.uni-due.de, shirley.knauer@uni-due.de

*** Department of Supramolecular Chemistry*
dennis.aschmann@uni-due.de, marcel.mertel@uni-due.de, martin.ehlers@uni-due.de, carsten.schmuck@uni-due.de

**** Department of Structural and Medicinal Biochemistry, ZMB*
christine.beuck@uni-due.de, peter.bayer@uni-due.de

University of Duisburg-Essen, 45117 Essen, Germany

Survivin was found to be upregulated in virtually all types of human cancers. It is associated with resistance against chemo- and radiotherapy, an increased tumor recurrence and an abbreviated patient survival, making it a promising target for cancer therapy. Survivin is involved in two key processes of carcinogenesis. As a member of the IAP family, it exhibits anti-apoptotic functions, but is also necessary for proper chromosome segregation during mitosis[1, 2].

Our project aims to interfere with Survivin´s (patho)biological role during cell death and proliferation using novel supramolecular ligands to target surface-accessible glutamate/aspartate residues either on Survivin´s Histone H3 binding site or its nuclear export signal (NES), which mediates interaction with the export receptor Crm1.

We were able to identify several promising candidate ligands affecting Survivin/Crm1 and Survivin/Histone H3 interaction as well as Survivin dimer formation in cell-based FRET- and proximity ligation (PLA) assays. With NMR titration experiments, we could map binding of one peptide ligand to acidic amino acid residues on Survivin´s surface spanning across the Histone H3 binding site. Currently, we are setting up additional cellular assays to investigate an effect on Survivin´s anti-apoptotic and mitotic functions.

References:

1. S. K. Knauer et al.: The survivin-Crm1 interaction is essential for chromosomal passenger complex localization and function. *EMBO Rep.* **2006**, *7*, 1259-1265.

2. S. K. Knauer et al Survivin's dual role: an export's view. *Cell Cycle.* **2007**, *6*, 518-521.

TALK NOTES

Improved "Experimental" EPR Parameters through First-Principles Computation

Anja Massolle[1,2], Thomas Dresselhaus[1,2], Steffen Eusterwiemann[1], Carsten Doerenkamp[3] , Hellmut Eckert[3] , Armido Studer[1] , and Johannes Neugebauer[1,2]

[1]Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Germany. studer@uni-muenster.de, j.neugebauer@uni-muenster.de

[2]Center for Multiscale Theory and Computation, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Germany.

[3]Institut für Physikalische Chemie, Westfälische Wilhelms-Universität Münster, Corrensstrasse 28/30, 48149 Münster, Germany. Instituto de Física em São Carlos, Universidade de São Paulo, Avenida Trabalhador Saocarlense 400, São Carlos, SP 13566-590, Brazil. eckerth@uni-muenster.de

a.massolle@uni-muenster.de

Typically, experimental EPR spectra are analyzed in terms of a fit to an effective Hamiltonian. Among others, hyperfine coupling constants are obtained from this fit. If too many free parameters are included in the model the extracted constants may be ambiguous, since several sets of parameters may represent the EPR spectra equally well.

Verdazyl radicals possess four ^{14}N nuclei inside their six-membered ring, which already leads to quite complex spectra. Additional, typically rather weak, couplings occur with ^{1}H nuclei of aromatic substituents at the 1- and 5- position of the verdazyl ring. Often, a high-quality fit of experimental spectra can be achieved without considering these additional couplings. As we point out here the large number of ^{1}H couplings does have a significant effect on the spectrum. We established an efficient and accurate computational protocol to calculate EPR parameters[1]. As a part of this protocol a molecular dynamics simulation based on the quantum mechanically derived force field[2] is performed. The obtained trajectory is sampled at different time steps. For each snapshot, EPR properties are calculated. Afterwards EPR spectra are simulated based on the averaged results. This protocol was applied to a number of verdazyl radicals[1,3]. A high-quality fit is obtained from the calculated EPR parameters, and the fitted values do not deviate much from the calculated ones.

References:

1. A. Massolle, T. Dresselhaus, S. Eusterwiemann, C. Doerenkamp, H. Eckert, A. Studer and J. Neugebauer: Towards reliable references for electron paramagnetic resonance parameters based on quantum chemistry: the case of verdazyl radicals. *Phys. Chem. Chem. Phys.*. **2018**, *20*, 7661–7675.

2. S. Grimme: A General Quantum Mechanically Derived Force Field (QMDFF) for Molecules and Condensed Phase Simulations. *J. Chem. Theory Comput.*. **2014**, *10*, 4497–4514.

3. S. Eusterwiemann, T. Dresselhaus, C. Doerenkamp, O. Janka, O. Niehaus, A. Massolle, C. G. Daniliuc, H. Eckert, R. Pöttgen, J. Neugebauer, A. Studer: Cooperative Magnetism in Crystalline *N*-Aryl-Substituted Verdazyl Radicals: First-Principles Predictions and Experimental Results. *Chem. Eur. J.*. **2017**, *23*, 6069–6082.

TALK NOTES

6×His-tagged chemical probes for quantitative affinity enrichment mass spectrometry

Florian Schulz, Farnusch Kaschani and Markus Kaiser

**Department of Chemical Biology, University of Duisburg-Essen, 45141 Essen*
florian.schulz@uni-due.de

In chemical proteomics, small molecule probes are utilized to profile proteins based on their functional properties. One of these functional technologies is activity-based protein profiling (ABPP). This technique enables direct monitoring of the availability of enzyme active sites. An extension of the ABPP approach is Proteome Reactivity Profiling (PRP) where probes with a broad specificity are used to profile reactivity patterns in whole proteomes.

Here we report the synthesis and evaluation of two such broad band probes based on α chloroacetamide (CA) and α iodoacetamide (IA) reactive moiety. Both probes are directed against with the thiol group in cysteine residues. To facilitate the enrichment of target proteins, the reactive groups are linked via an alkyl chain to a hexahistidine-tag for simplified affinity enrichment (e.g. on Ni-IDA IMAC resin). The probes were evaluated by labelling E. coli lysates followed by affinity enrichment on Ni-IDA resin. Incorporation of the probe was verified by Western blotting with a specific 6×His antibody and parallel quantitative label-free mass spectrometry. The whole protocol was adapted to a 96-well format and allows parallel screening of several hundred samples. First experiments in E. coli indicate cysteine containing thioredoxin and glutharedoxins as probe binding partners identified by LC-MS/MS.

All in all, we show that our chemical probes are suitable for Nickel affinity enrichment and that the described protocol is a valuable addition to the proteomics tool box.

References:

1. Keilhauer, E.C., Hein, M.Y. and Mann, M.: Chemical strategies for activity-based proteomics. *Mol Cell Proteomics*. **2015**, *1*, 120–135.

2. Barglow, K.T. and Cravatt, B.F.: Discovering Disease-Associated Enzymes by Proteome Reactivity Profiling. *Chem Biol.* **2004**, *11*, 1523-31.

TALK NOTES

Phosphorus(III) superbase vs. phosphorus(V) superacid

Paul Mehlmann, Fabian Dielmann

Institut für Anorganische und Analytische Chemie, Westfälische Wilhelms-Universität Münster; dielmann@wwu.de

p_mehl02@uni-muenster.de

As part of our program to enhance the donor strength of phosphines, we reported a new approach to highly electron-rich phosphines based on the use of imidazolin-2-ylidenamino groups directly attached to the phosphorus atom.[1] These phosphines are excellent electron donor ligands and display a new class of phosphorus(III) superbases. Furthermore, the first stable phosphorus(V) dication was synthesised by oxidation of P(NI*i*Pr)$_3$.

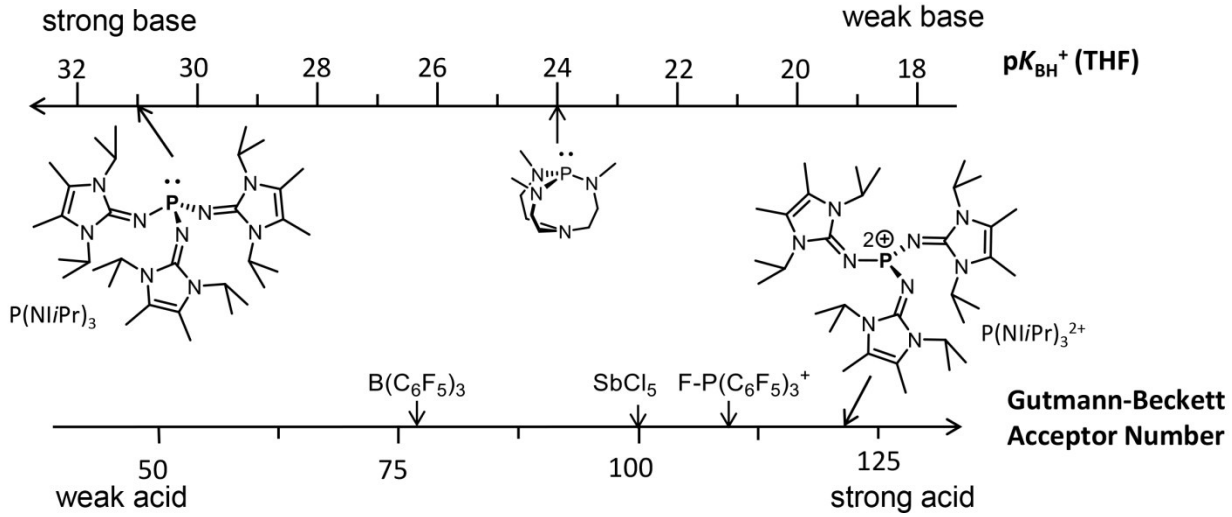


Figure 1 pK_{BH}^+ and Gutmann-Beckett values of P(NI*i*Pr)$_3$ and P(NI*i*Pr)$_3^{2+}$ respectively and selected bases and acids for comparison.

The determination of the phosphines basicity reveals pK_{BH}^+(THF) values of up to 31.0.The Lewis acidity of P(NI*i*Pr)$_3^{2+}$ was determined by the Gutmann-Beckett method to be 115 (Figure 1). Thus, P(NI*i*Pr)$_3$ is the strongest reported nonionic phosphorus(III) superbase[2] and P(NI*i*Pr)$_3^{2+}$ is a remarkble strong Lewis acid. The unique electronic properties of these phosphine and phosphonium dication provide new prospects in small molecule activation.

References:

1. M. Wünsche, F.Dielmann *et al*, *Angew. Chem. Int. Ed.* **2015**, *54*, 11857-11860.
2. P. Mehlmann, F. Dielmann *et al.*, *Chem. Eur. J.*, **2017**, *23*, 5929-5933.

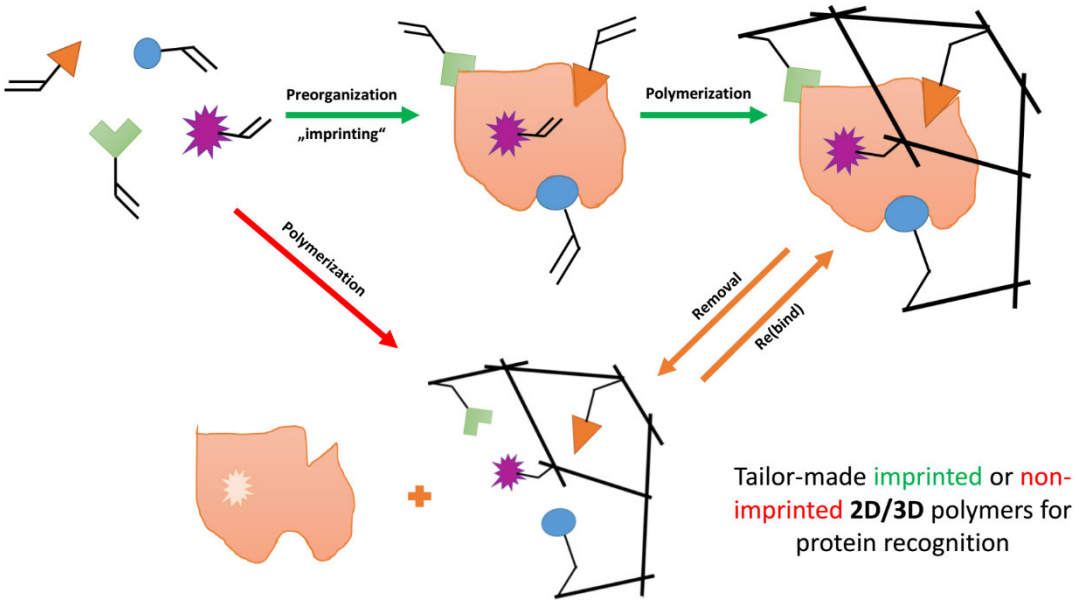
TALK NOTES

(Non-)Imprinted Polymers by Tailor-made Affinity Monomers for Proteins

K. Kujawski[1], Prof. T. Schrader[1]

[1]*Department of Organic Chemistry, University of Duisburg-Essen, Universitätsstr. 7, 45117 Essen, Germany,* kyra.kujawski@uni-due.de

During the past two decades, there was an exponential increase of research containing molecular imprinted materials. It started from ions to small molecules over peptides and finally reached macromolecules and proteins, viruses, DNA and cells. The field of protein imprinting and recognition is just about to be further investigated and developed.[1] We faced up to this challenging task and developed *tailor-made* molecular non-imprinted (NIP) and imprinted (MIP) polymers in two versions, hydrogels and nanoparticles. In contrast to leading literature, we use a special designed and synthesized monomer library to create specific polymers for a certain target. With the help of the amino acid complementary monomers, we want to enable a design of highly specific and selective polymers which can e.g. block protein or enzymatic functions, hinder protein-protein interactions or act like synthetic antibodies.[2] The high affinity of our two main functional monomers could be demonstrated also in imprinted biosensors for trypsin with a detection limit below picomolar (pM) concentrations.[3]



References:

1. M. E. Byrne, V. Saliam: Review, *Int. Journal of Pharmaceutics;* **2008**, *364*, 188–212.

2. Y. Hoshino, H. Koide, T. Urakami, H. Kanazawa, T. Kodama, N. Oku, K. Shea: Recognition, Neutralization, and Clearance of Target Peptides in the Bloodstream of Living Mice by Molecularly Imprinted Polymer Nanoparticles: A Plastic Antibody, *JACS;* **2010**, *132*, 6644–6645.

3. G. Ertürk, M. Akhoundian, K. Kujawski, S. Shinde, S. Y. Yeung, M. Hedström, T. Schrader, B. Mattiasson, B. Sellegren: Ultrasensitive Protein Sensor Based on Microcontact Imprinting – Complementary Match of Supramolecular and Dynamic Chemistry, **2018**, *submitted*.

TALK NOTES

Supramolecular Polymerization of a Pd(II)-BODIPY complex

Beatriz Matarranz García-Patos[a], Jörn Droste[b], Gustavo Fernández Huertas[a], Michael R. Hansen[b]

[a] Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut, Correnstraße 40, 48149 Münster, fernandg@uni-muenster.de
[b]Westfälische Wilhelms-Universität Münster, Institut für Physikalische Chemie, Correnstraße 40, 48149 Münster, mhansen@uni-muenster.de
matarran@uni-muenster.de

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

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

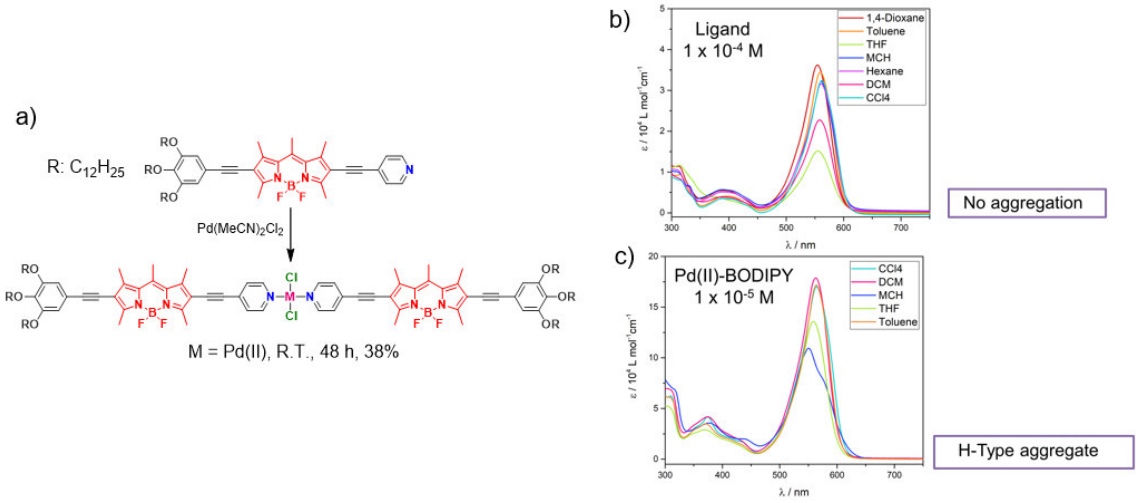


Figure 1. a) Synthetic pathway of Pd(II)-BODIPY complex. b) Solvent dependent UV/Vis spectra of ligand (1 x 10^{-5} M). c) Solvent-dependent UV/Vis spectra of Pd(II)-BODIPY complex (1 x 10^{-5} M).

References:

1. G. Ulrich, R. Ziessel and A. Harriman, *Angew. Chem., Int. Ed.*, **2008**, *47*, 1184.
2. C. Rest, R. Kandanelli and G. Fernández, *Chem. Soc. Rev.*, **2015**, *44*, 2543.

TALK NOTES

Reconstitution of p97-mediated unfolding with pure components

Matthias Kracht, Johannes van den Boom, Hemmo Meyer

Molekularbiologie I, Fakultät für Biologie, Universität Duisburg-Essen Universitätsstr. 5, 45117 Essen, matthias.kracht@uni-due.de

The AAA+ ATPase p97 (also known as VCP, Cdc48 in yeast, Ter94 in flies) plays important roles in several cellular processes such as ER-associated protein degradation, chromatin associated degradation, autophagy or membrane fusion. Its molecular function is to bind and unfold ubiquitinated substrate proteins to facilitate their degradation by the proteasome. p97 is a hexamer with each subunit containing an N-terminal domain (N-domain) for interaction with substrate adaptor proteins, as well as two ATPase domains (D1 and D2). The latter two form hexameric rings with the D1 domains stacked on top of the D2 domains. The exact mechanism by which a substrate protein is processed by p97 is subject of intensive research. Recent advances have led, for the first time, to recapitulation of p97-mediated unfolding of a ubiquitinated model substrate with pure components[1,2]. Our goal is to set up and further develop this assay in our laboratory in order to address and understand p97-mediated mechanisms by a combination of novel supramolecular chemistry and genetically encoded crosslink approaches. For this purpose, we expressed a fluorescent protein with an N terminal diubiquitin moiety in E. coli. and established an in vitro system for polyubiquitination, resulting in branched K48 linked chains. Upon incubation of the substrate with p97 and its cofactor Ufd1-Npl4, the unfolding activity of p97 will be determined by measuring the decrease of fluorescence. The effect of compounds that target distinct structural elements will be tested.

References:

1. EE. Blythe, KC. Olson, V. Chau V, RJ. Deshaies: Ubiquitin- and ATP-dependent unfoldase activity of P97/VCP•NPLOC4•UFD1L is enhanced by a mutation that causes multisystem proteinopathy. *PNAS*. **2017**, *114* (22), E4380-E4388.
2. N.O. Bodnar, T.A. Rapoport: Molecular Mechanism of Substrate Processing by the Cdc48 ATPase Complex. *Cell*. **2017**, *169* (4), 722-735.e9.

TALK NOTES

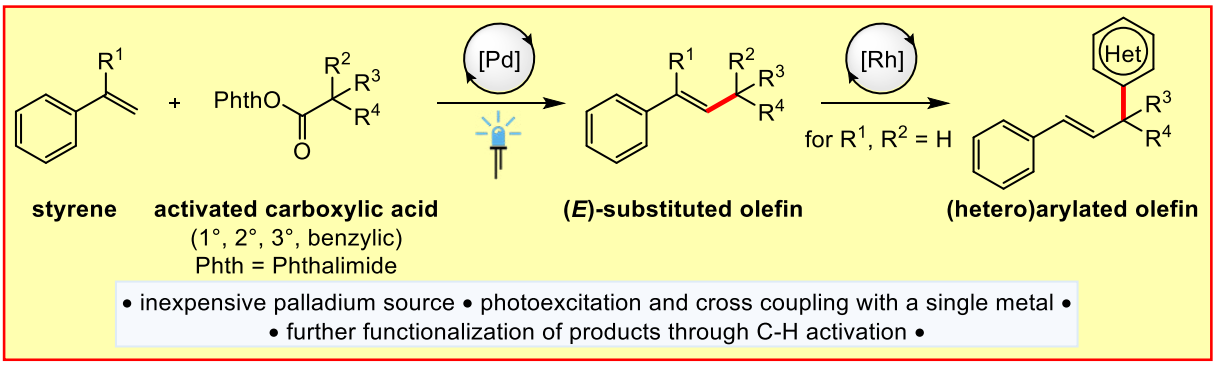
Palladium-Catalyzed Decarboxylative Heck-Type Coupling of Activated Aliphatic Carboxylic Acids and the Application in Cross-Dehydrogenative Allylic (Hetero)arylation

Maximilian Koy, Frederik Sandfort, Adrian Tlahuext-Aca, Andreas Lerchen, Tobias Knecht, Johannes B. Ernst, Linda Quach, Klaus Bergander, Constantin G. Daniliuc, Frank Glorius

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster

koy@uni-muenster.de

Olefins represent a widely-used class of functional groups in organic synthesis and material science. Thus, the development of new methods for the preparation of multisubstituted alkenes with complete stereocontrol is highly desirable. The Heck reaction is among the most fundamental reactions in the portfolio of synthetic organic chemists to create substituted carbon-carbon double bonds. While the formation of $C(sp^2)$–$C(sp^2)$ bonds is largely established, analogous assembly of $C(sp^2)$–$C(sp^3)$ connectivity is more challenging with traditional methods. Here, we present the coupling of *N*-hydroxyphthalimide esters derived from aliphatic carboxylic acids with electronically diverse styrenes to deliver substituted olefins with perfect (*E*)-selectivity. This method is exceptionally mild and relatively inexpensive $Pd(PPh_3)_4$ is used as the catalyst. Mechanistic studies for this process revealed a radical process initiated through excitation of a Pd(0) species with visible light.[1] To showcase the utility of the products obtained through this methodology, selected molecules were further functionalized through a rhodium catalyzed cross-dehydrogenative (hetero)arylation of the allylic $C(sp^3)$-H bond.[2]



References:

1. M. Koy, F. Sandfort, A. Tlahuext-Aca, L. Quach, C. G. Daniliuc, F. Glorius, *Chem. Eur. J.* **2018**, *24*, 4552-4555.

2. A. Lerchen, T. Knecht, M. Koy, J. B. Ernst, K. Bergander, C. G. Daniliuc, F. Glorius, *submitted*.

TALK NOTES

Solid-State NMR Spectroscopy and its Application on Organic FLPs and Inorganic BNH Polymers

***Robert Knitsch*[a], Delong Han[b], Torsten Beweries[b], Xiaoming Jie[c], Gerald Kehr[c], Gerhard Erker[c], Hellmut Eckert[a,d], Michael Ryan Hansen[a]**

[a] Westfälische Wilhelms-Universität Münster, Institut für Physikalische Chemie, Corrensstr. 28/30, 48149 Münster, [b] Leibniz-Institut für Katalyse an der Universität Rostock e.V., Albert-Einstein-Str. 29a, 18059 Rostock, [c] Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut, Corrensstr. 40, 48149 Münster, [d] Institute of Physics Sao Carlos, University of Sao Paulo, Sao Carlos, SP 13460-590

r.knitsch@uni-muenster.de

Structure characterisation of the solid-state is of great importance in solid matter material sciences as the structure is closely related to many important properties as conductivity, durability, reactivity etc. However, solid-state structure characterisation can be challenging, especially in amorphously ordered compounds, which are not accessible via x-ray diffractometry. For such materials solid-state NMR spectroscopy is the ideal tool for structure characterisation as the first and second coordination sphere of observed nuclei can be probed in detail. This presentation will shortly introduce into solid-state NMR techniques before discussing its application on B-P frustrated Lewis Pairs (FLP) and BNH polymers in detail. FLPs have gained great attention in the field of metal free catalysis over the last decade. Their unique reactivity results from frustration due to favoured bond formation between the Lewis centres prevented by sterically demanding groups.[1,2]
On the other side the BNH polymers resulting from catalytic dehydrogenation of hydrazine borane, often discussed as hydrogen storage material,[3] might be used as precursors for boron nitrogen ceramics. As the properties of these ceramics strongly depend on the B-N-H network, structure characterisation of this amorphous material is important.

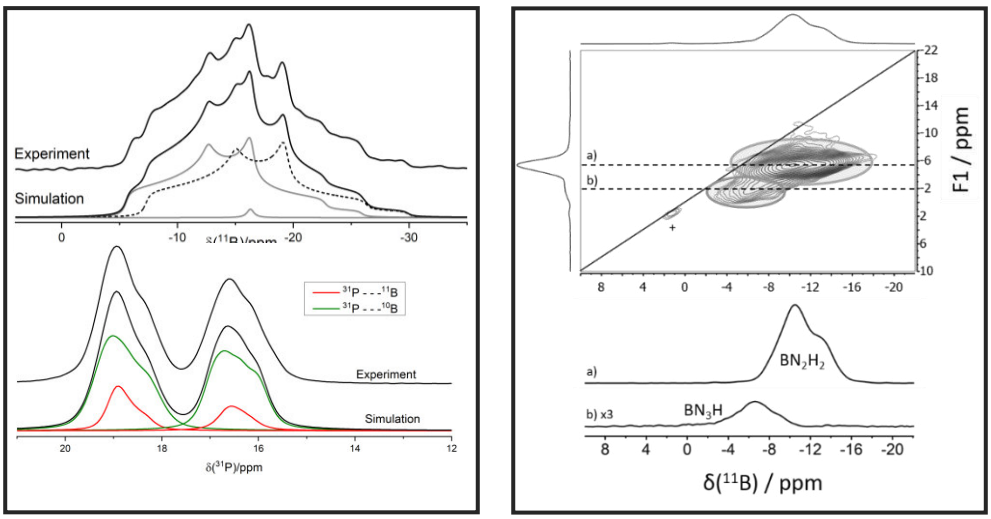


Figure 1: (Left) Exemplary ^{11}B (top) and ^{31}P solid-state NMR spectra of a B-P-FLP macrocycle. (Right) 2D solid-state ^{11}B MQMAS experiment of a BNH polymer obtained via dehydrogenation of hydrazine borane.

References:

[1] Douglas W.Stephan, JACS, **2015**, *137*, 10018-10032.
[2] Douglas W.Stephan, Gerhard Erker, *Angew. Chem. Ed.* **2010**, *49*, 46-76.
[3] Romain Moury, Umit B. Demirici, *Energies*, **2015**, *8*, 3118-3141.

TALK NOTES

Ultrasmall Gold Nanoparticles for Protein-Specific Targeting: Investigation by in-depth NMR Spectroscopy

Tatjana Ruks[1], Christine Beuck[2], Torsten Schaller[3], Felix Niemeyer[3], Manfred Zähres[4], Kateryna Loza[1], Marc Heggen[5], Ulrich Hagemann[6], Christian Mayer[4], Peter Bayer[2], Matthias Epple[1]

[1] Inorganic Chemistry and Center for Nanointegration Duisburg-Essen (CENIDE), University of Duisburg-Essen, Germany

[2] Institute of Biology and Center for Medical Biotechnology (CMB), University of Duisburg-Essen, Germany

[3] Organic Chemistry, University of Duisburg-Essen, Germany

[4] Physical Chemistry, University of Duisburg-Essen, Germany

[5] Ernst Ruska-Center for Microscopy and Spectroscopy with Electrons, Forschungszentrum Jülich GmbH, Germany

[6] Interdisciplinary Center for Analytics on the Nanoscale (ICAN) and Center for Nanointegration Duisburg-Essen (CENIDE), University of Duisburg-Essen, Germany

Tatjana.ruks@uni-due.de

Ultrasmall gold nanoparticles (AuNPs) with a diameter below 2 nm are promising as specialized carriers for targeted drug delivery. Functionalized with specific binding motifs, they open up innovative opportunities in a wide range of applications, e.g. nanomedicine. A possible application is the specific targeting of protein-epitopes.

A versatile approach to the functionalization with specific epitope-binding motifs is covalent binding of the gold-surface with sulfur-containing molecules, e.g. L-cysteine. NMR spectroscopy gives valuable insights into the characteristics of the binding situation on the surface.

Functionalized AuNPs were prepared by reduction of $HAuCl_4$ with $NaBH_4$ in presence of peptides which leads to in situ functionalization by strong Au-S-binding via cysteine. Here, the hexapeptide CGGpTPA, that is known to address the WW domain of the protein hPin1, was attached.

The attachment of the peptide to the AuNPs was detected by NMR spectroscopy, i.e. 1D-^{1}H NMR spectroscopy and 2D-^{1}H,^{1}H-TOCSY NMR spectroscopy. ^{1}H-DOSY and ^{15}N-DOSY NMR spectroscopy enabled the determination of the hydrodynamic particle diameter in excellent agreement with the metallic core diameter by high-resolution transmission electron microscopy. Specific protein binding was demonstrated by 2D-^{1}H,^{15}N-HSQC NMR spectroscopy. By titration of CGGpTPA-functionalized gold nanoparticles with the ^{15}N-labeled protein hPin1, specific interaction with the WW domain was observed.

TALK NOTES

Self-Assembly of Redox- and Hypersound-Responsive Supramolecular Nanocontainers

Wilke C. de Vries, David Grill, Maren Wissing, Yao Lu, Jurriaan Huskens, Armido Studer, Volker Gerke, Bart Jan Ravoo

Institute of Organic Chemistry, University of Münster, 48149 Münster

W.deVries@wwu.de

The supramolecular assembly of responsive materials holds great promise for the precise design and versatile modular fabrication of functional materials with diverse applications. For example, self-assembled nanocontainers show a high potential as vehicles for intracellular delivery, nanoreactors or protective shells for biomolecules.[1]

In this contribution, we demonstrate the supramolecular assembly of stimulus-responsive nanocontainers comprising a self-assembled cyclodextrin vesicle core and a supramolecular anchored polymer shell.[2] The supramolecular design allows for a modular modification of building blocks resulting in distinct functions and response to different external stimuli. Additionally, the surface of the nanocontainers can be functionalized readily with bioactive ligands facilitating their molecular recognition by proteins.[3] Importantly, the permeability of these nanocontainer assemblies can be precisely controlled by redox-stimulus or hypersound of gigahertz frequency enabling the loading and unloading of hydrophilic payload.[2,3] An incorporation of responsive cyclodextrin host amphiphiles as anchor for the guest-functionalized polymer shell allows for a controlled degradation of the nanocontainer and a highly specific release of hydrophobic or amphiphilic lipid cargos. These functional nanocarriers are employed successfully to deliver fluorescent probes, toxins and labelled lipids into cultured cells. Currently, we apply this concept to study the intracellular distribution of labelled lipids and dynamic processes at membrane interfaces.

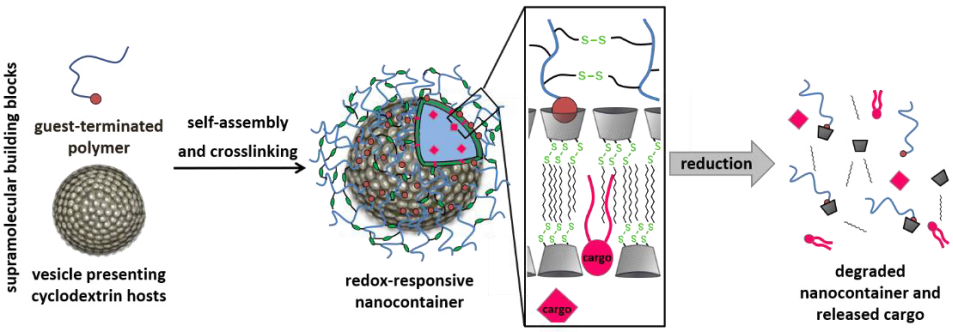


Figure. Supramolecular assembly and degradation of a redox-responsive nanocontainer.

References:

1. Palivan, C. G.; Goers, R.; Najer, A.; Zhang, X.; Car, A.; Meier, W. *Chem. Soc. Rev.* **2016**, *45*, 377-411.
2. De Vries, W. C.; Grill, D.; Tesch, M.; Ricker, A.; Nüsse, H.; Gerke, V.; Studer, A.; Ravoo, B. J. *Angew. Chem. Int. Ed.* **2017**, *56*, 9603-9607; *Angew. Chem.* **2017**, *129*, 9732-9736.
3. De Vries, W.; Tesch, M.; Studer, A.; Ravoo, B. J. *ACS Appl. Mater. Interfaces* **2017**, *48*, 41760-415766.

TALK NOTES

N-Heterocyclic Carbenes as Novel Surface Modifiers in Organic Field-Effect Transistors: Improved Stability and Contact at the Interface

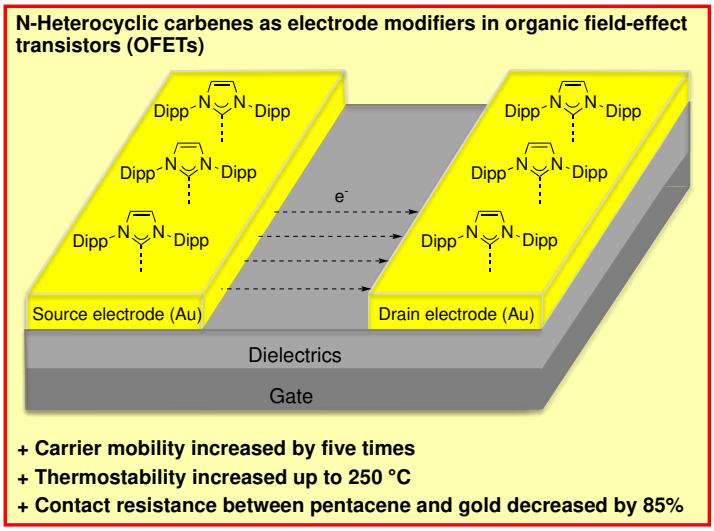
Matthias Freitag, Aifeng Lv, Kathryn M. Chepiga, Andreas H. Schäfer,

Lifeng Chi, Frank Glorius

Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut, Corrensstraße 40, 48149 Münster, Germany; glorius@uni-muenster.de

m_frei24@uni-muenster.de

In recent years, N-heterocyclic carbenes (NHCs) have become a powerful ligand class for the functionalization of noble metal surfaces like gold because of their widespread structural and electronic diversity and their very strong carbene-metal bond.[1] NHCs on gold surfaces were shown to be remarkably stable while exposed to thermal, chemical or oxidative stress, rendering these ligands especially interesting for the application as electrode modifiers in high performance electronics. Moreover, NHCs are known to be strongly electron donating and to reduce the work function of gold.[2]



Driven by these unique properties, we used NHCs to modify the electrodes of pentacene organic field-effect transistors.[3] While usually thiols are used as electrode modifiers to reduce the contact resistance at the organic-inorganic interface, these electrodes suffer from oxidative or thermal degradation of the modifier layer. By applying the NHC IPr on the electrodes, we were able to decrease the contact resistance at the pentacene-gold interface by 85%. Even after annealing the electrodes for 2 h at 200 °C before pentacene deposition, the charge carrier mobility of the pentacene transistor did not decrease.
This work shows the first application of N-heterocyclic carbenes in pentacene organic field-effect transistors, resulting in an increased performance.

References:

1. M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485.
2. H. K. Kim, A. S. Hyla, P. Winget, H. Li, C. M. Wyss, A. J. Jordan, F. A. Larrain, J. P. Sadighi, C. Fuentes-Hernandez, B. Kippelen, J.-L. Brédas, S. Barlow and S. R. Marder, *Chem. Mater.* **2017**, *29*, 3403.
3. A. Lv, M. Freitag, K. M. Chepiga, A. H. Schäfer, F. Glorius, L. Chi, *Angew. Chem. Int. Ed.* **2018**, *57,* 4792.

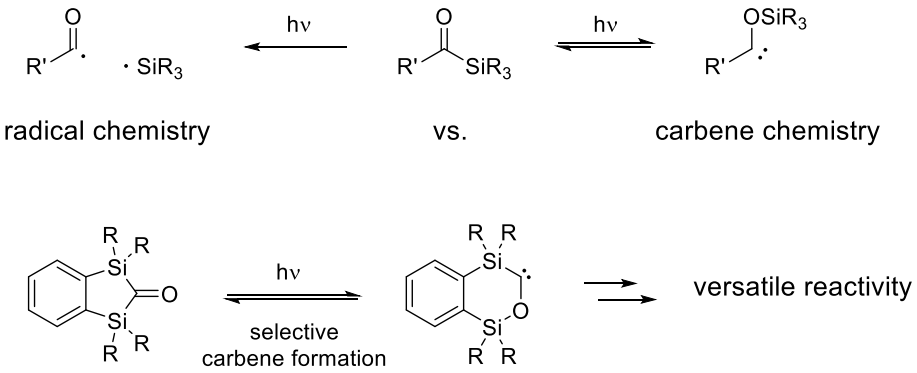
TALK NOTES

Cyclic Acylsilanes: Give it the Green Light!

Constantin Stuckhardt, Armido Studer

Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut
c.stuckhardt@wwu.de

Acylsilanes are exciting compounds drawing a lot of attention in synthetic organic chemistry and material science, which is for good cause.[1] Basis for most of their popular applications is the possibility to cleave the bond between the silyl group and the acyl moiety homolytically. The fission of this fragile bond can occur as a consequence of an n-π* transition which can be excited by irradiation with visible light. Photolysis of acylsilanes gives rise to either a pair of a silyl and an acyl radical or to a siloxycarbene, which is formed by migration of the silyl group to the oxygen atom. A perennial challenge is hence to find ways to push reactions into the carbene pathway while the undesired competing formation of radicals is circumvented. Installing the acylsilane functionality in a cyclic system will provide an anchor that connects the allegedly formed radical pair. Due to the spatial proximity between the silyl and the acyl radical both will recombine and form the siloxycarbene selectively. Considering the general ubiquity of carbene intermediates, a method for the selective light-mediated generation of siloxycarbenes can find promising applications to many fields of chemistry.



References:

1. H. Zhang, D. L. Priebbenow, C. Bolm: Acylsilanes: Valuable Organosilicon Reagents in Organic Synthesis. *Chem. Soc. Rev.* **2013**, *42*, 8540−8571.

2. a) A. G. Brook, H. W. Kucera, R. Pearce, Photolysis of 1,1-Diphenylsilacyclohexanone in Diethyl Fumarate. The Trapping of a Siloxycarbene by an Electron-Deficient Olefin. *Can. J. Chem.* **1971**, *49*, 1618−1621; b) A. G. Brook, R. Pearce, J. B. Pierce, Nucleophilic Attack of Siloxycarbenes on Carbonyl Groups. The Formation of Oxiranes. *Can. J. Chem.* **1971**, *49*, 1622−1628.

TALK NOTES

PARTICIPANTS

POSTERSESSION 1 29.08.18, 14:45
Aschmann, Dennis
Bluemke, Anika
Bruchhage, Julia
Bruninghoff, Kira
Droste, Jorn
Dudziak, Alexander
Duong, Qhi-Nhi
Erkelenz, Michael
Jaekel, Andreas
Kamba, Bianca
Killa, Matthias
Klahr, Kevin
Klepel, Florian
Kötter, Alexander
Martinewski, Katja
Marek, Jasmin

POSTERSESSION 2 30.08.18, 10:20
Meiners, Annika
Nguyen, Duy Thao
Pedroza, Laura
Rau, Kristina
Rebmann, Philipp
Riebe, Steffen
Scholz, Linus
Seifert, Daniel
Sriskantharajah, Abbna
Stegemann, Pierre
Tötsch, Niklas
Walstein, Kai
Wissing, Maren
Wübker, Anna-Lena
Zimmermann, Alexander

POSTER ABSTRACTS

Polycationic Supramolecular Ligands for Targeting Survivin

Dennis Aschmann [a], **C. Vallet** [b], **Carsten Schmuck** [a]*

[a] Institute of Organic Chemistry, University of Duisburg-Essen, Universitätsstrasse 7,

D-45141, Essen (Germany). [b] Department of Molecular Biology II, University of Duisburg-Essen, Universitätsstrasse 2, D-45117, Essen (Germany).
E-mail: dennis.aschmann@uni-due.de

Protein-protein interactions (PPIs) are involved in almost all biological processes, thus also in processes which lead to diseases.[1] Therefore the proteins involved offer potential targets to specifically modify PPIs and thus to intervene in disease progression. One of this proteins is Survivin which is associated with cancer.[2] Survivin is present in healthy cells only at low concentrations but is overexpressed in malignomas. It is a member of the apoptosis-inhibiting proteins (IAPs) and is involved in the formation of the INCEP complex at mitosis. Thus, it is a promising target for the development of new cancer therapies. Therefore, there is interest in the development of ligands which are able to bind specifically and with a high affinity to such proteins. For this purpose, different amino acids are functionalized with the tailor-made artificial binding motif guanidiniocarbonyl pyrrole cation (GCP) with different scaffolds to obtain a large variety of ligands, which are investigated with regard to their binding properties to different proteins.[3]

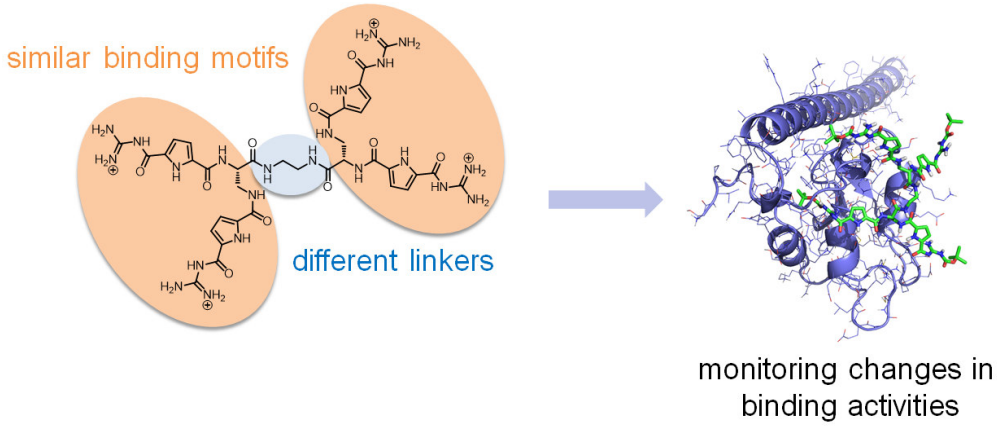


Figure 1. Schematic presentation of the development which should lead to ligands which

References:

1. Nogueira-Ferreira, R.; Vitorino, R.; Ferreira-Pinto, M. J.; Ferreira, R.; Henriques-Coelho, T., Exploring the role of post-translational modifications on protein-protein interactions with surviving, *Arch. Biochem. Biophys.* **2014**, *538*, 64–70.

2. Altieri, D. C., Survivin, cancer networks and pathway-directed drug discovery, *Nat. Rev. Cancer* **2008**, *8*, 61-70.

3. Jiang, Q.-Q.; Sicking, W.; Ehlers, M.; Schmuck, C., Discovery of potent inhibitors of human β-tryptase from pre-equilibrated dynamic combinatorial libraries, *Chem. Sci.* **2015**, *6*, 1792.

POSTER NOTES

Role of HTRA1 in the prion-like transmission of Tau aggregates in tauopathies

Anika Blümke[1] and Michael Ehrmann[1]

[1]University Duisburg-Essen, Centre for Medical Biotechnology, Universitätsstraße 2, 45117 Essen

Anika.Bluemke@uni-due.de

The abnormal aggregation of the microtubule-associated protein Tau into fibrillar deposits is a hallmark of neurodegenerative tauopathies, such as Alzheimer's disease. Tau pathology spreads along neural networks through the intercellular transfer of low-order Tau oligomers, or seeds (1,2). In a prion-like manner, Tau seeds are secreted into the extracellular space and subsequently endocytosed by neighboring cells. Upon internalization, seeds nucleate the fibrillization of endogenous Tau via direct protein-protein contact (2).

Here we show that the highly conserved serine protease HTRA1 disintegrates Tau fibrils in a cellular model of Tau aggregation. This model is based on HEK293T cells overexpressing Tau tagged to CFP or YFP. Treatment of these Biosensor cells with Tau seeds results in intracellular aggregation and thus in an increased FRET signal. Concomitant overexpression of HTRA1 counteracts Tau seeding and reduces the FRET signal. Further, a Tau spreading model was developed based on the indirect co-culture of HEK293T cells harboring Tau aggregates and Biosensor cells. Co-culture triggered the infection of Biosensor cells with Tau seeds, which was reduced in the presence of HTRA1. Additionally, the co-culture of HEK293T cells overexpressing HTRA1 and SH-SY5Y cells revealed spreading of HTRA1, which might display a further mechanism of impairing Tau propagation.

Taken together, our data indicate that HTRA1 counteracts Tau seed transmission underlining its vital role in tauopathies.

References:

1. de Calignon, A. et al.: Propagation of tau pathology in a model of early Alzheimer's disease. *Neuron.* **2012,** *73* (4), 685-697.

2. Holmes, Brandon B., et al.: Proteopathic tau seeding predicts tauopathy in vivo. *Proc. Natl. Acad. Sci.* **2014,** *111* (41), E4376-E4385.

POSTER NOTES

Versatile reactions of monomeric Al-Hydrazides as Active LEWIS Pairs

Julia S. Bruchhage, Werner Uhl

Westfälische Wilhelms-Universität Münster, Institut für Anorganische und Analytische Chemie
Julia.Bruchhage@uni-muenster.de

Monomeric Al/N based active LEWIS pairs were obtained by hydroalumination of hydrazones with different dialkylaluminium hydrides. The products feature strained three-membered AlN_2-heterocycles with a short Al-N polar covalent and a long Al-N donor-acceptor bond. Cleavage of the coordinative Al-N bond led to the formation of an active LEWIS pair, which was able to activate a variety of small molecules in a cooperative manner. [1,2,3] The Active LEWIS-Pair **1** showed a unique reactivity towards isocyanates and isothiocyanates. Depending on the stoichiometric ratio of the starting materials the insertion of one or two molecules of phenyl isocyanate into the Al-N bond was observed, the latter reaction yielded the unusual linear dimer of the isocyanate. [3] The nucleophilic reaction of **3** with carboxylic acid chlorides opens facile access to various unprecedented and highly functionalized organic after hydrolysis. Beyond that, the Al-N based LEWIS-Pair **1** is a very effective catalyst for the oligomerization of suitable monomers, such as methyl vinyl ketone or methyl methacrylate.

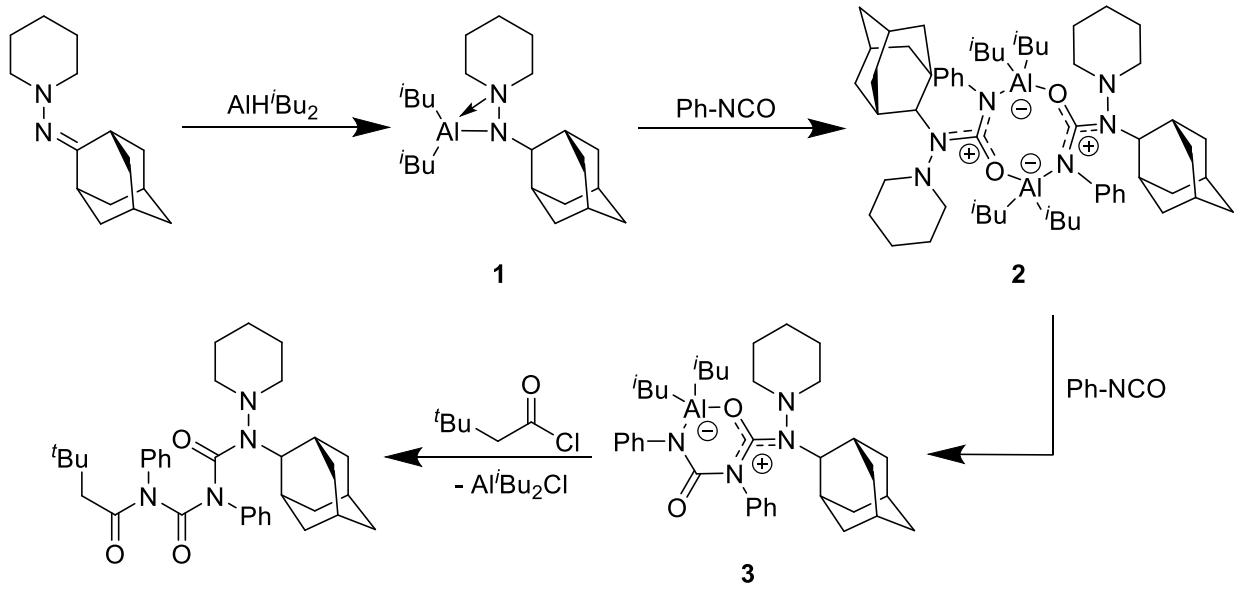


Figure 1: Synthesis of a monomeric Al/N based LEWIS pair and insertion of one and two molecules of phenyl isocyanate. **3** reacts with electrophiles to afford oligo-functional secondary products.

References:

1. T. Holtrichter-Rößmann, C. Rösener, J. Hellmann, W. Uhl, E.-U. Würthwein, R. Fröhlich, B.Wibbeling, *Organometallics* **2012**, *31*, 3272.
2. F. Hengesbach, X. Jin, A. Hepp, B. Wibbeling, E.-U. Würthwein, W. Uhl, *Chem. Eur. J.* **2013**, *19*, 13901.
3. W. Uhl, J. S. Bruchhage, M. Willeke, A. Hepp, J. Kösters, *Eur. J. Inorg. Chem.* **2016,** 2721.

POSTER NOTES

Investigation of protein-protein interactions in the SUMO pathway

Kira Brüninghoff, Wolfgang Dörner, Kim F. Taupitz, Henning D. Mootz

Westfälische Wilhelms-Universität Münster, Institut für Biochemie, Wilhelm-Klemm-Str. 2, 48149 Münster, Germany

k.brueninghoff@uni-muenster.de

Posttranslational modifications are an important mechanism to regulate cellular events including signal transduction and protein interactions by influencing protein activity, stability and conformation. Apart from the modification with small chemical moieties like phosphate or acetyl groups, target proteins can also be covalently linked with small proteins like ubiquitin or SUMO (small ubiquitin-like modifier). The SUMOylation of target proteins provide a new binding site mediating a non-covalent interaction with proteins that contain a SUMO-interaction motif (SIM). Thousands of proteins are SUMOylated in the cell and misregulation of the SUMO pathway is related to neurodegenerative diseases.
This study aims to investigate the SUMO interaction network in more detail by identifying SIM-mediated SUMO interaction partners. Due to the transient nature of the SUMO-SIM interaction, the purification and identification of the resulting protein complex is challenging. To stabilize the SUMO-SIM recognition, a novel covalent capture strategy is used. A genetically encoded photoinducible crosslinker is incorporated in the SIM binding interface of SUMO such that after UV irradiation SUMO-SIM interaction partners are linked covalently.
This photocrosslinking approach will be applied to enrich SUMO binding partners from mammalian cell extracts and identify the bound proteins by tandem mass spectrometry. In regards to this, proteins interacting with conjugated SUMO probes are of special interest.

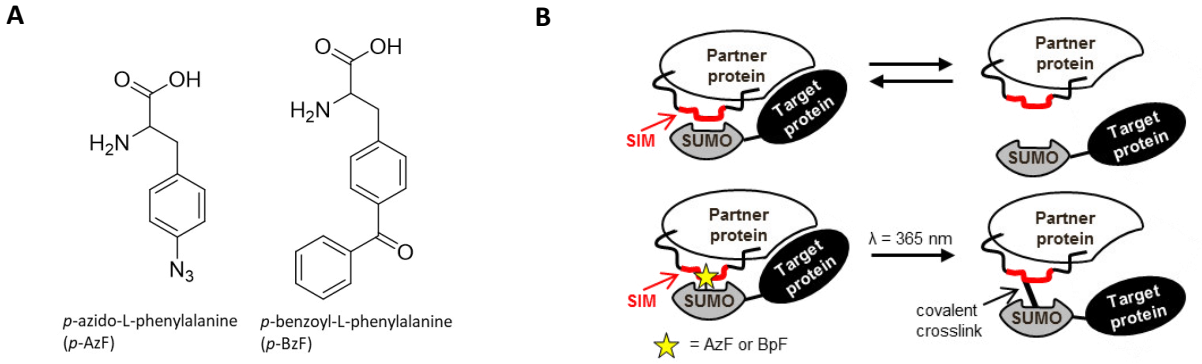


Figure 1: A. Unnatural amino acids incorporated for photocrosslinking. **B.** Concept of photoinducible crosslinking as a tool to study SIM-SUMO mediated interactions in multi protein complexes.

References:

1. K. F. Taupitz, W. Dörner, H. D. Mootz, Covalent capturing of transient SUMO-SIM interactions using unnatural amino acid mutagenesis and photocrosslinking. *Chem. Eur. J.* **2017**, *23*, 5978-5982.

POSTER NOTES

Solid-State NMR on Supramolecular BODIPY-Complexes

Jörn Droste[a], Alexander Rödle[b], Gustavo Fernández[b], Michael Ryan Hansen[a]

[a] Westfälische Wilhelms-Universität Münster, Institut für Physikalische Chemie, Corrensstr. 28/30, 48149 Münster

[b] Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut, Corrensstr. 40, 48149 Münster

joern.droste@uni-muenster.de

BODIPY dyes have recently attracted significant interest due to their favourable optoelectronic properties and flexibile chemical substitution possibilities.[1] Moreover, BODIPY dyes have been shown to aggregate in an H-type or J-type fashion, which directly influences their optical properties.[2] The combination of a large planar π-system and hydrogen-bonding via amide groups attached to BODIPY molecules leads to a cooperative self-assembly of H-type aggregates.[3] By replacing the substituent at the meso-position of the BODIPY core an additional interaction exists, see Figure 1a. However, the interaction of the here chosen ligands is expected to show negative cooperativity based on steric hindrance possibly leading to a transformation from H- to J-aggregates, see Figure 1b.

The resulting solid-state structures of the different meso-substituted supramolecular BODIPY-complexes are investigated by multinuclear solid-state NMR experiments supported by DFT calculations. On this basis, the substituent-depending stacking is investigated and for each of the three different BODIPY molecules a stacking motive can be proposed.

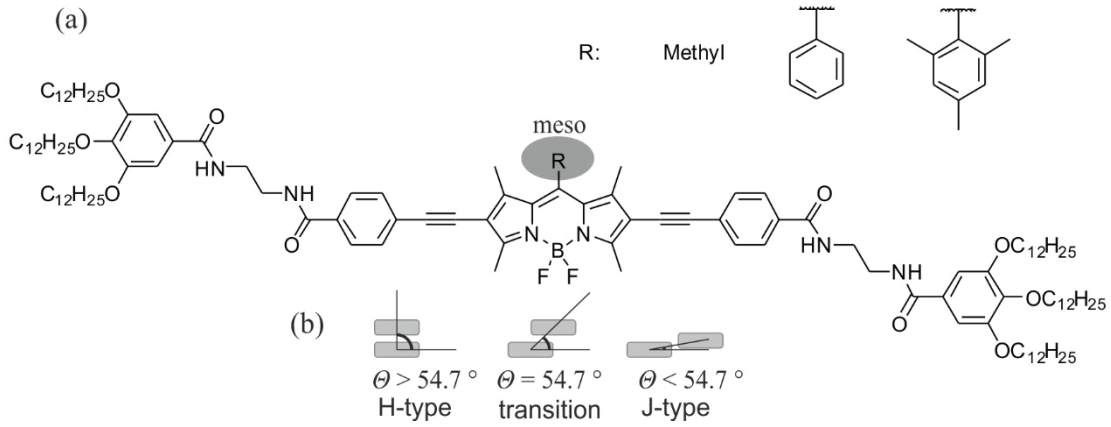


Figure 1. (a) Chemical structure of the investigated BODIPY molecules with different meso-substituents R. (b) Schematic illustration of the possible H- and J-type aggregation.

References:

1. G. Ulrich, R. Ziessel, A. Harriman: The Chemistry of Fluorescent BODIPY Dyes: Versatility Unsurpassed. *Angew. Chem. Int. Ed.* **2008**, *47*, 1184-1201.

2. A. Rödle, M. Lambov, C. Mück-Lichtenfeld, V. Stepanenko and G. Fernández: Cooperative nanoparticle H-type self-assembly of a bolaamphiphilic BODIPY derivative in aqueous medium. *Polymer*. **2017**, *128*, 317-324.

3. A. Rödle, B.Ritschel, C- Mück-Lichtenfeld, V. Stepanenko, G. Fernández: Influence of Ester versus Amide Linkers on the Supramolecular Polymerization Mechanisms of Planar BODIPY Dyes. *Chem. Eur. J.* **2016,** *22*, 15772-15777.

POSTER NOTES

Molecular analysis of outer kinetochore assembly in budding yeast

Alexander Dudziak, Stefan Westermann

University of Duisburg-Essen, Department of Molecular Genetics I,
alexander.dudziak@uni-due.de

The persistence of eukaryotic life depends on the faithful segregation of chromosomes during mitotic cell division. This process requires the mitotic spindle which is composed of dynamic microtubules generating the force required for chromosome movement and kinetochores which provide the physical linkage between chromosomes and microtubules. Kinetochores are large multi-protein complexes which assemble on specialized centrosomes (Figure 1). The different subcomplexes of the kinetochore fulfill various functions such as centromere binding, recruitment of components of the spindle assembly checkpoint and microtubule binding[1]. The Dam1 complex of *Saccharomyces cerevisiae* is a key factor for attaching kinetochores to dynamic microtubules. The heterodecameric complex oligomerizes into rings that completely embrace and track depolymerizing microtubules[2]. Binding of the Ndc80 complex, another major component of the outer kinetochore, to the Dam1 ring complex may couple the kinetochore to dynamic microtubules and thus enable chromosome movement by harnessing the forces generated by microtubule depolymerization[3].
The formation and modulation of the kinetochore-microtubule binding interface requires a regulated interplay between the core kinetochore and various microtubule-associated proteins. In this study, the mechanism of the interaction between the Dam1 complex and the autonomous plus-end tracking protein Bim1 is studied in molecular detail using a combination of biochemical in-vitro reconstitution and genetic experiments in *S. cerevisiae*.

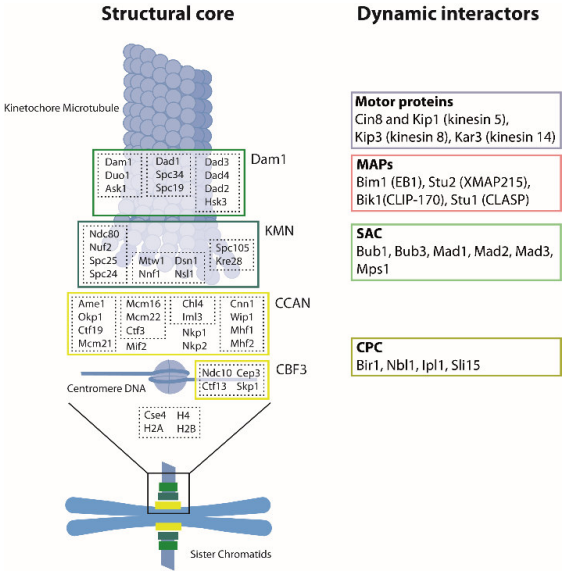


Figure 2: Schematic illustration of the budding yeast kinetochore

References:

1. Biggins, S. The composition, functions, and regulation of the budding yeast kinetochore. *Genetics* **2013**, *194*, 817–846.

2. Westermann, S. *et al.* The Dam1 kinetochore ring complex moves processively on depolymerizing microtubule ends. *Nature* **2006**, *440*, 565–569.

3. Lampert, F., Hornung, P. & Westermann, S. The Dam1 complex confers microtubule plus end-tracking activity to the Ndc80 kinetochore complex. *J. Cell Biol.* **2010**, *189*, 641–649.

POSTER NOTES

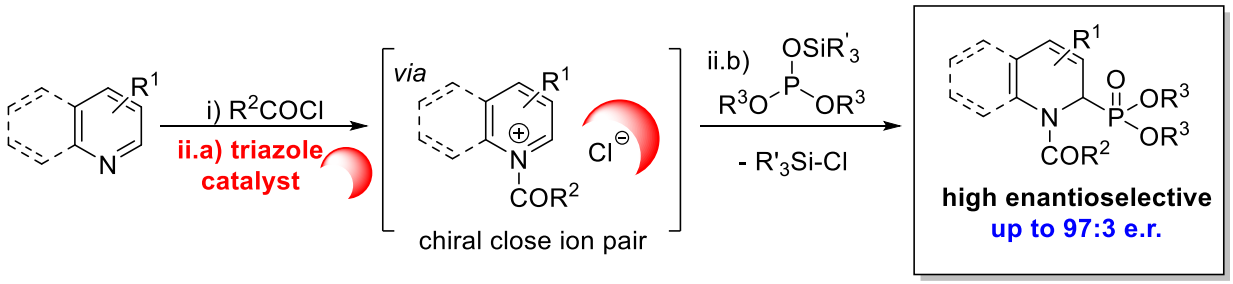
Triazole-Based Anion-Binding Catalysis for the Enantioselective Dearomatization of *N*-Heteroarenes with P-Nucleophiles

Qui-Nhi Duong, Theresa Fischer, Olga García Mancheño*, Münster/DE

Organisch-chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Qui-Nhi.duong@wwu.de

Chiral α-amino phosphonic acid derivatives are essential bioactive structures for the pharmaceutical and medicinal industry as well as valuable building blocks in organic synthesis.[1a] However, known syntheses pathways of chiral *N*-heterocyclic α-amino phosphonic acids are challenging and require hash reaction conditions. Hence, new simplified synthetic methods showing milder conditions are highly desirable. In this regard, the asymmetric dearomatization of isoquinolines with phosphites employing thiourea-based anion-binding catalysts has recently been reported.[1b] Motivated by these results, we decided to explore the enantioselective dearomatization of more challenging substrates such as quinolines and pyridines using phosphorous nucleophiles with our recently developed triazole-based H-donor catalysts, which already showed superior performance in the dearomatization reactions of such *N*-heteroarenes.[2]

In this work, an anion-binding catalysed approach for the first asymmetric synthesis of heterocyclic α-amino phosphonates through nucleophilic dearomatization of quinolines and pyridines is presented.[3] Chiral tetrakistriazoles (TetraTri) were employed as efficient hydrogen-bond donor catalysts through formation of a chiral closed ion-pair with *in situ* formed *N*-acyl salts. Treatment with various phosphorous nucleophiles such as silyl protected dialkyl phosphites and trialkylphosphites provided the corresponding products in complete or high regioselectivities and excellent enantioselectivities for both quinolines (up to 97:3 e.r) and the more demanding pyridine substrates (up to 89:11 e.r.). In this way, a new efficient method was developed to give easy access to substituted chiral cyclic α-amino phosphonates and phosphonic acid derivatives.



References:

1. a) V. P. Kukhar, H. R. Hudson, Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity, *John Wiley & Sons, Chichester*, *UK*, **2000**. b) A. R. Choudhury, S. Mukherjee, *Chem. Sci.* **2016**, *7*, 6940.
2. a) M. Zurro, S. Asmus, S. Beckendorf, C. Mück-Lichtenfeld, O. García Mancheño, *J. Am. Chem. Soc.* **2014**, *136*, 13999. b) O. García Mancheño, S. Asmus, M. Zurro, T. Fischer, *Angew. Chem. Int. Ed.* **2015**, *54*, 8823. c) M. Zurro, S. Asmus, J. Bamberger, S. Beckendorf, O. García Mancheño, *Chem. Eur. J.* **2016**, *22*, 3785. d) T. Fischer, J. Bamberger, O. García Mancheño, *Org. Biomol. Chem.* **2016**, *14*, 5794.
3. T. Fischer, Q.-N. Duong, O. García Mancheño, *Chem. Eur. J.* **2017**, *23*, 5983.

POSTER NOTES

Nanopositioning of Supramolecular Ligands on DNA Origami for Multivalent Protein Recognition

Michael Erkelenz[1], Richard Kosinski[2], Barbara Saccà[2], Christian Ottmann[3], Carsten Schmuck[4], Thomas Schrader[5], Sebastian Schlücker[1]

[1]University Duisburg-Essen, Physical Chemistry I, 45141 Essen, Germany
[2]University Duisburg-Essen, Bionanotechnology, 45141 Essen, Germany
[3]University of Technology Eindhoven, Chemical Biology, 5600 MB Eindhoven, Netherlands
[4]University Duisburg-Essen, Supramolecular Chemistry, 45141 Essen, Germany
[5]University Duisburg-Essen, Organic Chemistry, 45141 Essen, Germany
michael.erkelenz@uni-due.de

The ability of supramolecular ligands like GCP and the molecular tweezer CLR01 to bind proteins is based on their non-covalent interactions at accessible residues of proteins which can be localised, for example, by X-ray crystallography or molecular dynamics simulations.[1] The design of a modular platform with many precisely positioned low-affinity protein-binding supramolecular ligands and an overall high avidity could be the next step for protein recognition in biomedical applications.[2] The combination with a programmable DNA origami platform enables the binding of proteins in their native states via nanopositioned supramolecular ligands resulting in high avidity. The controlled deposition of the ligands on the DNA origami is achieved by hybridising complementary ssDNA strands: One strand protrudes out of the origami and catches the second strand, which itself is functionalized with an ExoS peptide or another supramolecular ligand. As a gold standard for binding 14-3-3 with high affinity, a short peptide derived of the binding motif of the ExoS enzyme (*Pseudomonas aeruginosa*) is used.

In first proof-of-principle experiments, the association of the protein 14-3-3 with a DNA origami anchored ExoS peptide is tested by gel electrophoresis as well as atomic force microscopy (AFM) for a selective binding motive.[3]

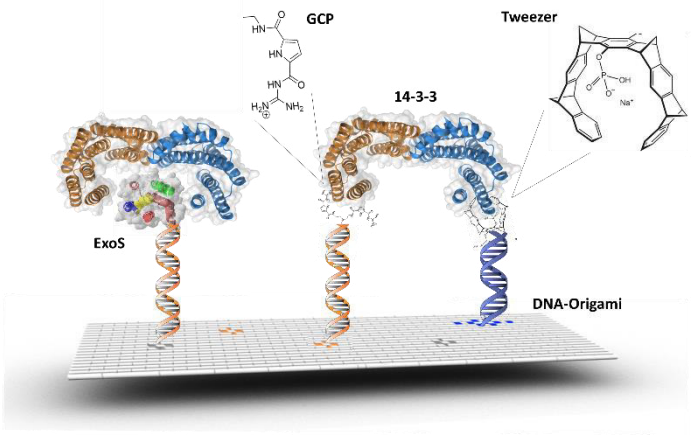


Figure 3: Binding of 14-3-3 via the supramolecular ligands GCP and Tweezer nanopositioned on DNA Origami and binding of 14-3-3 with an ExoS peptide as gold standard.

References:

1. J. N. Grad, A. Gigante, C. Wilms, J. N. Dybowski, L. Ohl, C. Ottmann, C. Schmuck & D. Hoffmann, *J. Chem. Inf. Model.* **2018**, *58*, 315-327.

2. A. Sprengel, P. Lill, P. Stegemann, K. Bravo-Rodriguez, E.-C. Schöneweiß, M. Merdanovic, D. Gudnason, M. Aznauryan, L. Gamrad, S. Barcikowski, E. Sanchez-Garcia, V. Birkedal, C. Gatsogiannis, M. Ehrmann & B. Sacca, *Nat. Commu.* **2017**, *8*, 14472.

POSTER NOTES

Exploring the Chemical Toolbox for Protein Encapsulation in DNA-Origami Cages

Andreas Jaekel, Michelle Hechler, Barbara Saccà

Bionanotechnology, Centre for Biotechnology/Faculty of Biology, Universität Duisburg-Essen

Andreas.jaekel@uni-due.de

Placing ligands and molecules with high spatial resolution is the unprecedented advantage of DNA nanotechnology. Using this method, proteins, lipids and distinct reaction partners can be arranged in close proximity and predefined orientations, gaining new insights into protein cascades and programmable reaction chains. Especially, binding of different proteins to DNA origami surfaces or their encapsulation within DNA-origami cages led to some unforeseen results on their activity.[1,2] Until now, most of these systems are based on the covalent modification of amino acid side chains to bring the desired proteins reliably to their designated position. However, previous studies have shown that covalent attachment of DNA to a protein surface may alter protein behavior, making the differentiation between surface modification and DNA proximity effects on enzyme activity and stability challenging.[3] Additionally, these reactions are often not regioselective resulting in mixtures of DNA-protein species. For this reason, alternative and more general ways to scaffold proteins onto DNA surfaces are currently under investigation to enable researchers to address structural and functional questions in a more accurate fashion (Figure 1). Our goal is to develop enhanced protein-tags and molecular tweezers for the highly regioselective and non-covalent attachment of proteins to DNA based structures.

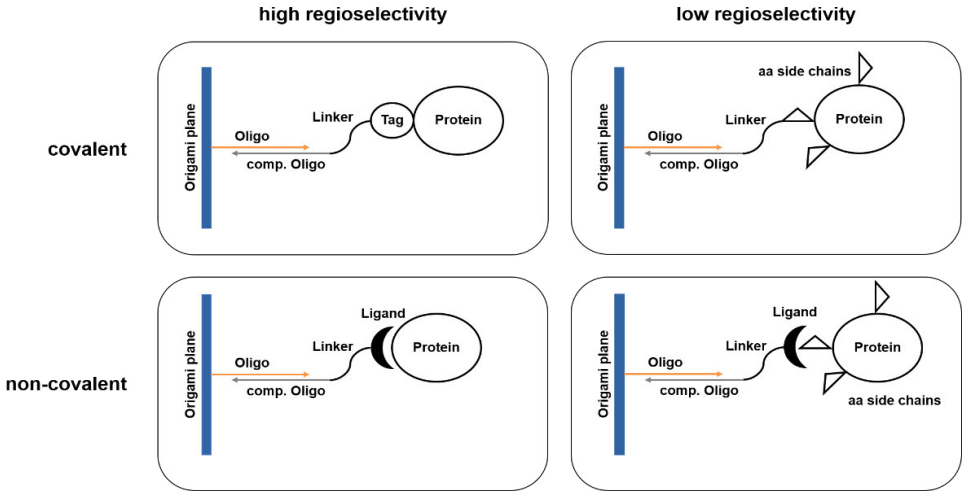


Figure 1. Different strategies for binding proteins to DNA-origami based structures.

References:

1. Guido Grossi, Andreas Jaekel, Ebbe Sloth Andersen, Barbara Saccà: Enzyme-functionalized DNA nanostructures as tools for organizing and controlling enzymatic reactions. *MRS Bulletin.* **2017**, *12*, 920-924.
2. Zhao, Zhao, Jinglin Fu, Soma Dhakal, Alexander Johnson-Buck, Minghui Liu, Ting Zhang, Neal W. Woodbury, Yan Liu, Nils G. Walter, Hao Yan: Nanocaged enzymes with enhanced catalytic activity and increased stability against protease digestion. *Nature Communications*. **2016**, 10619.
3. Glettenberg, Maximilian, and Christof M. Niemeyer: Tuning of Peroxidase Activity by Covalently Tethered DNA Oligonucleotides. *Bioconjugate Chemistry*. **2009**, *5*, 969–75.

POSTER NOTES

Reversible modulation of epigenetic information by application of molecular tweezers

Bianca E. Kamba[1], Thomas Schrader[2], Peter Bayer[1]

[1]University of Duisburg-Essen, Research Group Structural and Medical Biochemistry, Centre for Medical Biotechnology (ZMB), 45117 Essen, Germany.
E-mail: bianca.kamba@uni-due.de
[2]University of Duisburg-Essen, Institute of Organic Chemistry, 45117 Essen, Germany.

Histones are nucleosomal proteins interacting with stretches of chromosomal DNA. These interactions are predominantly maintained by basic amino acids, e.g. lysine residues. The epigenetic gene control is regulated by covalent post-translational modifications of histones. Those modifications act by switching transcriptional on and off states in gene expression, e.g. by enabling or disabling attractive histone:DNA interactions [1, 2]. The acetylation of lysine residues in nucleosomal proteins affects DNA binding by decreasing their basicity and hence their degree of protonation. This leads to a weakness of the histone:DNA interaction [3]. Consequently, hidden transcriptional sites become accessible. The aim of this work is the reversible modulation of epigenetic information by application of molecular tweezers. We would like to investigate if the supramolecular entrapment of lysine sidechains in $H4_{1-23}$ histone peptides by molecular tweezers and the concomitant charge neutralization can functionally mimic the acetylation state, and thereby weaken protein:DNA interaction as observed under epigenetically controlled acetylation. $H4_{1-23}$ contains 5 lysines, 4 of which can be acetylated *in vivo* (lysines 5, 8, 12, and 16; lysine 20 is methylated *in vivo).* Finally the tweezers should be modified in such a way that they will selectively address a preferred region at the $H4_{1-23}$ (**H4:** Ser-Gly-**Arg**-Gly-**Lys**-Gly-Gly-**Lys**-Gly-Leu-Gly-**Lys**-Gly-Gly-Ala-**Lys**-**Arg**-His-**Arg**-**Lys**-Val-Leu-**Arg**) N-terminus without impairing other acetylation sites therein.

References:

1. M.M. Müller and T.W. Muir. Histones: At the Crossroads of Peptide and Protein Chemistry, *Chem. Rev.* **2015**, *115*, 2296−2349.

2. L. Hong, G.P. Schroth, H.R. Matthew, P. Yaus, and E. M. Bradbury. Studies of the DNA Binding Properties of Histone H4 Amino Terminus. *The Journal of Biological Chemistry* **1993**, *268*, 305-314.

3. L.N. Mishra, S. Pepenella, R. Rogge, J.C. Hansen & J.J. Hayes. Acetylation Mimics Within a Single Nucleosome Alter Local DNA Accessibility In Compacted Nucleosome Arrays. Scientific Reports **2016**, *6*, Article number: 34808.

POSTER NOTES

Geometry Optimizations in a Subsystem DFT formalism - A Structural Benchmark Study

Kevin Klahr, Johannes Neugebauer

Theoretische Organische Chemie, Organisch-Chemisches Institut and Center for Theory and Multiscale Computation, Westfälische Wilhelms-Universität, Corrensstr. 40, 48149 Münster, Germany

k_klah01@uni-muenster.de, j.neugebauer@uni-muenster.de

Subsystem DFT (sDFT), a subsystem approach to density functional theory which uses Frozen Density Embedding (FDE), is an efficient alternative to Kohn-Sham density functional theory (KS-DFT) for complex chemical systems.[1] By partitioning the total electron density into a set of smaller subsystem densities, the ansatz introduces a favorable scaling with the number of subsystems.

Here, we present a structural benchmark of sDFT geometries using the analytical sDFT gradient implementation in SERENITY.[2] Since the method is inherently well suited for the calculation of weakly interacting systems, the S22 and A24 test sets serve as references. The three most commonly used functional combinations in the context of sDFT (LDA/TF, PW91/PW91k and BP86/LLP91 + D3(BJ)) are tested thoroughly, with the intent of challenging the previously used strategy to rely on error cancellation effects between exchange-correlation and nonadditive kinetic-energy approximations for medium-range dispersion as is typical for PW91/PW91k[3]. The results show that structures obtained with BP86/LLP91 including explicit D3(BJ) dispersion correction are superior to their LDA/TF and PW91/PW91k counterparts.

References:

1. Jacob, C.R., Neugebauer, J.: Subsystem density-functional theory. *WIREs Comput. Mol. Sci.* **2014**, *4*, 325–362.

2. Unsleber, J. P., Dresselhaus, T., Klahr, K., Schnieders, D., Böckers, M., Barton, D., Neugebauer: SERENITY: A Subsystem Quantum Chemistry Program. *J. Comput. Chem.* **2018**, *39*, 788–798.

3. Dulak, M., Kamiński, J. W., Wesolowski, T. A.: Equilibrium Geometries of Noncovalently Bound Intermolecular Complexes Derived from Subsystem Formulation of Density Functional Theory. *J. Chem. Theory Comput.* **2007**, *3*, 735–745.

POSTER NOTES

The combination of Guanidinocarbonyl Pyrrol Cation and Precise Oligomers to Create Modulators of Protein-Protein Interactions

M. Killa, C. Schmuck*

University of Duisburg-Essen, Universitätsstrasse 7, D-45141 Essen
matthias.killa@uni-due.de

The binding of small ligands to protein surfaces is usually based on aromatic and electrostatic or hydrophobic interactions. [1] Therefore the developed guanidinocarbonyl pyrrol cation (GCP) is ideal to bind carboxylates even in polar solvents. [2] To address several binding sites on the surface at the same time with surface-binding-groups, a polar scaffold bridging these groups is necessary. The precision oligomers developed by Hartmann *et al.* are perfect for this usage. The length of the scaffolds can be adjusted and different functional groups can be added for rational designed ligands. The oligomers are also water-soluble, which is perfect for biological applications. [3] The combination of GCP and precise oligomers allows the rational design of protein-protein-interaction modulators.

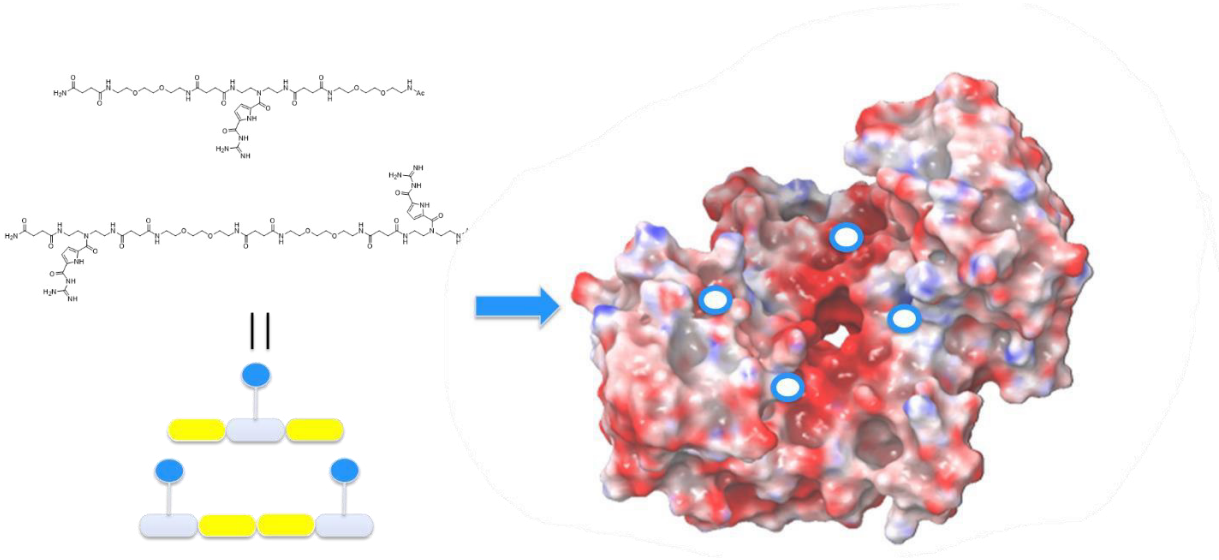


Fig. 1: Two small GCP-oligomers can address different binding sites on a 14-3-3 protein.

References:

1. Q.Jiang, L. Bartsch, W. Sicking, P. R. Wich, D. Heider, D. Hoffmann, C. Schmuck, *Org. Biomol. Chem.*, **2013**, *11*, 1631–1639.
2. C. Schmuck, *Eur. J. Org. Chem.* **1999**, 2397-2403.
3. Daniela Ponader, Felix Wojcik, Figen Beceren-Braun, Jens Dernedde, and Laura Hartmann, *Biomacromolecules*, **2012**, *13*, 1845−1852.

POSTER NOTES

Photoinduced Formation of Supramolecular Structures using Disulfide-Based Dynamic Covalent Chemistry

F. Klepel, S. Sagebiel, B. J. Ravoo

Center for Soft Nanoscience, Busso-Peus-Str. 10, University of Münster, 48161 Münster, Germany, florian.klepel@uni-muenster.de

In recent years there have been some notable examples of light induced dynamic covalent chemistry.[1,2] To contribute to this topic, we adapted the photoinduced radical disulfide metathesis for our dynamic covalent chemistry.[3]

The mechanism of the exchange is a simple radical chain reaction, were the initiation is the homolytical cleavage of the sulfur-sulfur bond and can be achieved by a common handheld UV lamp. The mixed product can be formed by propagation as well as termination. This offers the opportunity to build dynamic covalent systems that are dormant and can be activated on demand. Such systems are catalyst free, since the UV-active component is part of the molecular design.

In a first example, we could show hydrogelation by irradiation of a solution of a single asymmetric disulfide. Upon irradiation two additional symmetrical disulfides are generated. One of those molecules turns the sample into a hydrogel.

We have since worked on implementing this chemistry into other nanoscaled systems, such as dynamically exchanged ligands on silica nanoparticles for molecular recognition, as well as a dynamic combinatory library of amphiphiles.

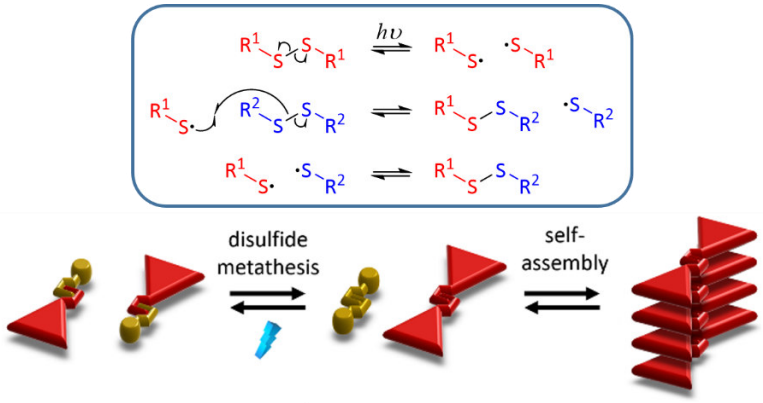


Figure 1. Mechanism of the photoinduced radical disulfide metathesis and scheme of a photoinduced hydrogel based upon this chemistry.

References:

1. J. Li, J. M. A. Carnall, M. C. A. Stuart, S. Otto, *Angew. Chem. Int. Ed.* **2011**, *50*, 8384–8386.
2. A. Fuhrmann, R. Göstl, R. Wendt, J. Kötteritzsch, M. D. Hager, U. S. Schubert, K. Brademann-Jock, A. F. Thünemann, U. Nöchel, M. Behl, et al., *Nature Communications* **2016**, *7*, 13623.
2. F. Klepel, B. J. Ravoo, *Org. Biomol. Chem.* **2017**, *15*, 3840-3842.

POSTER NOTES

MD Simulation of SIM/SUMO complexes

Alexander Kötter, Andreas Heuer

Institut für Physikalische Chemie, WWU Münster, a_koet04@wwu.de

The interaction of the small ubiquitin related modifier (SUMO) with the SUMO interacting motif (SIM), a 4 to 5 amino acid long sequence of varying chemical composition, plays an important role in many cellular processes. We perform atomistic molecular dynamics simulations and apply accurate free energy methods in order to understand the underlying properties on a microscopic scale from a structural and thermodynamic perspective. In particular we are interested in the dependence of the standard binding free energy on the protonation state of acidic side chains in the SIM in different orientations.

POSTER NOTES

Unique Reactivity of Enantioselective Catalysis by Using Short, Structurally Defined DNA Hairpins as Scaffold for Hybrid Catalysts

Jasmin J. Marek and Ulrich Hennecke

University of Münster, Organic Chemistry Institute, Corrensstraße 40, D-48149 Münster
ulrich.hennecke@uni-muenster.de

The use of DNA-based hybrid catalysts in asymmetric synthesis was first demonstrated by *B. Feringa* and *G. Roelfes* in 2005.[1] In a copper(II)-catalyzed *Diels-Alder* reaction of azachalcone **1** and cyclopentadiene (**2**) the main product *endo*-**3** was generated with an enantiomeric excess of up to 99% *ee*. Since then, the concept of DNA-based asymmetric catalysis has been applied to a variety of different reactions, however, the structure of the catalyst and its mode of activation has remained.

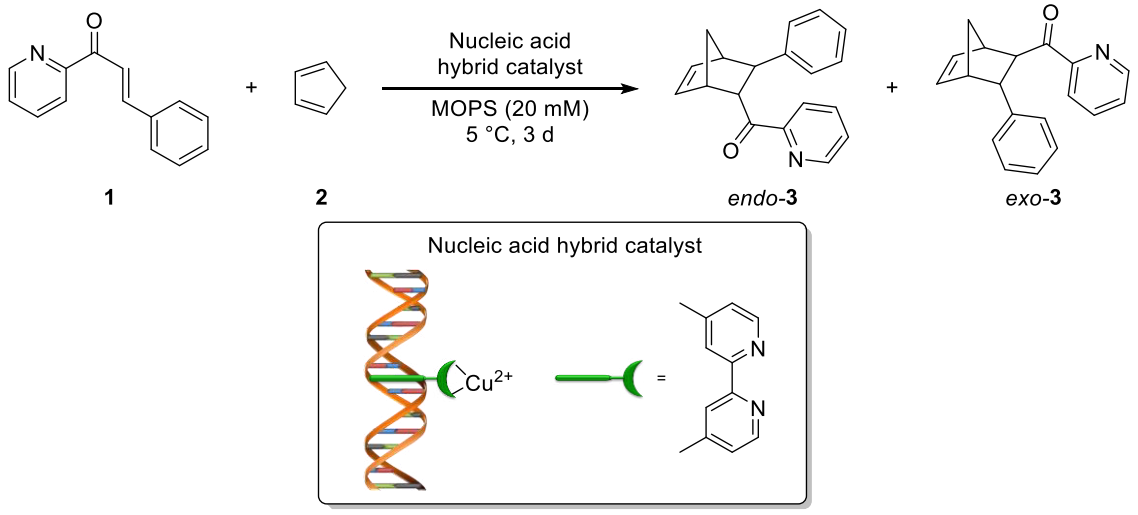


Figure 1: Nucleic acid-based asymmetric *Diels-Alder* reaction.

Recently we demonstrated that also hybrid catalysts based on short RNA-double strands and DNA-RNA-hybrid helices can be used in asymmetric catalysis.[2] Depending on the formed secondary structure of the nucleic acid different selectivities can be observed and an enantiomeric excess of up to 73% *ee* can be achieved. To understand the influence of nucleic acid secondary structure on catalysis, we reduced the complexity of the used system and turned to nucleic acid hairpins.[3] Again, the use of both, RNA and DNA nucleotides, demonstrated the observed effects of different secondary structures on catalytic usability. With DNA hairpins an enantiomeric excess of up to 96% *ee* can be achieved while RNA hairpins show lower activity.

References:

1. G. Roelfes, B. L. Feringa, *Angew. Chem. Int. Ed.* **2005**, *44*, 3230–3232.
2. J. J. Marek, U. Hennecke, *Chem. Eur. J.* **2017**, *23*, 6009–6013.
3. J. J. Marek, R. P. Singh, A. Heuer, U. Hennecke, *Chem. Eur. J.* **2017**, *23*, 6004–6008.

POSTER NOTES

Active Al-N Based Lewis Pairs towards Small Molecules

K. Martinewski, W. Uhl

Institut für Anorganische und Analytische Chemie*, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149, Münster*

k_mart05@uni-muenster.de

We recently reported on the synthesis of aluminium-nitrogen based active Lewis pairs. They were obtained on a facile route by hydroalumination of ynamines with dialkylaluminium hydrides. These Al-N based Lewis pairs show a nice and unprecedented reactivity towards small molecules.[1, 2]

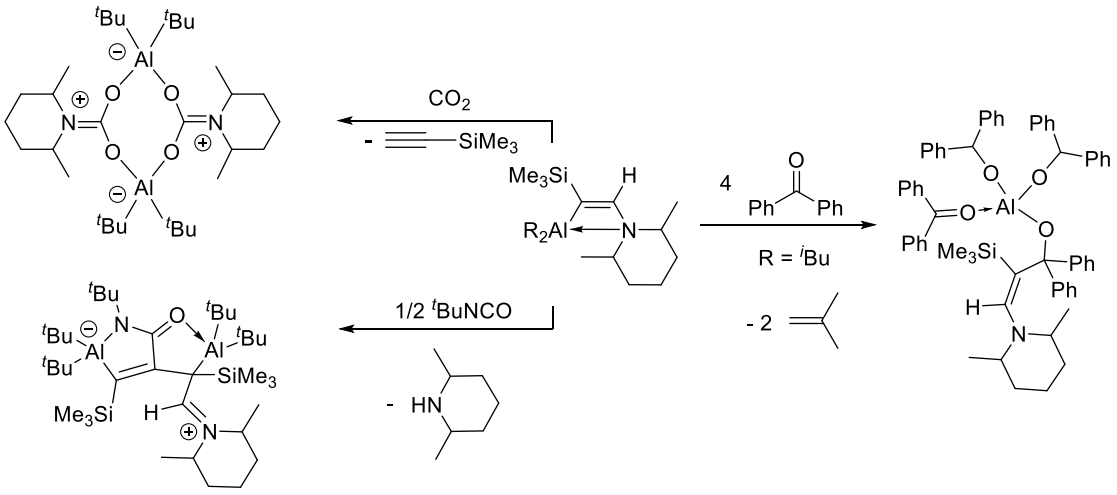


Figure 1 Reactivity of Al-N based active Lewis pairs.

An 8-membered heterocycle was obtained by treating the active Lewis pair with CO_2, which inserted into the Al-N bond and initiated trimethylsilylacetylene elimination. Activation of *tert*-butyl isocyanate results in an unprecedented reaction with pseudo-dimerization of the Lewis pair by condensation and formation of two concomitant new C-C bonds. In a unique reaction four molecules of benzophenone reacted by insertion and activation of the terminal Al-C bonds.

References:

[1] T. Holtrichter-Rößmann, C. Rösener, J. Hellmann, W. Uhl, E.-U. Würthwein, R. Fröhlich, B. Wibbeling, *Organometallics*, **2012**, *31*, 3272.

[2] K. Martinewski, T. Holtrichter-Rössmann, C. Roesener, A. Hepp, E.-U- Würthwein, W. Uhl, *Chem. Eur. J.*, **2017**, *23*, 6129–6141.

POSTER NOTES

Rational targeting of intracellular protein transport signals by supramolecular ligands

Annika Meiners*, Sandra Bäcker*, Cecilia Vallet*, Lisa Oelschläger*, Christian Heid, Inesa Hadrovic**, Christine Beuck***, Peter Bayer***, Thomas Schrader**, Shirley K. Knauer***

** Department of Molecular Biology II, Centre for Medical Biotechnology (ZMB), annika.meiners@uni-due.de*

***Department of Organic Chemistry*

**** Department of Structural and Medicinal Biochemistry, Centre for Medical Biotechnology*

University of Duisburg-Essen, 45117 Essen, Germany

The protein Survivin is overexpressed in most types of cancer cells and considered to be a cytoprotective factor, correlating with a resistance against chemo- and radiotherapy[1]. It features a nuclear export signal (NES) which is recognized by the export receptor Crm1. This interaction is required for the cytoprotective activity of Survivin and thus represents a promising target for novel anti-cancer approaches[2]. Since Crm1 does not only serve as an export receptor for Survivin but has many cargos, targeting Crm1 would not specifically inhibit the nuclear export of Survivin. Our project aims to specifically target the NES on Survivin's surface using supramolecular ligands like diphosphate tweezers. Although these basic tweezer molecules already bind to surface-exposed lysine residues, we included additional peptide modifications to shield Survivin's NES region. Binding was demonstrated by ITC measurements and directed to specific amino acids within and near the NES by NMR experiments. Biochemical pulldown assays as well as fluorescence anisotropy measurements showed that the molecular tweezers interfere with the Survivin/Crm1 interaction. To further confirm the binding site, we are currently generating different Survivin point mutants of the amino acids supposedly involved in tweezer binding. Moreover, we aim to further increase binding affinity and specificity of the tweezers using additional recognition units or combining multiple tweezers with appropriate linker molecules.

References:

1. Unruhe, B., Schröder, E., Wünsch, D., & Knauer, S. K.: An old flame never dies: survivin in cancer and cellular senescence. *Gerontology*. **2015**, *62* (2), 173-181.

2. Knauer, S. K., Krämer, O. H., Knösel, T., Engels, K., Rodel, F., Kovács, A. F., ... & Brieger, J. Nuclear export is essential for the tumor-promoting activity of survivin. *The FASEB Journal.* **2007**, *21* (1), 207-216.

POSTER NOTES

Microcontact Printed Patterns of N-Heterocyclic Carbenes on Gold Substrates

D. Thao Nguyen[+], Matthias Freitag[+], Martin Körsgen, Sebastian Lamping, Andreas Rühling, Andreas H. Schafer, Martin H. Siekman, Heinrich F. Arlinghaus, Wilfred G. van der Wiel, Frank Glorius, and Bart Jan Ravoo

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Germany
Center For Soft Nanoscience, Busso-Peus-Straße 10, 48149 Münster, Germany
E-mail: dt.nguyen@wwu.de

In recent years N-heterocyclic carbenes (NHCs) have emerged as a promising class of ligands for metals substrates utilizing their unique bond strength and electronic properties. The adoption of NHCs as innovative ligands for nanoparticles has led to many insights into the nature of the metal-to-NHC bond.[1]
The lessons drawn from those studies were then transferred to flat metal substrates for the development of novel electronics, chip-based sensors and other nanomaterials. To this end, researches mostly focused on decorating flat gold surfaces with NHC in a homogenous manner.[2]
Herein, we present the first example of NHC functionalized gold surfaces with spatial control using bench stable NHC precursors and microcontact printing.[3] The obtained micropatterns have proven to be thermally stable, conducting and resilient towards backfilling with an additional NHC. With this knowledge in hand, the creation of novel nanodevices can be envisioned.

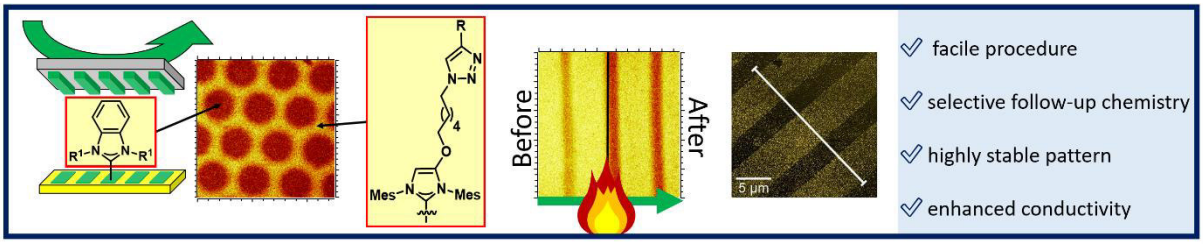


Figure 4. NHCs printed on gold by microcontact printing offers desirable properties needed for novel electronic devices.

References:

1. S. Engel, E. Fritz, B. J. Ravoo, *Chem. Soc. Rev.* **2017**, *46*, 2057.

2. A. V. Zhukhovitskiy, M. J. MacLeod, J. A. Johnson, *Chem. Rev.* **2015**, *115*, 11503.

3. D. T. Nguyen[+], M. Freitag[+], M. Körsgen, S. Lamping, A. Rühling, A. H. Schäfer, M. H. Siekman, H. F. Arlinghaus, W. G. van der Wiel, F. Glorius, B. J. Ravoo, *Angew. Chem. Int. Ed.* ***2018***, *57*, 1.

[+] These authors contributed equally to this work.

POSTER NOTES

Implications for HTRA1 in Systematic Light Chain Amyloidosis

Laura Pedroza[1], Kamilla Ripkens[1], Michael Ehrmann[1]

[1]University Duisburg-Essen, Centre for Medical Biotechnology, Universitätsstraße 2, 45117 Essen
Laura.pedroza@uni-due.de, Kamilla.Ripkens@uni-due.de, Michael.Ehrmann@uni-due.de

Systemic Light Chain Amyloidosis (AL-Amyloidosis) is a protein folding disorder of the antibody light chain. In AL-Amyloidosis an abnormal plasma cell clone secrets high amounts of free light chain without the corresponding heavy chain leading to extracellular deposits in form of amyloid fibrils in the ECM around organs and in tissues consequently resulting in tissue damage and organ death. Current treatment options focus on inhibiting the formation of new deposits by applying aggressive chemotherapy or stem cell transplantation (1).

The highly conserved serine protease HTRA1 is implicated in protein quality control as well as the regulation of signaling pathways and is mainly secreted into the extracellular space (2). Previous studies demonstrate that HTRA1 facilitates the dissociation of amyloid Tau fibrils occurring in Alzheimer's disease thus promoting subsequent proteolysis (3). Since β-sheet structures are hallmarks of amyloid protein fibrils, we address the question whether amyloid light chain fibrils are also substrates of HTRA1.

This study will produce patient derived recombinant light chains and amyloid fibrils to investigate the dissociation potential of proteolytically inactive HTRA1 as well as proteolytic clearance. To address the variances, i.e. that every patient produces a specific light chain, fibrils extracted from patients' fat tissue will also be analysed. Ultimately, we hope that our basic research will produce results that can serve as a basis for new treatment options.

References:

1. Ramirez-Alvarado, M: Amyloid Formation in Light Chain Amyloidosis. *Curr. Top. Med. Chem.* **2013**, *12* (22), 2523–2533.
2. Clausen, T., Kaiser, M., Huber, R., & Ehrmann, M.: HTRA proteases: regulated proteolysis in protein quality control. *Nature Reviews. Molecular Cell Biology*. **2011**, *12* (3), 152–162.
3. Poepsel, S., Sprengel, A., Sacca, B., Kaschani, F., Kaiser, M., Gatsogiannis, C., Ehrmann, M: Determinants of amyloid fibril degradation by the PDZ protease HTRA1. *Nat. Chem. Biol.* **2015**, *11* (11), 862–869.

POSTER NOTES

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

Kristina Rau[1], Andrea Rentmeister[1,2]

[1] *Institute of Biochemistry, University of Münster, D-48149 Münster, Germany*

k_rau001@uni-muenster.de

Epitranscriptomics is an emerging research field focusing on RNA modifications and their cellular functions. Until now, more than 150 reversible and irreversible RNA modifications are known, but their biological roles are mainly unknown. The most abundant internal mRNA modification is N^6-methyladenosine (m^6A). The methylation is realized by a methyltransferase complex and can be recognized by various reader proteins in the nucleus and cytoplasm. The "demethylases" FTO and AlkBH5 remove the methyl group, resulting in a dynamically regulated modification in RNA [1]. Current research elucidates several cellular roles of m^6A on splicing, translation and mRNA decay with impacts on stem cell development and cancer. Until now, the specific role of each m^6A site remains unknown. We aim to investigate the effect of single m^6A positions on its mRNA fate using sequence-specific demethylation. To reach this specificity, we want to make use of the RNA-binding protein RCas9 [2]. This approach will be realized *in vitro* and in human cell lines.

References:

1. Meyer, K.D. and S.R. Jaffrey: Rethinking m(6)A Readers, Writers, and Erasers. *Annu. Rev. Cell Dev. Biol.* **2017**, *33*, 319-342.
2. O'Connell, M.R., B.L. Oakes, S.H. Sternberg, A. East-Seletsky, M. Kaplan, and J.A. Doudna: Programmable RNA recognition and cleavage by CRISPR/Cas9. *Nature*. **2014**, *516*, 263-266.

POSTER NOTES

Enhancing Molecular Tweezer Selectivity – a Conceptional Approach via Dynamic Combinatorial Libraries

Philipp Rebmann[1], Thomas Schrader[1]

[1]Universität Duisburg Essen, Universitätsstr. 7, 45117 Essen, philipp.rebmann@uni-due.de

The molecular tweezer CLR01 is known to be a selective host molecule for lysine- and arginine side chains even on proteins. The complexation of one of these amino acids on the protein surface can induce blocking of hot spots and lead to inhibition of protein-protein interactions. As an example, PARP-1, which is important for DNA quality control, is inhibited by the diphosphate tweezer due to competition with a key lysine residue.[1]

However, the prototype phosphate tweezer in principle recognizes all accessible lysine and arginine residues on a protein surface randomly and thus lacks selectivity. It would be desirable to functionalize the parent tweezer with established binding motifs for other frequent amino acids found in the immediate environment of a critical lysine or arginine. Such motifs have indeed been created by us as binding monomers for the construction of protein-selective affinity copolymers.[2]

Our now embarked concept involves covalent fusion of known amino acid binders and the molecular tweezer within a dynamic combinatorial library. It will be assembled from several branched oligomeric tweezer aldehydes which form hydrazones with a selection of different hydrazine-functionalized amino acid binders. A commercially available PARP-1 assay will be employed to identify the best binders. Their structure and binding properties can provide new insight into the structural prerequisites for efficient PARP-1 inhibition.

References:

1. Wilch, C., Talbiersky, P., Berchner-Pfannschmidt, U., Schaller, T., Kirsch, M., Klärner, F.-G., Schrader, T.: Molecular Tweezers Inhibit PARP-1 by a New Mechanism. *Eur. J. Org. Chem.* **2017,** 2223–2229.

2. Gilles, P., Talbiersky, P., Bastkowski, F., Klärner, F.-G., Schrader, T.: High-Affinity Copolymers Inhibit Digestive Enzymes by Surface Recognition. *Biomacromolecules* **2017**, *130*, 1772–1784

POSTER NOTES

Ether-Based Luminophores with Aggregation-Induced Emission Properties

Steffen Riebe, Jens Voskuhl*

Institute of Organic Chemistry, University of Duisburg-Essen, Universitätsstrasse 7, D-45117, Essen (Germany), steffen.riebe@uni-due.de

The need of novel efficient fluorophores for the recognition and labeling of biomolecules such as proteins enzymes and cells is one of the most challenging disciplines in modern biosupramolecular chemistry. Our group uses a phenomenon called aggregation-induced emission.[1] Molecules with this ability show fluorescence, contrary to normal fluorophores, when aggregated or in the solid state. Recently we found a novel class of facile ethers of chalcogens with this remarkable characteristic. Our system can be easily modified and was used for the detection of proteins and bacteria.[2] Furthermore we investigated the formation of fluorescent micelles using hydrogen bonding.[3] Currently a couple of different compounds were investigated concerning their fluorescence properties. Interestingly delayed fluorescence was observed for specific compounds leading to the assumption, that and intersystem crossing to a triplet state occurs leading to a long lived fluorescence state, termed phosphorescence.

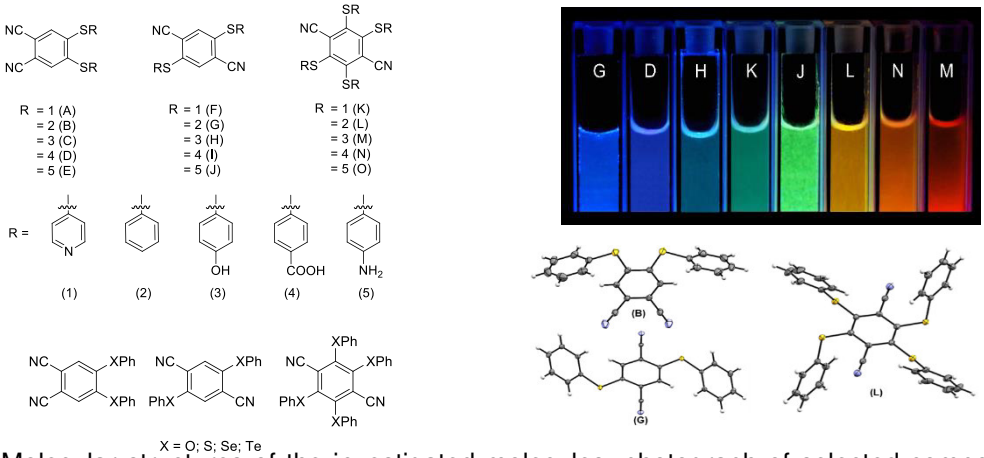


Fig.1: Molecular structures of the investigated molecules, photograph of selected compounds, when dispersed in water under UV-light irradiation and X-ray structures of compounds B, G and L.

References:

1. Luo, J. Xie, Z. Lam, J. W. Y. Cheng, L. Chen, H. Qiu, C. H. S. Kwok, H. S. Zhan, X. Liu, Y. Zhu D. Tang, B. Z. *Chem. Commun.*, **2001**, *0*; 1740-1741.
2. Frisch, H. Spitzer, D. Voskuhl, J. Besenius, P. *Org. Biomol. Chem*, **2016**, *14*, 5574-5579.
3. Schmidt, B. Sankaran, S. Stegemann, L. Strassert, C. A. Jonkheijm, P. Voskuhl, J. *J. Mat. Chem. B,* **2016**, *4*, 4732-4738.

POSTER NOTES

Investigating the Effect of Missing Inter-Subsystem Charge-Transfer Excitations in Subsystem TDDFT

L. Scholz[1, 2], J. Neugebauer[1, 3]

[1]Organisch-Chemisches Institut and Center for Multiscale Theory and Computation, Westfälische Wilhelms-Universität, Corrensstraße 40, 48149 Münster, Germany

[2]l.scholz@uni-muenster.de, [3]j.neugebauer@uni-muenster.de

For TDDFT-based calculations of response properties, e.g. excitation energies, of extended systems, fragmentation and embedding methods such as subsystem DFT and Frozen Density Embedding (FDE) [1–3] can be applied. Herein, three substantial approximations need to be considered: First, a restricted basis set is usually used compared to supermolecular calculations. Second, an approximate kinetic energy potential and kernel are employed. Third, charge-transfer (CT) excitations between subsystems are inherently omitted. While the first two error sources might have mild effects on local excitations, the third issue definitely creates a qualitative difference to supermolecular calculations.

FDE-TDDFT introduces another error, consisting in only intrasubsystem, i.e. local, excitations. Delocalized excitations as linear combination of various excitations on different subsystems can be obtained with Coupled FDE (FDEc) [2], which was developed especially for the description of excitonically coupled chromophores with a few prominent, intense low-energy excitations, but can also be used for more general problems. But even in FDEc, the issue concerning intermolecular charge-transfer excitations persists. In this work, we analyze the effects of such charge-transfer contributions by explicit comparisons of FDEc and supermolecular spectra over a broad spectral range.

References:

1. M. E. Casida, T. A. Wesołowski: Generalization of the Kohn–Sham Equations with Constrained Electron Density Formalism and Its Time-Dependent Response Theory Formulation. *Int. J. Quantum Chem.* **2004**, *96.6*, 577–588.

2. J. Neugebauer: Couplings between electronic transitions in a subsystem formulation of time-dependent density functional theory. *J. Chem. Phys.* **2007**, *126.13*, 134116.

3. J. Neugebauer: On the calculation of general response properties in subsystem density functional theory. *J. Chem. Phys.* **2009**, *131.8*, 1–12.

POSTER NOTES

Specific and sensitive recognition of proteins with aggregation-induced emission

Daniel Seifert[1], Steffen Riebe[2], Jens Voskuhl[2], Peter Bayer[1]

[1]University of Duisburg-Essen, Structural and Medical Biochemistry, Center for Medical Biotechnologie (ZMB), 45117 Essen, Germany. E-mail: Daniel.Seifert@uni-due.de
[2]University of Duisburg-Essen, Institute of Organic Chemistry, 45117 Essen, Germany

daniel.seifert@uni-due.de

Intrinsic labeling e.g. using organic fluorophores, inorganic quantum dots or fluorescent proteins like GFP is used for the detection of specific proteins in living cells. However, all of these luminophores lack at least one important feature. While quantum dots are highly cytotoxic and fluorescent proteins can interfere with other proteins, commercial luminophores are highly susceptible to photobleaching. In contrast, fluorophores with aggregation-induced emission (AIEgens) showed good cell compatibility and a high photostability[1]. Here we report on a thiophtalonitrile dye that is based on the work of Voskuhl and Jonkheijm[2]. This AIE is easily amenable for chemical modification. We modified this AIEgen by adding short peptides via copper(I) catalyzed alkyne-azide cycloaddition (CuAAC) and are now able to monitor specific binding events to proteins. As model target protein, we used the WW-domain of the human peptidyl-prolyl isomerase Pin1. By varying the linker between the AIE and the protein, we like to investigate the influence of distance on binding constant and maximum fluorescence intensity. In future, we like to test our AIEgen for detection, localization and quantification of certain proteins in living cells.

References:

1. Shi, H.; Liu, J.; Geng, J.; Tang, B. Z.; Liu, B. Specific detection of integrin αvβ3 by light-up bioprobe with aggregation-induced emission characteristics. *Journal of the American Chemical Society* **2012**, *134*, 9569–9572.
2. Schmidt, B.; Sankaran, S.; Stegemann, L.; Strassert, C. A.; Jonkheijm, P.; Voskuhl, J. Agglutination of bacteria using polyvalent nanoparticles of aggregation-induced emissive thiophthalonitrile dyes. *J. Mater. Chem. B.* **2016**, *4*, 4732–4738.

POSTER NOTES

Multivalent Molecular Tweezers as Molecular Cork for Protein Pores

A. Sriskantharajah, T. Schrader

University of Duisburg-Essen, Universitätsstraße 7, 45117 Essen
abbna.sriskantharajah@uni-due.de

Nowadays molecular tweezers have been developed as supramolecular tools which selectively address accessible lysines and arginines on protein surfaces. [1] This unique interaction has been used to interfere with pathologic protein aggregation and also to inhibit protein protein interactions. We asked ourselves if multiple tweezers could also be utilized to explore and block the function of protein pores due to the presence of multiple copies of basic amino acids. One such example is the segregase p97 which is relevant for protein quality control inside cells. It contains a central dynamic pore which runs through the whole self-assembled protein machinery and is discussed to take place in recognition and unfolding of lesioned protein termini. The precise function of the pore and its mechanism of action are still unclear.[2]

We now decided to synthesize a symmetrical multivalent tweezer array with defined distances and a rigid core containing aromatic systems, which can target the spherical arrangement of lysines or arginines lining the pore wall. This tailored hybrid tweezer oligomer should be able to bind cooperatively and tightly to the ring of basic amino acids and hence prevent unfolded peptide strands to penetrate the pore. To this end, we have attached an azide function to the parent tweezer and will employ “click” chemistry to couple multiple tweezers to different oligoalkyne scaffolds. This can be the first example of an artificial plug for a protein pore.

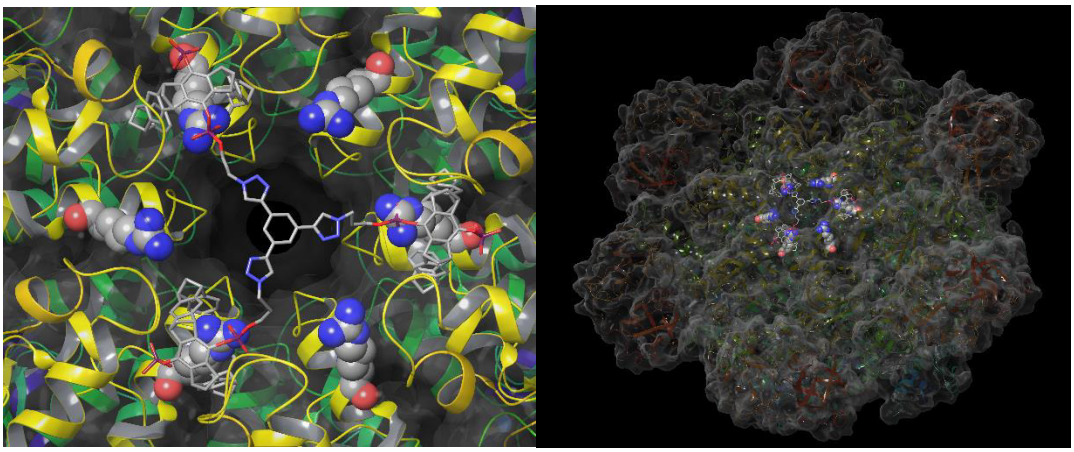


Figure 5 Segregase p7 with multivalent molecular tweezer cork.

References:

[1] M. Fokkens, T. Schrader, F.-G. Klärner, *J. Am. Chem. Soc.* **2005**, *127*, 14415-14421.

[2] V. E. Pye, I. Dreveny, L. C. Briggs, C. Sands, F. Beuron, X. Zhang, P. S. Freemont: Going through the motions: The ATPase cycle of p97. *J. Struct. Biol.* **2006**, *156*, 12–28.

POSTER NOTES

Understanding protein mechanisms using chemically-designed DNA architectures

Pierre Stegemann, Michael Ehrmann and Barbara Saccà

Bionanotechnology, Centre for Biotechnology/Faculty of Biology, Universität Duisburg-Essen

pierre.stegemann@uni-due.de

Structural DNA nanotechnology uses the unique recognition properties of the DNA molecule to realize two- and three-dimensional finite-sized objects of desired shape and full molecular addressability.[1] Using this strategy, we recently realized one of the largest DNA-protein complexes of semisynthetic origin held in place exclusively by spatially defined supramolecular interactions.[2] In our approach, the collective and convergent action of multiple peptide ligands pre-oriented towards the surface of the DegP protease is exploited to strengthen the binding affinity, circumventing the need for covalent protein tagging and favoring the formation of a 1:1 host-guest complex (Figure 1). Preliminary results have shown the putative role of the DNA envelope in preventing protein degradation and enhancing its enzymatic activity towards a natural substrate (unpublished results). Our goal is to investigate this issue in greater detail, revealing and possibly quantifying the contribution given by the different parameters of the system, including the geometry of the cage, the type and spatial arrangement of the peptide ligands and the oligomerization state of the protein cargo. We envisage that through the engineering of the chemical space around the protein, this method will enable to control and better understand the mechanisms behind the allosteric regulation of DegP activity, and more in general, will open the way to a new approach to explore protein events at the molecular level.

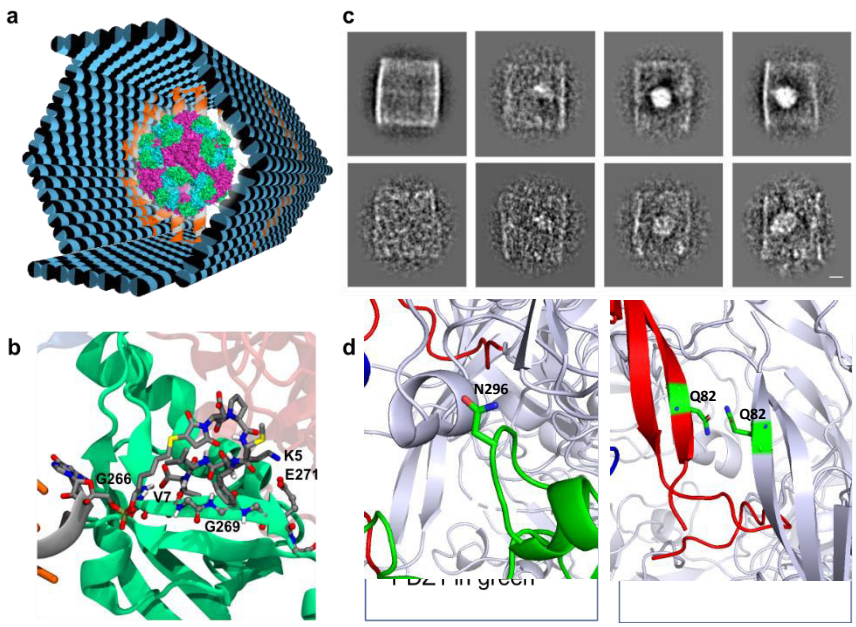


Figure 1. DNA-driven encapsulation of single protein molecules. (**a**) Molecular model of the DNA origami cage used for encapsulation of the DegP protease. (**b**) The protein is bound inside the cage through non-covalent interactions with peptide motifs. (**c**) EM characterization of the unbound and DegP6, DegP12 and DegP24 bound cages. (**d**) Details of the genetically modified DegP6 for improved structural studies.

References:

1. N. C. Seeman, *Nature* **2003**, *421*, 427-431.
2. A. Sprengel, P. Lill, P. Stegemann, K. Bravo-Rodriguez, E. C. Schöneweiß, M. Merdanovic, D. Gudnason, M. Aznauryan, L. Gamrad, S. Barcikowski, E.Sanche-Garcia, V. Birkedal, C. Gatsogiannis, M. Ehrmann, B. Sacca, **2016**.

POSTER NOTES

Modeling Polymer Assisted Protease Self-Digest

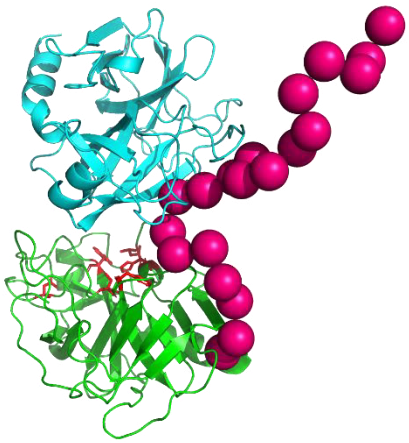
Niklas Tötsch, Daniel Hoffmann

Department of Bioinformatics and Computational Biophysics, Universität Duisburg-Essen, Universitätsstraße 2, 45117 Essen, niklas.toetsch@uni-due.de

Serine proteases cleave peptide bonds in proteins and play a crucial role in various physiological functions such as digestion and blood coagulation. Poor regulation can cause medical emergencies by e.g. enzymatic digestion of gastrointestinal walls. Conventional protease inhibitors suffer from low efficiency and selectivity as well as high biodegradability.

Copolymers have been found to inhibit proteases. Many protein-polymer complexes are enabled by multiple weak interactions resulting in a strong avidity. A few polymers inhibit proteases substoichiometrically by accelerating the proteases' self-digest. Physiologically, autolysis has been indicated a "fail-safe" mechanism to avoid damaging high concentrations of proteases.

The system size, including at least two proteases and a polymer, as well as the vast conformational space of very flexible polymers pose great challenges to computational models on a molecular level. We use a variety of computational tools such as docking and Molecular Dynamics simulations to describe and understand the system or parts thereof at different levels of complexity and detail.



References:

1. P. Gilles, K. Wenck, I. Stratmann, M. Kirsch, D. Smolin, T. Schaller, H. de Groot, A. Kraft, T. Schrader: High-Affinity Copolymers Inhibit Digestive Enzymes by Surface Recognition. *Biomacromolecules.* **2017**, *18*, 1772–1784.
2. Y. Lv, J. Zhang, H. Wu, S. Zhao, Y. Song, S. Wang, B. Wang, G. Lv, X. Ma: A protease inhibition strategy based on acceleration of autolysis. *Chem. Commun.* **2015**, *51*, 5959–5962.

POSTER NOTES

Design of surface-functionalized ultrasmall gold nanoparticles for controlled protein targeting through click chemistry

Selina Beatrice van der Meer, Kateryna Loza, Peter Bayer, Christine Beuck and Matthias Epple

Inorganic Chemistry and Center for Nanointegration Duisburg-Essen (CeNIDE), University of Duisburg-Essen, Universitätsstr. 7, 45141 Essen, Germany
selina.van-der-meer@uni-due.de

Surface-functionalized ultrasmall gold nanoparticles (diameter of 2 nm) allow a specific targeting of epitopes on a protein surface as they are smaller than most proteins.[1] This is of special interest to influence the function or the conformation of a protein, e.g. to influence its function.[1] A surface functionalization of the gold nanoparticle with azide groups and a subsequent click reaction, i.e. a copper-catalyzed azide-alkyne (CuAAC) cycloaddition, permits an orthogonal covalent conjugation under mild conditions.[2]
Azide-terminated ultrasmall nanoparticles were prepared by reducing tetrachloroauric acid in the presence of azide-carrying cysteine-containing tripeptide.[3] Functional molecules with an alkyne function were covalently attached to the particles by CuAAC click chemistry. The hydrodynamic diameter of the functionalized gold nanoparticles was measured by diffusion ordered NMR spectroscopy (DOSY). Disc centrifugal sedimentation (DCS) and transmission electron microscopy (TEM) showed the dispersion state of the nanoparticles and the diameter of the metallic core. The successful click reaction to the azide-functionalized gold nanoparticles was demonstrated by ^{13}C-NMR with ^{13}C-labelled alkyne propargyl alcohol as model compound clicked to the gold nanoparticle surface.

References:

1. M. Kopp, S. Kollenda, M. Epple: Nanoparticle-Protein Interactions: Therapeutic Approaches and Supramolecular Chemistry. *Acc. Chem. Res.* **2017**, *50*, 1383-1390.
2. C. Kolb, M.G. Finn, K.B. Sharpless: Click Chemistry: Diverse Chemical Function from a Few Good Reactions. *Angew. Chem. Int. Ed.* **2001**, *40*, 2004-2021.
3. B. Schuetze, C. Mayer, K. Loza, M. Gocyla, M. Heggen, M. Epple: Conjugation of thiol-terminated molecules to ultrasmall 2 nm-gold nanoparticles leads to remarkably complex ^{1}H-NMR spectra *J. Mater. Chem. B.* **2016**, *4*, 2179-2189.

POSTER NOTES

CENP-C is recruited to the centromere through multivalent interactions within the CCAN meshwork

Kai Walstein, Dongqing Pan, Dorothee Vogt and Andrea Musacchio

Department of Mechanistic Cell Biology, Max Planck Institute of Molecular Physiology, Otto-Hahn-Straße 11, 44227 Dortmund, Germany

kai.walstein@mpi-dortmund.mpg.de

In metazoans, the centromere is defined by an enrichment of the histone H3 variant centromere protein A (CENP-A).[1] CENP-A recruits at least two subunits of the constitutive centromere associated network (CCAN), which forms the inner layer of the kinetochore. CENP-C, the largest CCAN member, directly binds CENP-A nucleosomes, mediated by two sequence-related motifs localized in the central and C-terminal region of CENP-C. Using analytical size exclusion chromatography (SEC), we compared the binding of an N-terminal and a C-terminal CENP-C fragment to CENP-A nucleosomes. We found, that both individual CENP-C fragments can bind to CENP-A nucleosomes. The interaction of both CENP-C fragments with CENP-A required a functional CENP-C motif. In HeLa cell experiments we found, that mutation or deletion of both CENP-C motifs did not abolish the centromere localization of CENP-C. However, mutation of either the CENP-HIKM or the CENP-LN binding site significantly reduced the recruitment of CENP-C to the centromere. Using purified proteins, we can finally show, that the CENP-LN and CENP-HIKM subcomplexes are able to rescue the binding of CENP-A to a CENP-C mutant harboring two non-functional CENP-A binding motifs.

References:

1. Earnshaw, W.C. and N. Rothfield: Identification of a family of human centromere proteins using autoimmune sera from patients with scleroderma. *Chromosoma.* **1985**, *91* (3-4), 313-321.

POSTER NOTES

Two Metals are better than One! – Cooperative Effects of AuPd-Nanoalloy Catalysts in Alkyne *Z*-Semihydrogenation

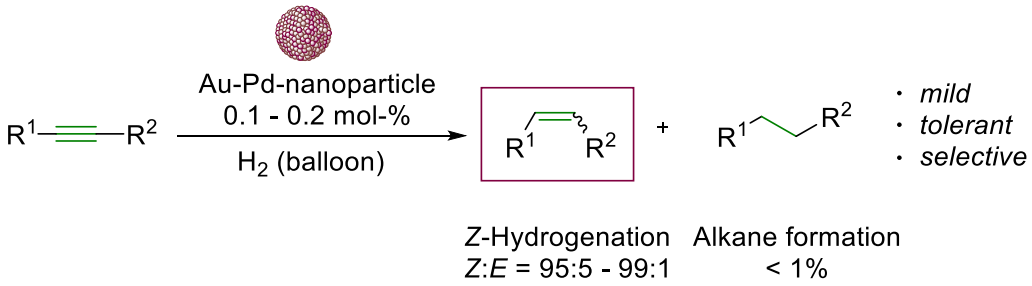
M. Wissing, A. Studer

WWU Münster, Organisch-Chemisches Institut, Corrensstraße 40, 48149 Münster

maren.wissing@uni-muenster.de

The synthesis of *Z*-alkenes by chemo- and stereoselective hydrogenation of alkynes is a key step in the synthesis of vitamins and natural products and is also a relevant reaction in polymer industry.[1] Over the past years, different metal nanoparticles - mostly consisting of palladium - have been developed as catalysts for this transformation. In these systems the reactivity of palladium often has to be adjusted by poisoning with sulfur or phosphorous containing additives to avoid over-hydrogenation and isomerization.[2] However, this catalyst poisoning often also leads to a loss of activity.

Our approach lies in the use of mixed AuPd-nanoparticles.[3] In these systems the incorporation of gold into the palladium particles offers the possibility to tune the selectivity while at the same time it increases the activity. With this strategy the amount of catalyst can be reduced by 90% compared to corresponding monometallic Pd-nanoparticles, clearly documenting the cooperative effect exerted by the two metals. Moreover, the catalyst performs well under mild conditions, tolerates many functional groups and can be recycled at least 4 times



References:

1. Á.Molnár, A. Sárkány, M. Varga: Hydrogenation of carbon–carbon multiple bonds: chemo-, regio- and stereo-selectivity. *J. Mol. Catal. A: Chem.* **2001**, *173*, 185-221.

2. K. C. K. Swamy, A. S. Reddy, K. Sandeep, A. Kalyani: Advances in chemoselective and/or stereoselective semihydrogenation of alkynes. *Tetrahedron Lett.* **2018**, *59*, 419–429.

3. M. Wissing, M. Niehues, B. J. Ravoo, A. Studer: Mixed AuPd-Nanoparticles as Highly Active Catalysts for Alkyne *Z*-Semihydrogenation. *Eur. J. Org. Chem.* **2018**, 3403–3409.

POSTER NOTES

Solid-state NMR on frustrated aluminum-phosphorus Lewis-pairs

Anna-Lena Wübker[a], Hellmut Eckert[a,b] and Michael Ryan Hansen[a].

[a]*Westfälische Wilhelms-Universität Münster, Institut für Physikalische Chemie, Corrensstraße 28/30, 48148 Münster, Germany*

[b]*Universidade de São Paulo, Instituto de Fisica de São Carlos, São Carlos, Brasil*

a.wübker@uni-muenster.de

In the neutralization reaction of Lewis acids and bases strong adducts are formed. In Frustrated Lewis pairs (FLPs) this neutralization reaction is prevented due to the steric and electrical influences of their ligands. This frustration leads to excellent catalytic activity for the activation and splitting of small molecules or for the building of adducts and polymers.[1] Therefore, FLPs have become increasingly studied in recent years since they represent potential substitutes for transition metals in organic catalysis. This increases the importance of structural analysis as well as the investigation of their reaction behavior.[2]

Previous solid-state NMR investigations in our group mostly were done at boron phosphorus FLPs. Aluminum provides a stronger acidity, a higher variety in the possible ligands, and an easier formation reaction compared to boron. However, aluminum shows much higher quadrupolar coupling constants (>15 MHz) compared to boron (<5 MHz), making the characterization of such compounds less straight forward using solid-state NMR spectroscopy. To overcome this problem, special pulse sequences, like the WCPMG,[3] were developed for the acquisition of broad NMR spectra, which combined with frequency-stepping enables the recording of static ultra-wideline ^{27}Al NMR spectra. Here, we report the first ^{27}Al{^{1}H} WCPMG NMR spectra for some aluminum-phosphorus FLPs and the challenges in determining the heteronuclear dipolar coupling between ^{27}Al and ^{31}P for such systems.

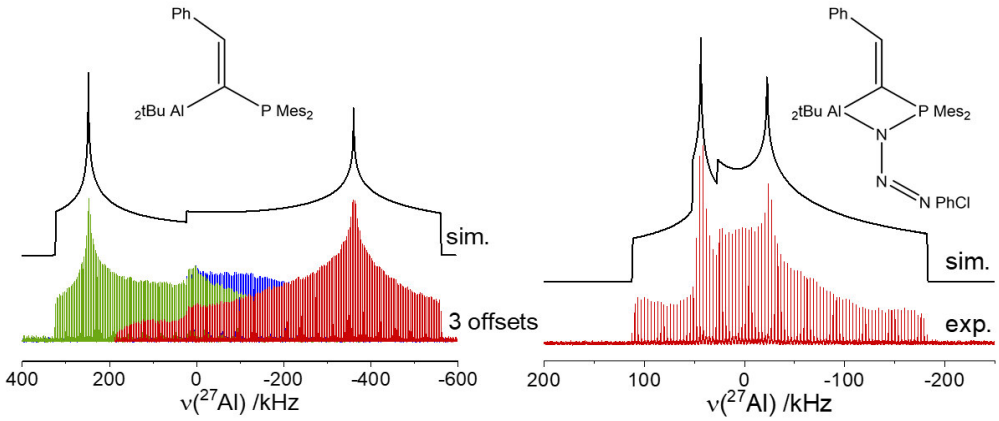


FIGURE 1. ^{27}Al{^{1}H} WCPMG NMR spectra of an Al-P FLP and an azidoadduct of the same Al-P FLP. The simulations (black) were done using the QUEST programm.

Acknowledgements:

We thank the working group of Prof. Uhl from the WWU Münster for preparing the investigated compounds.

References:

1. D. W. Stephan, G. Erker: *Angew. Chem. Int. Ed.* **2010**, *49*, 46-76.
2. T. Wiegand, M. Siedow, H. Eckert, G. Kehr, G. Erker: *Isr. J. Chem.* **2015**, *55*, 150-178.
3. L. A. O´Dell, R. W. Schurko: *Chem. Phys. Lett.* **2008**, *464*, 97-102.

POSTER NOTES

Developing Supramolecular Taspase Inhibitors with Dynamic Combinatorial Libraries

Alexander Zimmermann, Carsten Schmuck*

Institute of Organic Chemistry, University of Duisburg-Essen, Universitätsstraße 7, 45117 Essen,

Alexander.Zimmermann@uni-due.de

The enzyme TASP1 (Threonine aspartase 1) is overexpressed in primary human cancer cells. This protease coordinates cell proliferation and apoptosis. Therefore, Taspase inhibitors may serve as an anti-cancer therapeutic target.[1] In 2012 a patent with novel Taspase inhibitors was published.[2] These inhibitors contain a lot of donor acceptor pairs that can interact with TASP1. The binding motif **G**uanidiunio**c**arbonyl **p**yrrole (**GCP)**, developed by the Schmuck group, also contains many donor acceptor pairs.[3] That is why we generated compounds that are derived from the patent and contain GCP as basic structur. To identify potent inhibitors, it is necessary to generate a great number of different compounds. **D**ynamic **C**ombinatorial **C**hemistry (**DCC**) has the advantage to generate a great set of different compounds, so called **D**ynamic **C**ombinatorial **L**ibraries (**DCL**s). Assays of DCLs show the most biological active substances and enable the optimization of structures. With the help of DCC we want to achive an optimized Taspase inhibitor.

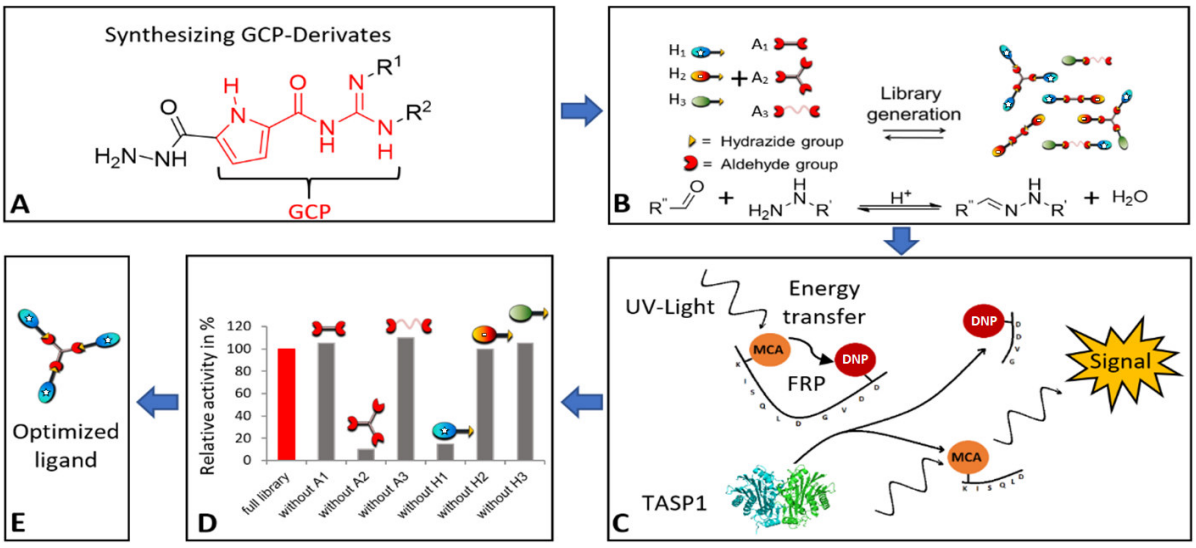


Figure 1.: A) GCP derivates have to be synthesized. **B)** Development of a DCL. An aldehyde reacts with a hydrazide to a hydrazone. A lot of compounds become created. **C)** An enzyme assay is conducted. TASP1 cleaves a substrate resulting in separating the Forster Resonanz Pair (FRP). The slower the signal increases the higher the inhibitory impact is. **D)** The full Library with every compound is compared with sub libraries where one compound (corresponding hydrazide = $H_{1\text{-}3}$) or scaffold (corresponding aldehyde = $A_{1\text{-}3}$) is missing. If the signal of the sub library is lower compared to the full library the missing compound or scaffold is an important building block for a potent Taspase inhibitor. **E)** Shows an optimized ligand as a result of the DCL.

References:

1. Chen, D. Y.; Liu, H.; Takeda, S.; Tu, H.; Sasagawa, S.; Van Tine, B. A.; Lu, D.; Cheng, E. H-Y.; Hsieh, J. J-D. *Cancer Res.* **2010**, *70* (13), 5358-5367.
2. Hsieh, J.; Cheng, E. Washington University, St. Louis, US 2012/0015990 A1, **2012**.
3. Schmuck, C.; Heil, M. *Org. Lett.* **2001**, *3* (9), 1253-1256.

POSTER NOTES

LIST OF PARTICIPANTS

Aschmann, Dennis, Institute of Organic Chemistry, University of Duisburg Essen (UDE), dennis.aschmann@uni-due.de

Blümke, Anika, Centre for Medical Biotechnology, University of Duisburg Essen (UDE), Anika.Bluemke@uni-due.de

Bruchhage, Julia, Institut für Biochemistry, University of Münster (WWU), k.brueninghoff@uni-muenster.de

De Vries, Wilke, Institute of Organic Chemistry, University of Münster (WWU), W.deVries@wwu.de

Droste, Jorn, Institut of Physical Chemistry, University of Münster (WWU), joern.droste@uni-muenster.de

Dudziak, Alexander, Department of Molecular Genetics I, University of Münster (WWU), alexander.dudziak@uni-due.de

Duong, Qui-Nhi, Institute of Organic Chemistry, University of Münster (WWU), Qui-Nhi.duong@wwu.de

Erkelenz, Michael, Physical Chemistry I, University of Duisburg Essen (UDE), michael.erkelenz@uni-due.de

Freitag, Matthias, Institute of Organic Chemistry, University of Münster (WWU), m_frei24@uni-muenster.de

Hayduk, Matthias, Institute of Organic Chemistry, University of Duisburg Essen (UDE), matthias.haydukduk@uni-due.de

Henning, Klaasen, Institute of Organic Chemistry, University of Münster (WWU), h_klaa01@uni-muenster.de

Jaekel, Andreas, Bionanotechnology, Centre for Biotechnology/Faculty of Biology, University of Duisburg Essen (UDE), Andreas.jaekel@uni-due.de

Kamba, Bianca, Centre for Medical Biotechnology, University of Duisburg Essen (UDE), bianca.kamba@uni-due.de

Killa, Matthias, Institute of Organic Chemistry, University of Duisburg-Essen (UDE), matthias.killa@uni-due.de

Klahr, Kevin, Theoretic Organic Chemistry, University of Münster (WWU), k_klah01@uni-muenster.de

Klepel, Florian, Center for Soft Nanoscience, University of Münster (WWU), florian.klepel@uni-muenster.de

LIST OF PARTICIPANTS

Knitsch, Robert, Institute of Physical Chemistry, University of Münster (WWU), r.knitsch@uni-muenster.de

Kollenda, Sebastian, Inorganic Chemistry and Centre for Nanointegration, University of Duisburg Essen (UDE), sebastian.kollenda@uni-due.de

Kötter, Alexander, Institute of Physical Chemistry, University of Münster (WWU), a_koet04@wwu.de

Koy, Maximilian, Institute of Organic Chemistry, University of Münster (WWU), koy@uni-muenster.de

Kracht, Matthias, Institute of Biology, University of Duisburg-Essen (UDE), matthias.kracht@uni-due.de

Kujawski, Kyra, Institute of Organic Chemistry, University of Duisburg-Essen (UDE), kyra.kujawski@uni-due.de

Marek, Jasmin, Institute of Organic Chemistry, University of Münster (WWU), j_mare02@uni-muenster.de

Martinewski, Katja, Institut of Inorganic and Analytical Chemistry, University of Münster (WWU), k_mart05@uni-muenster.de

Massolle, Anja, Institute of Organic Chemistry, Center for Multiscale Theory and Computation, University of Münster (WWU), a.massolle@uni-muenster.de

Matarranz, Beatriz, Institute of Organic Chemistry, University of Münster (WWU), matarran@uni-muenster.de

Mehlmann, Paul, Institut of Inorganic and Analytical Chemistry, University of Münster (WWU), p_mehl02@uni-muenster.de

Meiners, Annika, Centre for Medical Biotechnology, University of Duisburg-Essen (UDE), annika.meiners@uni-due.de

Nguyen, Duy Thao, Institute of Organic Chemistry, University of Münster (WWU), dt.nguyen@wwu.de

Pedroza, Laura, Centre for Medical Biotechnology, University of Duisburg-Essen (UDE), laura.pedroza@uni-due.de

Rau, Kristina, Institute of Biochemistry, University of Münster (WWU), k_rau001@uni-muenster.de

Rebmann, Philipp, Institute of Organic Chemistry, University of Duisburg-Essen (UDE), philipp.rebmann@uni-due.de

Riebe, Steffen, Institute of Organic Chemistry, University of Duisburg-Essen (UDE), steffen.riebe@uni-due.de

LIST OF PARTICIPANTS

Roling, Lena, Institute of Organic Chemistry, University of Münster (WWU), lena.roling@uni-muenster.de

Ruks, Tatjana, Inorganic Chemistry and Center for Nanointegration, University of Duisburg-Essen (UDE), Tatjana.ruks@uni-due.de

Scholz, Linus, Center for Multiscale Theory and Computation, University of Münster (WWU), l.scholz@uni-muenster.de

Schönrath, Isabell, Institut of Inorganic and Analytical Chemistry, University of Münster (WWU), isabell@muellerlab.org

Schulz, Florian, Institutet of Chemical Biology, University of Duisburg-Essen (UDE), florian.schulz@uni-due.de

Seifert, Daniel, Center for Medical Biotechnologie, University of Duisburg-Essen (UDE), daniel.seifert@uni-due.de

Sriskantharajah, Abbna, Institute of Organic Chemistry, University of Duisburg-Essen (UDE), abbna.sriskantharajah@uni-due.de

Stegemann, Pierre, Centre for Biotechnology/Faculty of Biology, University of Duisburg-Essen (UDE), pierre.stegemann@uni-due.de

Stuckhardt, Constantin, Institute of Organic Chemistry, University of Münster (WWU), c.stuckhardt@wwu.de

Toetsch, Niklas, Department of Bioinformatics and Computational Biophysics, University of Duisburg-Essen (UDE), niklas.toetsch@uni-due.de

Vallet, Cecila, Centre for Medical Biotechnology, University of Duisburg-Essen (UDE), cecilia.vallet@uni-due.de,

Van der Meer, Selina, Inorganic Chemistry and Center for Nanointegration, University of Duisburg-Essen (UDE), cecilia.vallet@uni-due.de

Walstein, Kai, Department of Mechanistic Cell Biology, Max Planck Institute of Molecular Physiology, kai.walstein@mpi-dortmund.mpg.de

Wissing, Maren, Institute of Organic Chemistry, University of Münster (WWU), maren.wissing@uni-muenster.de

Wübker, Anna-Lena, Institute of Physical Chemistry, University of Münster (WWU), a.wübker@uni-muenster.de

Zimmermann, Alexander, Institute of Organic Chemistry, University of Duisburg-Essen (UDE), Alexander.Zimmermann@uni-due.de

Notes