

"In-the-box" ideas awarded €2M in NWO-TOP programme

Chemists from the UvA and the RUG are starting a large-scale collaboration on "Catalysis in Confined Spaces", a TOP-PUNT project which was awarded 2M euros this week by the Netherlands Organisation for Scientific Research (NWO). The groups of Profs. Gadi Rothenberg, Joost Reek and Ben Feringa have joined forces to tackle this challenge.

This five-year project will connect homogeneous, heterogeneous and biocatalysis by researching a simple yet baffling question: How does a catalyst work when it is constrained in a small "box" of nanometric dimensions? This may seem trivial, but being "close to the wall" is very different than being "in the middle of the crowd", as any student who has been to a large music festival will tell you.

Now, researchers from the Sustainable Chemistry Research Priority Area at the UvA and from the Stratingh Institute for Chemistry at the RUG will try and unravel this mystery. The grant will be used to fund eight PhD projects, supervised by dr. Jarl Ivar van der Vlucht, dr. Stefania Grecea, dr. Raveendran Shiju, dr. David Dubbeldam, dr. Jan van Maarseveen, prof. dr. Bas de Bruin, prof. dr. Wesley Browne, and dr. Sander Wezenberg.

The project will cement the ties between the chemistry departments of the UvA and the RUG, bringing together expertise in homogeneous catalysis, heterogeneous catalysis, and biocatalysis and organic synthesis.

Rothenberg, who has coordinated the proposal, is very happy with the result: "When we started thinking about catalysis in confined spaces, we quickly realised that this is an intricate problem that can only be solved by a coordinated effort. We got eight high-quality scientists to collaborate on writing these PhD projects. The concept wherein all of the results, methods and equipment will be shared by all researchers increases the chances of the project's success".

Vidi grant for Anna Hirsch and Edwin Otten



Drug discovery is a challenging undertaking. In a context where the pharmaceutical industry finds it increasingly difficult to develop new drugs, efficient access to novel molecular scaffolds is urgently needed. Dr. Anna Hirsch has been awarded a NWO Vidi grant to use dynamic combinatorial chemistry (DCC) in combination with fragment-based drug design, (de novo) structure-based drug design (SBDD) and multicomponent reactions to accelerate the drug-discovery process. Taken together, this research will further our knowledge of the molecular basis of DCC applied to targets of biomedical interest, lead to novel molecular scaffolds, interaction modes, bio-active compounds and ways to efficiently initiate the drug discovery process. The impact of this research extends to the health and well-being of society.

Dr. Edwin Otten has been awarded a NWO Vidi grant to develop new catalysts based on earth-abundant, inexpensive elements. In order to replace the precious metal catalysts that are currently in use, this project will develop a new strategy to mimic the reactivity of these metals. The prevalence of catalysts based on precious metals is due to their versatile electronic properties that allow redox-reactions in 2-electron steps, which are key to many important chemical transformations. This type of reactivity is generally not accessible to other (non-precious) elements. By making use of organic ligands that can participate in redox-reactions, the aim of this research is to replicate the catalytic properties of precious metals to non-scarce elements.



The Hanse Catalysis Symposium

On Friday May 29 the first Hanse Catalysis symposium took place.

A long time ago both Groningen as well as Rostock belonged to the Hanseatic League, which was an early form of a free trade zone. Most of the Hanseatic Cities were indeed harbours.

Today Groningen and Rostock have a common interest in catalysis and that is the reason why the LIKAT (Rostock) and the Stratingh Institute for Chemistry came together for a one day symposium on catalysis.

The main interest topics during the symposium were homogeneous catalysis, spectroscopy in relation to catalysis, catalytic conversion of renewable resources and these were addressed during two plenary lecture, 13 oral communications and a large number of posters from both institutions.

The symposium was a great success!

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

- Burke and seven coworkers at the University of Illinois at Urbana-Champaign, Urbana, USA developed a broadly applicable automated process for the synthesis of 14 distinct classes of small organic molecules. And, very importantly, they also discovered a catch-and-release chromatographic purification protocol applicable to all of the corresponding intermediates. For medicinal chemists, often interested in preparing a large number of compounds for testing, these synthesis machines, that allow automated carbon-carbon bond-formation approaches, are of great potential importance. Burke's work, that increases the flexibility of what one can make in libraries, has been discussed in some detail by Katharine Sanderson in a two-page review in Nature Reviews. *Li, J., Ballmer, S.G., Gillis, E.P., Fujii, S., Schmidt, M.J., Palazzolo, A.M.E., Lehmann, J.W., Morehouse, G.F., Burke, M.D., Science 2015, 347, 1221-1226. Sanderson, K., Nature Reviews, 2015, 14, 299-300.*
- Hans-Jörg Schneider wrote an interesting review about the limitations and extensions of the lock-and-key concept, also stressing the differences between gas state, solution and solid state structures. Perhaps unexpectedly, the formation of supramolecular complexes depends not only, and often even not primarily, on an optimal geometric fit between host and guest. Induced fit, allosteric interactions, different binding mechanisms, medium effects and pH effects may lead to variations of binding constants by orders of magnitude. And in aqueous solutions hydrophobic interactions may be of significant importance. The review reports a nice series of examples leading to a much better insight into the formation and

stability of supramolecular complexes. *Schneider, H.J., Int.J.Mol.Sci., 2015, 16, 6694-6717.*

- A highly efficient and selective hydrogenation of aldehydes in the presence of ketones in addition to olefins can be carried out using an [(ethylenediamine)(dppe)Ru(OCOt-Bu)₂] complex [dppe=1,2-bis(diphenylphosphino)ethane] under base-free conditions. It was demonstrated that even the sensitive 1,6-ketoaldehydes gave the desired ketoalcohols in high yields and with a 94-99% overall selectivity. Many functional groups can be tolerated in this synthetic procedure, including epoxides, carboxylic acids, esters, amides and nitriles, showing the potential synthetic utility of the catalyst. *Bonomo, L., Kermorvan, L., Dupau, P., ChemCatChem, 2015, DOI 10.1002/cctc.201500006.*
- Zhang, Yue and Cheng, with colleagues from the USA, Japan and China reported the selective assembly behaviors of a class of precisely defined, nanosized giant tetrahedra. These were constructed by placing different polyhedral oligomeric silsesquioxane (POSS) molecular nanoparticles at the vertices of a rigid tetrahedral framework. Precise positional interactions were introduced by designed symmetry breaking of these giant tetrahedra. This resulted in diverse selectively assembled, highly ordered supramolecular lattices. One of them was a Frank-Kasper A15 phase, resembling the essential structural features of certain metal alloys but at a larger scale. It is argued that a subtle competition between the persistent molecular geometry and the deformability driven by interaction terms dictates the selective assembly of the giant tetrahedra. *Huang, M., Hsu, C-H., Wang, J., Mei, S., Dong, X., Li, Y., Li, M., Liu, H., Zhang, W., Aida, T., Zhang, W-B., Yue, K., Cheng S.Z.D., Science 2015, DOI 10.1126/science.aaa2421.*
- In a joint project of scientists from China, Spain, Germany and Saudi Arabia it is shown that the power conversion efficiency of quantum-dot-sensitized solar cells (QDSCs) can be increased by about 20% via treatment of the QD-sensitized photoanode with a novel sequential inorganic ZnS/SiO₂ double layer. This procedure leads to strong inhibition of interfacial recombination processes in QDSCs and is also providing improved cell stability. Understanding of the recombination control was obtained by employing several physical techniques. *Zhao, K., Pan, Z., Mora-Seró, I., Cánovas, E., Wang, H., Song, Y., Gong, X., Wang, J., Bonn, M., Bisquert, J., Zhong, X., J.Am.Chem.Soc. 2015, DOI 10.1021/jacs.5b01946.*
- Lactimidomycin is a glutarimide-containing macrolide which displays a wide range of biological effects including cytotoxicity, anti-fungal activity, and inhibition of DNA/protein biosynthesis. It is also a potential anticancer drug. A total synthesis has now been achieved at the University of Minnesota, starting from (E)-2-methyl-2-pentenoic acid and using minimal functional group protection. Key steps are a copper-catalyzed ene-yne coupling/alkyne reduction tandem reaction, a Kobayashi vinylogous aldol reaction and a Marshall propargylation reaction. It is probably the shortest route to lactimidomycin intermediates with a similar structure. *Li, W., Georg, G.I., Chem.Comm. 2015, DOI 10.1039/c5cc02571k.*
- Detailed molecular dynamics simulations, performed at the University of Queensland, Brisbane, Australia, have shown why cyclopropane fatty acids, which are widespread in bacteria, disrupt the lipid packing in lipid bilayers. There are two main reasons: (1) they favor the occurrence of gauche defects in the chains and (2) they enhance fluidity by increasing the lipid lateral diffusion. However, at the same time, they generally induce a greater degree of order than unsaturated fatty acids of the same configuration and limit the rotation about the bonds surrounding the cyclopropane ring. Thus, cyclopropane fatty acids possess a dual function. They stabilize membranes against adverse conditions while simultaneously promoting membrane fluidity. Interestingly, there are important differences in the effects of cis- and trans-monocyclopropanated fatty acids. *Poger, D., Mark, A.E., J.Phys.Chem.B 2015, DOI 10.1021/acs.jpcc.5b00958.*
- Lowry, Walsh, and Khosla from Stanford University reviewed 11 metabolic pathways that have been the subject of recently reported in vitro reconstitution studies. Taking a subset of four

case studies within these 11 examples, it is argued that the remarkable organic chemistry occurring in biological systems obeys the fundamental principles of organic chemistry, and that the relevant chemical mechanisms are just those that we also encounter in conventional synthetic organic routes. Therefore it seems clear that the fine details of the kinetics, mechanistic pathways, and the identity of the organic products of enzymatic transformations can all be evaluated by in vitro reconstitution of metabolic pathways. *Lowry, B., Walsh, C.T., Khosla, C., Synlett. 2015, DOI 10.1055/s-0034-1380264.*

- In a second brief paper in Nature Chemistry, Bruce Gibb further reviews what is known about the about 100 organic compounds that have been detected in the Solar System. The “plausibility of life” (POL) considers a fluid medium, a source of energy and constituents (particularly thiols, i.e. unsaturated polymers) and conditions compatible with polymeric chemistry as key to POL. After discussing several gas and ice giants, Gibb concentrates his attention on Titan, the second largest moon in the Solar System, first discovered by Christiaan Huygens in 1655. A cascade of organic chemistry has been detected. The rain on Titan is composed of liquid methane or a methane/ethane mixture. The largest methane sea is somewhat larger than the Caspian Sea. A second mission to Titan, planned for the future, could bring us highly interesting material from Titan’s surface. Gibb concludes: “...if there is such a thing as reincarnation, I want to come back as an organic chemistry student analyzing data from the mission and trying to replicate Titan chemistry in the fumehood for my PhD.....” *Gibb, B.C., Nature Chem.2015, DOI 10.1038/nchem.2241.*

Finally I like to wish all my readers a most pleasant and relaxing summer holiday!

Jan Engberts

PhD Defences

Friday, June 5th

@11:00 Wenqiang Zou will defend his PhD thesis. **Title:** “Molecular Upconversion for Photovoltaics”.

Promotor: Prof. Dr. J.C. Hummelen. **Co-promotor:** Dr M.S. Pchenitchnikov

@ 16:15 Shaghayegh Abdolahzadeh will defend her PhD thesis. **Title:** “Catalysis in complex media”.

Promotor: Prof. Dr. W.R. Browne

Friday, June 19th

@11:00 Zhongtao Wu will defend his PhD thesis. **Title:** “Synthesis of natural products containing chiral tertiary alcohols and total synthesis of phorbacin B”. **Promotor:** Prof. Dr. A.J. Minnaard

Friday, June 26th

@9:00 Manuel Jäger will defend his PhD thesis. **Title:** “Selective oxidation of glycosides”. **Promotor:** Prof. Dr. A.J. Minnaard

New appointments



Gerard Roelfes

As of 1 May 2015

Professor in Biomolecular
Chemistry and Catalysis

Werkbespreking: Thursday morning 8.30 hrs, room 5111.0080

Jun 4th—Marco Wonink “Lowering the CO₂/CO overpotential by Fe-Porphyrin/FLP combinations”

Jun 11th—WORKWEEK

Jun 18th—Xinkai Qiu “System chemistry of self-assembled fibers”

Jun 25th— Dima Bederak “New Cu(I)-Mg(II) heterobimetallic chiral complexes for applications in asymmetric catalysis”

Jul 2nd—Jenny Douvogianni “Towards high-k polymers for OPVs”

Jul 9th—Paul Dockerty “Synthetic Brabantamide derivatives as antibacterial compounds and activity-based probes”

Jul 16th— Shuo Yang “Title to be announced”

Jul 23rd—Petra Erne “Mechanistic insight into dynamic liquid crystal systems which rotate micrometer-sized objects”

Jim Ottelé “Title to be announced”

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