

February 2017

## Innovation prize in medicinal/pharmaceutical chemistry for Anna Hirsch



Anna Hirsch has been awarded the "innovation prize in medicinal/pharmaceutical chemistry" of the German Chemical and the German Pharmaceutical Society. This prize honours excellent independent scientific work and publications in the fields of medicinal/pharmaceutical chemistry of scientists who obtained their PhD no longer than ten years ago. The prize will be awarded at the conference "Frontiers in Medicinal Chemistry", which will be held in Berne (Switzerland) from 12.–15.2.17.

## Highlights by Prof. dr. Jan B.F.N.Engberts

First of all, happy New Year to all my readers of the monthly highlights!

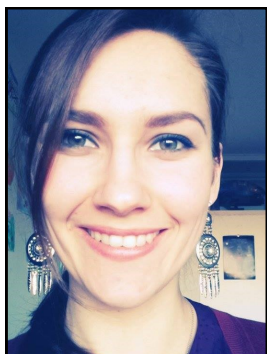
- The first paper I like to mention is a manuscript from our Stratingh Institute, written by Prof. Roelfes and three coworkers, which describes a beautiful reaction, the DNA-accelerated copper catalysis of Friedel-Crafts conjugate addition/enantioselective protonation reactions in water. It is a very efficient DNA-induced rate acceleration, the highest reported so far, due to the environment presented by a bimolecular scaffold. The authors propose that DNA is acting as a pseudophase in which all reaction components are concentrated, leading to a high effective molarity. The enantioselectivity of the product is explained by the involvement of additional second coordination sphere interactions. The results provide a powerful demonstration of the concept of DNA-based catalysis. *Garcia-Fernandez, A., Megens, R.P., Villarino, L., Roelfes, G., J.Am.Chem.Soc., 2016, DOI 10.1021/jacs.6b08295.*
- A group from Shanghai University reported a disulfide-catalyzed visible-light-mediated oxidative cleavage of C=C bonds and an olefin-disulfide charge-transfer complex. This photocatalytic method employed electron-rich aromatic disulfides as photocatalysts. In this procedure mono- and multi-substituted aromatic olefins could be converted into ketones and aldehydes at ambient temperatures. The unconventional homolysis of the aromatic S-S bond by visible light was tentatively explained by the formation of an intermediate olefin-disulfide charge-transfer complex. The exact mechanism is under further investigation. *Deng, Y., Wei, X-J., Wang, H., Sun, Y., Noël, T., Wang, X., Angew.Chem.Int.Ed., 2016, DOI 10.1002/anie.201607948.*
- Two scientists, working at the Universities of Illinois at Urbana, USA and the University of Lorraine, France, developed a methodology for the simulation of molecular motors at different scales. Millisecond-scale conformational transitions have their particular attention

because of their relevance for the study of molecular motors that convert chemical energy into mechanical work. A whole array of methods was employed for delivering a viable option for capturing the millisecond-scale motor steps of biological motors. The novel hybrid method was demonstrated for cyclodextrin-based motors and for V-type ATPases. *Singharoy, A., Chipot, C., J.Phys.Chem.B 2016, DOI 10.1021/acs.jpcc.6b09350.*

- The factors which control the reactivities and stereoselectivities of Diels-Alder reactions of substituted cyclopropenes with butadiene have been examined by Houk and a coworker at the University of California, Los Angeles. Based on results obtained with M06-2X density functional theory, they argue that the differences in reactivity are due to differences in hyperconjugative aromaticities and anti-aromaticities of the cyclopropenes.  $\sigma$ -Donor 3-substituents destabilize the ground state and enhance the reactivity. The opposite effect occurs for acceptors. The stereoselectivities respond to electrostatic, secondary orbital, and steric effects. *Levandowski, B. J., Houk, K.N., J.Am.Chem.Soc. 2016, DOI 10.1021/jacs.6b10463.*
- Chen and eight coworkers at Nankai University in Tianjin, China, showed that high photovoltaic performance small molecules can be designed and synthesized by tuning their HOMO levels. For this purpose they used an electron-withdrawing central unit with a large planar structure in the A-D-A type of small molecules. Their novel molecule was named DR3TBDD (with eight thiophene units) and contained an electron-withdrawing unit BDD as the central building block. A power conversion efficiency of 9.53% was achieved with a high open-circuit voltage. An attempt was made to attribute these important properties to structural units in the molecule. *Zhang, H., Liu, Y., Sun, Y., Li, M., Kan, B., Ke, X., Zhang, Q., Wan, X., Chen, Y., Chem.Comm. 2016, DOI 10.1039/c6cc07927.*
- As argued by Knowles and four coworkers at Princeton University, amidyl radicals are useful intermediates in a number of synthetically useful transformations. They now developed a novel approach for the formation of these radicals that overcomes limitations in previous methods. N-H bonds of N-alkyl amides were homolyzed via proton-coupled electron transfer. An excited-state iridium photocatalyst and a weak phosphate base cooperatively serve to remove both a proton and an electron from an amide in a concerted elementary step. The resultant amidyl radicals are then able to promote subsequent C-H abstraction and radical alkylation steps, leading to synthetically useful compounds, inaccessible by traditional hydrogen atom transfer approaches. Further mechanistic details were investigated in some detail. *Choi, G.J., Zhu, Q., Miller, D.C., Gu, C.J., Knowles, R.R., Nature, 2016, DOI 10.1038/nature19811.*
- We all know that carbon is tetravalent, being able to form four bonds to other atoms. The hexagonal planar ring structure of benzene represents our basic idea about aromaticity. However, in 1973 Prof. H.Hogeveen and his student Peter Kwant, in our department, were the first to prepare  $C_6(CH_3)_6^{2+}$  a species with a six-coordinate carbon atom. The structure was only based upon NMR spectroscopic analysis and reactivity studies. But now the structure of the hexamethylbenzene dication has been definitely confirmed by its X-ray crystal structure in a study by Seppelt and his coworker Malischewski at the Free University of Berlin. The dication was prepared as follows. Hexamethyl Dewar benzene epoxide was dissolved in  $HSO_3F/SbF_5$  (magic acid) and was crystallized as the  $SbF_6^-$  salt after addition of excess anhydrous HF at low temperature. The hexacoordinated carbon that is only bound to carbon atoms is without precedent. *Hogeveen, H., Kwant, P.W., Tetrahedron Lett. 1973, 14, 1665-1670 and Malischewski, M.Sc.M., Seppelt, K., Angew.Chem.Int.Ed., 2016, DOI 10.1002/anie.201608795.*
- The final paper that I like to mention is a highly interesting study by Pascal (University of Montpellier) and Pross (University of the Negev and Shanghai University). The title is "A Roadmap toward Synthetic Protolife". It contains a statement by Einstein: "the most powerful force in the Universe is compound interest". As argued previously by Pross, life is ultimately nothing but the material manifestation of exponential kinetics acting on particular material forms, which is nature's alternative path to persistent forms. The ultimate concept here is dynamic kinetic stability (DKS), meaning that a chemical system, potentially able to evolve towards biological complexity, needs to be driven by both exponential replicative growth and has to be in a dynamic, non-equilibrium and energy-fueled state (DKS). These systems possess remarkably different physical and chemical characteristics to regular chemical systems. It is claimed that these systems will now be experimentally accessible and that the door to the possible synthesis of simple protolife appears to be open. *Pascal, R., Pross, A., Synlett 2017, DOI 10.1055/s-0036-158940-3.*

Jan Engberts

## New Appointments



**Liubov Yakovlieva**

PhD student as of 1/1/2017

Group Walvoort



**Simona Bianca**

PhD student as of 16/1/2017

Group Minnaard



**Niek van der Zouwen**

PhD student as of 16/1/2017

Group Witte



**Spyros Bousis**

PhD student as of 16/1/2017

Group Hirsch



**Guillaume le Calvez**

PhD student as of 16/1/2017

Group Minnaard



**Vivek Kumar Mishra**

PostDoc as of 1/1/2017

Group Minnaard



**Sara Hernandez**

PostDoc as of 15/1/2017

Group Roelfes



**Renze Sneep**

Trainee as of 1/1/2017

with Theodora Tiemersman

## **PhD Defence**

### Friday, February 17<sup>th</sup>

@ **9:00 Olga Elena Castañeda Ocampo** will defend her PhD thesis. **Title:** "Shedding light on photosystem I— from charge-transport to bio-photovoltaics". **Promotores:** Prof. dr. R.C. Chiechi and Prof. Dr. A. Herrmann

### **Werkbespreking: Thursday morning 8.30 hrs, room 5111.0080**

**February 16<sup>th</sup>—Liliana Cozzoli** (PhD Roelfes) "Responsive DNA G-quadruplex micelles"

**February 23<sup>rd</sup>—Henriette Heideman** (PhD Feringa) "Directional Movement of Light-Driven Molecular Motors on Surfaces"

**March 2<sup>nd</sup>— Xingchen Yan** (PhD Harutyunyan) "Copper(I)-catalyzed enantioselective synthesis of chiral amides"

**March 9<sup>th</sup>—Yuchen Wei** (PhD Feringa) "Molecular motor in confined space"

**March 16<sup>th</sup>— Tao Yan** (PhD Barta) "Catalytic N-alkylation of unprotected amino acids with alcohols"

*If you have items for the next issue of this Newsletter, please send an e mail to the Stratingh Institute office: [Stratingh@rug.nl](mailto:Stratingh@rug.nl)*