

Clemens Mayer appointed assistant professor

Clemens Mayer (post-doc in the Roelfes group) will start his independent career from October 1st. The research carried out in his group will be centered around repurposing established genetic code expansion techniques for bioprocess strategies that enable the production of value-added compounds from readily available precursors. Specifically, the group will utilize orthogonal translation systems to evaluate or tailor both enzymatic and non-enzymatic reactivities.



New scientific coordinator for the Stratingh Institute



Gaël Schaeffer is the new scientific coordinator of the Stratingh Institute, replacing Cristina D'Arrigo who moved to Lugano. Gaël is also taking over from Marzia Nuzzolo the PhD coordinator function, so please refer to him for any questions related to this matter. He might not be unknown to some of you since he worked as a post-doc in the group of Sijbren Otto until not so long ago.

Johannes Klein has been awarded an NWO Start Up Grant on sustainable catalysis with gold

Johannes Klein receives an NWO START-UP grant of 0.4 million euros. START-UP grants are awarded to recently appointed faculty members for establishing their research groups.

Johannes' project is entitled "Sustainable Gold Catalysis: Radical Based C-H Bond Oxidations using Environmentally Benign Oxidants". The project aims to develop novel eco-friendly strategies for C-H bond activation reactions of organic molecules, which are commonly found in fossil fuels, pharmaceuticals and agrochemicals. Well done Johannes!



Zarief Hasrat - Selected for the Undergraduate Award



The work of Zarief Hasrat (Bachelor student in the Chiechi group), entitled ““High-Surface Area ZnO Photoanode for Microfluidic Biophotovoltaic Devices”, has been selected among the top 10% of the papers submitted to the Chemical & Pharmaceutical Sciences category of the [Undergraduate Awards](#). This award is the world’s leading undergraduate awards programme which recognises top undergraduate work, shares this work with a global audience and connects students across cultures and disciplines.

Zarief has been formally invited to the Global Undergraduate Summit, which will be taking place from the 12th to the 14th of November at Dublin’s historic venue, Croke Park. Congrats Zarief!

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

I would like to start with a citation from Jean Baptiste André Dumas:

“I have seen many phases of my life, but if I had to live my life again, I would always remain in my laboratory, for the greatest joy of my life has been to accomplish original scientific work, and, next to that, to lecture to a set of intelligent students”.

After these beautiful words, I will summarize some nice recent studies.

The first is a paper by MacMillan and five coworkers from the Merck Center for Process Chemistry and for Catalysis, the last at Princeton University. Although carbon-hydrogen bonds are the most abundant groups in organic molecules, a mild and general platform for the coupling of strong, neutral C(sp³)-H bonds with aryl electrophiles has not been realized. Now a protocol for these reactions is described, using a combination of light-driven, polyoxometalate-facilitated hydrogen atom transfer and nickel catalysis. Here carbon-centred radicals are formed from strong, neutral C-H bonds, which thereafter act as nucleophiles in nickel-mediated cross-coupling with aryl bromides yielding C(sp³)-C(sp²) cross-coupled products. A broad variety of complex, medically relevant products have been obtained from natural products and from chemical feedstocks by functionalization of sites that, employing traditional procedures, are unreactive. The yields obtained using the novel procedure are not very high, but most important is the potential to employ unactivated C-H bonds as nucleophiles in transition-metal-catalysed cross-coupling transformations.

Perry, I.B., Brewer, T.F., Sarver, P.J., Schultz, D.M., DiRocco, D.A., MacMillan, D.W.C., Nature 2018, DOI 10.1038/s41586-018-0366

Unexpected results have been found in an extensive mechanistic study by Hase and three coworkers at the Harbin Institute of Technology, at Harbin, China and the Texas Technical University. They examined in detail the dynamics of the reaction of $F-(CH_3OH)_n$ with CH_3CH_2Br as a function of n . Competing S_N2 substitution and $E2$ elimination are of central importance in preparative organic chemistry and it was studied how a gradual addition of CH_3OH affects the $S_N2/E2$ ratio. For the solvent-free reaction ($n=0$) the $E2$ mechanism dominates over the S_N2 process, but adding one solvating methanol molecule largely promotes the S_N2 mechanism through a strong stabilization of the transition state for substitution. This preference for substitution becomes more pronounced upon further solvation, concomitant with a strong suppression of the elimination reaction. An extensive experimental and theoretical analysis was made of how the interplay of energetics and dynamics is determining the mechanistic selectivity. Dynamical and/or steric effects account for the observed selectivity of the reaction channels. These novel results shed light on previous findings that gas-phase reactions are dominated by $E2$ mechanisms while the dynamics in solution are governed by S_N2 mechanisms.

Liu, X., Zhang, J., Yang, L., Hase, W.L., J. Am. Chem. Soc. 2018, DOI 10.1021/jacs.8b04529.

A JACS communication describes the first Ni-catalyzed regioselective hydrocyanation of terminal alkynes with $Zn(CN)_2$ as the cyanide source and water as the hydrogen source. The work was performed by Liu and two colleagues at the University of the Chinese Academy of Sciences at Shanghai, China. The reaction provides an efficient procedure for the preparation of functionalized vinyl nitriles with a broad range of structural diversity and under very mild reaction conditions. No hazardous HCN has been used. The reaction mechanism has not yet been studied in detail, but the authors propose that the first step involves formation of an $Ni(o)$ species by reduction of $Ni(acs)_2$ with Mn. A $Ni(II)$ intermediate is then generated by oxidative addition of water to $Ni(o)$. The following step is alkyne insertion to this intermediate via cis-addition of the $Ni-H$ bond (hydronicelation), yielding an alkenyl nickel complex. The following steps are uncertain but may involve oxidative addition of water as confirmed by deuterium-labeling experiments. Further mechanistic studies are currently ongoing.

Zhang, X., Xie, X., Liu, Y., J. Am. Chem. Soc., 2018, DOI 10.1021/jacs.8b02542.

The presence of water on Mars has long been suspected but not observed. Now Orosei at the Radioastronomic Institute in Bologna, Italy, with 21 coworkers at different Institutes, has now detected a 20-km-wide lake of liquid water underneath solid ice in the Planum Australe region. They suggest that the water is probably kept from freezing by dissolved salts and the pressure of the ice above. The experiments were carried out using radar measurements from the Mars Express spacecraft and radar profiles have been collected between May 2012 and December 2015. There appears to be no reason to conclude that the presence of water on Mars is limited to a single location. If Orosei's observations are correct, this is an extremely important finding and might be taken as evidence that there is, or has been, life on Mars. An interesting brief summary of the work has been published by Witze.

Orosei, R., Lauro, S.E., Pettinelli, E., Cicchetti, A., Corodini, M., Cosciotti, B., Di Paolo, F., Flamini, E., Mattei, E., Pajola, M., Soldovieri, F., Cartacci, M., Cassenti, F., Frigeri, A., Giuppi, S., Martufi, R., Masdea, A., Mitri, G., Nenna, C., Noschese, R., Restano, M., Seu, R., Science, 2018, DOI 10.1126/science.aar7268.

Witze, A., Nature, 2018, DOI 10.1038/d41586-018-05795-6.

Nucleophilic aromatic substitution (S_NAr) is a widely applied reaction in organic chemistry and in pharmaceutical research. It is generally accepted that these reactions occur via a two-step addition-elimination sequence via a discrete, non-aromatic Meisenheimer complex. It has now been shown by Jacobsen with three colleagues at Harvard University, Cambridge, USA, that prototypical S_NAr reactions proceed by concerted mechanisms. This was accomplished using $^{12}C/^{13}C$ kinetic isotope effects (KIE) and computational analyses. A new technique was employed for the KIE measurements that leverages the high sensitivity of ^{19}F as an NMR nucleus to establish the degree of isotope fractionation. The KIEs could be measured on 10 mg natural abundance material in one overnight acquisition. The mechanism of forming or breaking of C-F bonds was studied in great detail for 120 S_NAr reactions. In no case could a Meisenheimer intermediate be located by NMR or calculation. An important finding!

Kwan, E.E., Zeng, Y., Besser, H.A., Jacobsen, E.N., Nature Chemistry, 2018, DOI 10.1038/s41557-018-0079-7.

An extensive review (with 547 references!) of the possibilities for controlled biomolecule-biomaterial conjugation has been published in Chem.Rev. by Spicer, and two colleagues from the Karolinska Institute, Stockholm, Rutgers University, Piscataway and Imperial College, London. The conjugation of biomolecules is a method for modulation of specific cell behaviors and often the key role played by the specific conjugation strategy has been overlooked. The review is focused on the chemistry of biomolecule conjugation and provides a comprehensive summary of the key strategies for achieving controlled biomaterial functionalization. A particular conjugation strategy has to be carefully matched to the core material and end application. It may well occur that a method which is best in one scenario is totally inadequate for another case. Further innovative and interdisciplinary research will hopefully stimulate the design and production of new biomaterial systems with an enhanced bioactivity and efficacy and the use of novel and efficient conjugation techniques.

Spicer, C.D., Pashuck, E.T., Stevens, M.M., Chem. Rev., 2018, DOI 10.1021/acs.chemrev.8b00253.

If you perform a reaction in a solvent, the solvent is just considered as a medium in which the reactants encounter each other by diffusion. Although the reaction rates are influenced by solvation effects, the solvent is usually not considered to be a part of the reacting chemical species. But now it has been shown by Widmer and Schwartz, at the University of California at Los Angeles, using quantum simulations of the sodium dimer (Na_2), that the solvent not only controls the bond dynamics but also the chemical identity of the solute. This is the case when the local specific interactions between the solute and the solvent are energetically on the same order as those of a hydrogen bond. Dative bonding interactions between the solvent and Na atoms in tetrahydrofuran, lead to unique coordination states, that must cross a Gibbs energy barrier of about 8 $k_B T$ for interconversion. Each coordination state with its own dynamics and spectroscopic signatures provides evidence that indeed the solvent is necessary for identifying the “chemical identity” of condensed-phase chemical systems.

The provoking prediction of the formation of metastable coordination states with a distinct molecular identity for simple solutes such as Na_2 in liquid THF has been discussed by Peslherbe, also in Nature Chemistry.

Widmer, D.R., Schwartz, B.J., Nature Chemistry, 2018, DOI 10.1038/s41557-018-0066-z.

Peslherbe, G.H., Nature Chemistry, 2018, DOI 10.1038/s41557-018-130-8.

"The physics of infinity", an old and interesting question. The issue of infinity has been discussed by Ellis (University of Cape Town, South Africa), Meissner (University of Warsaw, Poland) and Nicolai (Max Planck Institute of Gravitation, Potsdam) in a recent paper in Nature Physics. It has often been proposed that things can be infinitely small, but also infinitely big. But scientists (among them David Hilbert) have also argued that infinity cannot exist in physical reality, neither in theory, nor in nature. A definite solution to this problem has far-reaching implications. Also zero cannot exist in physical reality, quantum field theory has shown that a vacuum is far from nothing. String theory in its current form cannot explain what precisely happens to space and time at the Planck scale. Also for very large systems it has been stated that in case the Universe would be infinite, it could never be proven. Claims for infinity, both for very small systems and for very large systems have to be proven, either observationally or theoretically. Such claims have not been realized so far.

Ellis, G.F.R., Meissner, K.A., Nicolai, H., Nature Physics, 2018, DOI 10.1038/s41567-018-0238-1.

A selection of recent publications from Stratingh members

- J. E. M. N. Klein, G. Knizia, "[cPCET versus HAT: A Direct Theoretical Method for Distinguishing X–H Bond-Activation Mechanisms](#)" *Angew. Chem. Int. Ed.* **2018**, 57, 11913-11917
- E. B. Pinxterhuis, P. Visser, I. Esser, J.-B. Gualtierotti, B. L. Feringa, "[Fast, Efficient and Low E-Factor One-Pot Palladium-Catalyzed Cross-Coupling of \(Hetero\)Arenes](#)" *Angew. Chem. Int. Ed.* **2018**, 57, 9452-9455
- J. J. Liu, G. Portal, S. Torabi, M. C. A. Stuard, X. Qiu, M. Koopmans, R. Chiechi, J. C. Hummelen, J. A. Koster, "[Side-chain effects on N-type organic thermoelectrics: A case study of fullerene derivatives](#)" *Nano Energy* **2018**, 183-191

Upcoming PhD Ceremonies

- **October 26th** at 12:45 - **Yanxi Zhang** (Chiechi group) - "The influence of conjugation in molecular tunneling junctions and nanofabrication"
- **November 2nd** at 12:45 - **Dowine de Bruijn** (Roelfes group) - "Bio-orthogonal metal catalysis for selective modification of dehydroalanine in proteins and peptides"

Werkbespreking

Thursday morning at 8:30, room 5111.0080

- **October 4th** - **Peter Kroon** (PhD Otto) - "Using molecular dynamics to study non-covalent assemblies and structure"
- **October 11th** - **Marco Wonink** (PhD Feringa) - "Valorization of electrochemically produced 2,5-dimethoxy-2,5-dihydrofuran"
- **October 18th** - **Niek van der Zouwen** (PhD Witte) - "New methodologies for the development of chemical probes"
- **October 25th** - **Piermichele Kobauri** (PhD Feringa) - "Structure-based photopharmacology"
- **November 1st** - **Alessandra de Santi** (PhD Barta) - "Exploring sustainable value chains from renewable resources"

New appointments



Marcel Eleveld (PhD)
Group Otto



Matthijs ter Harmsel (PhD)
Group Harutyunyan



Paul Adamski (PhD)
Group Otto



Reuben Leveson-Gower (PhD)
Group Roelfes



Jane Kardula (PhD)
Group Chiechi



Jeffrey Buter (Post-doc)
Group Feringa



Greg Boursalian (Post-doc)
Group Feringa



Maxim Galkin (Post-doc)
Group Barta

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