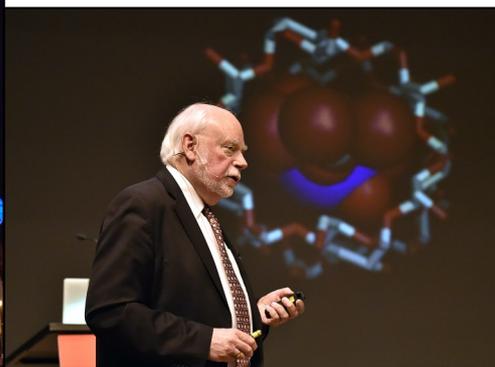


December 2017—January 2018



Dear colleagues,  
 I wish you all a Merry Christmas.  
 Instead of providing a comprehensive overview of 2017, I like to show you a few pictures of the Molecular Machines Nobel Conference. We can safely conclude this was a great success. It was heartwarming to experience the collaboration both from within the institute, many contributed in several ways to the organization, and from outside; the board of directors, and the Groningen Congress-bureau. This will long be remembered.

Adri Minnaard





### ERC consolidator for Syuzi Harutyunyan

Aromatic compounds are widely distributed in nature and some produced in multimillion metric ton scales annually. Recognized as fundamental synthetic materials, the chemistry of aromatics in which the aromaticity of the ring systems remains intact is well established. On the other hand, dearomatization reactions of arenes are an effective mechanism to convert simple planar aromatic compounds into chiral alicyclic systems. In this ERC-funded research program novel modalities to achieve dearomatization of electron-rich and electron-deficient arenes through Lewis acid activation followed by copper catalyzed carbon-carbon bond forming reactions will be developed. An important aspect is achieving dearomatization with the simultaneous installation of carbon-carbon bonds

in a regio- stereo- and enantioselective, and above all catalytic way.

### NWO-CCC grant for Marthe Walvoort

Marthe Walvoort is the recipient of an NWO-CCC grant on the theme 'Carbobotics: Pre/Probiotics mitigating the antibiotics burden'. In this project, she will generate novel carbohydrates inspired on the sugar coating of beneficial bacteria and investigate their impact on strengthening the immune system together with researchers at the UMCG. For more information, see:

<https://www.nwo.nl/actueel/nieuws/2017/enw/nieuwe-projecten-over-vermindering-antibioticagebruik-door-mens-en-landbouwhuisdier.html>



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

- Small dual hydrogen-bond donors like urea, thiourea and guanidinium ions are popular catalysts for a number of enantioselective transitions. However, their relatively weak acidic character is a clear disadvantage. Banik and Jacobsen, at Harvard University, have now developed a mode of acid-catalysis with chiral H-bond donors which enables enantioselective reactions of relatively unreactive electrophiles. They employed squaramides which interact with silyl triflates by binding the triflate counterion. In this reaction a stable, highly Lewis acidic, complex is formed. It is observed that squaramides react with silyl triflates by binding the triflate counterion and form a stable, highly Lewis acidic, complex. The silyl triflate-chiral squaramide combination promotes the generation of oxocarbenium intermediates from acetal substrates at low temperatures. A network of noncovalent interactions between the squaramide catalyst and the oxocarbenium triflate then controls enantioselectivity in the nucleophilic additions to the cationic intermediates. *Banik, S.M., Levina, A., Hyde, A.M., Jacobsen, E.N., Science 2017 DOI 10.1126/science.aa05894.w*
- Bryostatin 1 is a scarce marine-derived natural product that has been used in the treatment of HIV/AIDS, Alzheimer disease and in cancer immunotherapy. Its availability is limited and as a result clinical studies have not been sufficiently performed. Wender and nine colleagues from Stanford University have now carried out a synthesis of the compound in 29 total steps, 19 in the longest linear sequence with >80% average yield per step. Grams of

bryostatin 1 are now available which can be scaled to meet clinical needs (about 20 grams per year). Mechanistic studies are now possible as well as work on synthetically accessible analogs that could be more effective and better tolerated in comparative studies with cells. *Wender, P.A., Hardman, C.T., Ho, S., Jeffreys, M.S., Maclaren, J.K., Quiroz, R.V., Ryckbosch, S.M., Shimizu, A.J., Sloane, J.L., Stevens, M.C.; Science, 2017, 358, 218-223. DOI 10.1126/science.aan7969.*

- Tang, from the Hong Kong University of Science and Technology, together with fourteen coworkers from several other Chinese Universities, have answered the question how it is possible that three simple organic molecules with nonconjugated structures and “isolated” phenyl rings are able to emit visible light. Apart from the absorption of isolated phenyl rings, their photoluminescence (PL) in the aggregate state showed emission from a phenyl or 1,2,4-trimethylphenyl ring and chromophore formed by through-space interaction between methylene-linked phenyl rings. Excitation occurred by longer-wavelength UV light and excitation-dependent emission was found. The longer-wavelength emission, because of through-space interaction, was only found in the aggregate state due to the RIR mechanism. In the solid state high quantum yields of up to 69% can be reached. Through-space conjugation was supported by simulated results. The overall results suggest that traditional conjugated structures are not required for generating efficient light emission. *Zhang, H., Zheng, X., Xie, N., He, Z., Liu, J., Leung, N.L.C., Niu, Y., Huang, X., Wong, K.S., Kwok, R.T.K., Sung, H.H.Y., Williams, I.D., Qin, A., Lam, J.W.Y., Tang, B.Z., J.Am.Chem.Soc. 2017 DOI 10.1021/jacs.7b08592.*
- MacMillan with four coworkers at the Merck Center for Catalysis, Princeton University, developed an interesting new platform where aldehydes can undergo coupling with a variety of olefins to enantioselectively produce  $\alpha$ -alkyl carbonyl adducts. It is a visible light-mediated transformation involving a hydrogen atom and electron borrowing mechanism with three discrete catalytic cycles that are temporally matched to function in concert. Both intra- and intermolecular coupling of aldehydes leads to the production of both cyclic and acyclic products. The authors claim that the novel enantioselective coupling reaction that employs visible light will find utility in both research and industrial applications. *Capacci, A.G., Malinowski, J.T., McAlpine, N.J., Kuhne, J., MacMillan, D.W.C., Nature Chem. 2017, DOI 10.1038/NCHEM.2797.*
- In a recent issue of *J.Am.Chem.Soc.* appeared probably the first study of proton movement in hybrid organic-inorganic perovskites (HOIPs) using kinetic isotope effects. It was carried out by Bassani and Hirsch, with two colleagues, from the University of Bordeaux, France. The occurrence of proton tunneling in methylammoniumPbI<sub>3</sub> hybrid organic inorganic perovskites was demonstrated by studying the effect of isotopic labeling of the methylammonium (MA) component on the dielectric permittivity response. Two isotope effects were observed. Whereas deuteration of the ammonium group results in an acceleration of proton migration (an inverse primary isotope effect), deuteration of the methyl group leads to a normal isotope effect. The activation energies for proton migration were calculated to be 50 and 27 meV for the tetragonal and orthorhombic phases, respectively, that decrease upon deuteration of the ammonium group. Interestingly, the low activation barrier and the deviation from unity of the ratio of the pre-exponential factors ( $AH/AD = 0.3-0.4$ ) are consistent with a tunneling mechanism for proton migration. *Chen, Y-F., Tsai, Y-T., Hirsch, L., Bassani, D.M.; J.Am.Chem.Soc. 2017, DOI 10.1021/jacs.7b09526.*
- Doye and Bielefeld (University of Oldenburg, Germany) reported the first successful use of dimethylamine in catalytic hydroaminoalkylations of alkenes. In the past, many transition-metal-

catalyzed hydroaminoalkylations of alkenes have been performed, also in industrial processes, but not with the most important amines, methylamine and dimethylamine. Now, a relatively simple and cheap Ti-complex has been used as a catalyst, that has a number of advantages. One of them is, that the  $\alpha$ -C-H-activation strongly prefers methyl groups over methylene groups. In addition the catalyst possess excellent regioselectivity towards branched products. The reactions should be carried out in small ampoules to avoid significant outgassing of dimethylamine. The yields are decent to good and the selectivity is very good to excellent. A variety of functional groups is tolerated. Dihydroaminoalkylation products were also prepared in a one-pot synthesis with higher yields and selectivities. *Bielefeld, M.Sc.J., Doye, S., Angew. Chem.Int.Ed. 2017, DOI 10.1002/anie.201708959.*

- The final item this year is a very unusual reaction. It is a tunneling reaction, which is, as defined by Atkins, a quantum mechanical phenomenon in which a particle is found outside a confining potential despite its having insufficient energy to cross the barrier classically. Whereas hydrogen-tunneling is rather frequently observed in chemistry and biology, heavy-atom tunneling is rare. Zeng (Soochow University, China) and Abe (Suzhou University, China) with seven coworkers have now observed heavy-atom tunneling in trifluoroacetyl nitrene ( $\text{CF}_3\text{C}(\text{O})\text{N}$ ). Laser photolysis in cryogenic matrices of  $\text{CF}_3\text{C}(\text{O})\text{N}_3$  gave this nitrene which was characterized by IR and ESR spectroscopy. Rapid rearrangement with a half-life time less than 10 minutes and unusually large  $^{14}\text{N}/^{15}\text{N}$  kinetic isotope effects (1.18-1.33) provided  $\text{CF}_3\text{NCO}$  in solid Ar, Ne, and  $\text{N}_2$  matrices even at 2.8 K. The disappearance of  $\text{CF}_3\text{C}(\text{O})\text{N}$  through tunneling becomes much slower in chemically active toluene and 2-methyltetrahydrofuran at 5 K. *Wu, Z., Feng, R., Li, H., Xu, J., Deng, G., Abe, M., Bégué, D., Liu, K., Zeng, X., Angew.Chem. Int.Ed., 2017, DOI 10.1002/anie.201710307.*

Jan Engberts

## New appointments



Luo Ge

PhD—group Harutyunyan

1/11/2017



Elisabeth G. Sieders

PhD—group Witte

1/11/2017

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

**December 14<sup>th</sup>—Mira Holzheimer (PhD Minnaard)** - "Total synthesis of the mycobacterial glycolipid DAT2a and its non-natural analogue thio-DAT2a"

**December 21<sup>st</sup>—Mark Hoorens (PhD Feringa)** - "Glutamate transport inhibitors with photo-controlled activity"

**January 11<sup>th</sup>—Luuk Kortekaas (PhD Browne)** - "Title to be announced"

**January 18<sup>th</sup>—Zhuohua Sun (PhD Barta)** - "Complete lignocellulose conversion with integrated catalyst recycling yielding valuable aromatics and fuels"

**January 25<sup>th</sup>—Juan Chen (PhD Browne)** - "Title to be announced"

**February 1<sup>st</sup>—Andreas Hussain (PhD Otto)** - "Title to be announced"

**February 8<sup>th</sup>—Simone Romanini (PhD Harutyunyan)** - "Title to be announced"

## **Stratingh traditional Christmas Borrell**

The yearly "Christmas borrel" of the Stratingh Institute will take place on Wednesday December 20<sup>th</sup>, 2017. It will start at 16.00 and it will take place in room 5171.0415 (Het Oog), Linnaeusborg.

*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)*