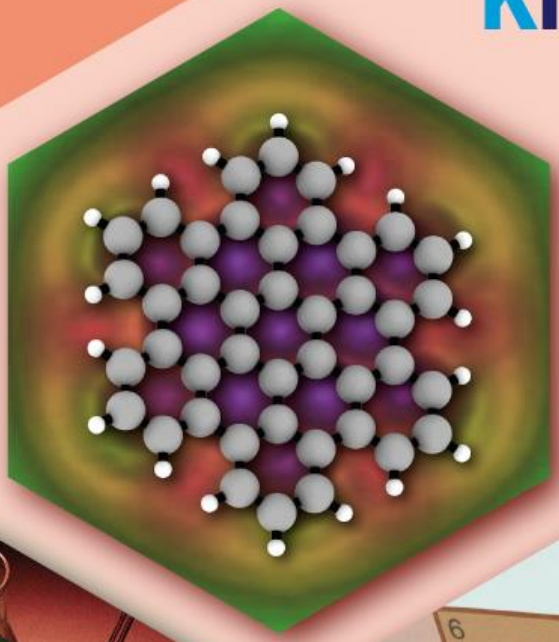
April 5th & 6th

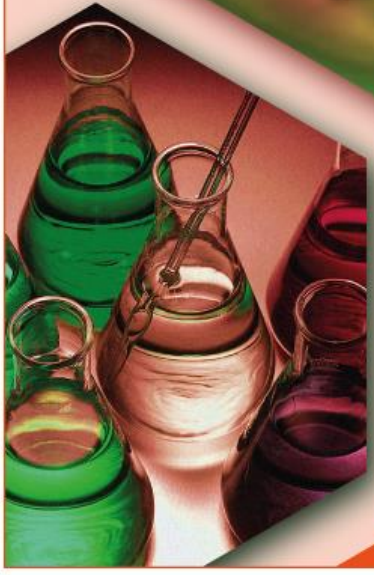
2018

International Wageningen Symposium on Organic Chemistry

Organic Chemistry Division

KNCV





www.kncv.nl/wageningen

Wageningen Symposium on Organic Chemistry

April 5th and 6th 2018
At the Wageningen International Congress Centre

Dear fellow Organic Chemists and Colleagues,

Our biannual Organic Chemistry celebration, the '2018 Wageningen Symposium on Organic Chemistry' is about to get started.

We believe we have put together a very stimulating program for you that like, in previous years, highlights the vivid and versatile field of Organic Chemistry. While in the past, the symposium often centered on a single theme, for this edition we have again opted to show the wide breadth of the field and have composed a program that covers different sub-disciplines of the field. Accordingly, this year's program includes contributions from excellent scientist on topics ranging from physical organic chemistry, materials/polymer science, catalysis to chemical biology and more. This year we have again included daily parallel sessions with presentations from national PhD students and postdocs to showcase the exciting research in our field at Dutch Universities.

Another part of the program is the announcement of the annual Backer prize that is awarded for the best PhD thesis in the Netherlands in the field of Organic Chemistry and is sponsored by the Backer foundation and the KNCV Organic Chemistry Division.

Importantly, organizing the symposium would not be possible without the financial support of our sponsors; Buchi, Screening Devices, Mettler-Toledo, Mercachem-Syncom, ChemConnection, Elsevier Reaxys, Wiley ChemPubSoc-Europe, InnoSyn and Aspen. We, therefore, would like to thank them for their support and invite you to visit their stands present here at the venue and their websites.

We look forward to a very successful symposium that you will hopefully enjoy just as much as we do. So enjoy, relax, interact with our speakers, and join the discussions!

On behalf of the KNCV Organic Chemistry Division,

Prof. dr. Jeroen Cornelissen

Chairman

Programme Thursday April 5h 2018

9:00 **Welcome & Coffee**

9:40 **Opening by Jeroen Cornelissen**

9:45 **Sir Fraser Stoddart (Northwestern University, USA, Sponsored by Wiley / ChemPubSoc)**
Materials Beyond Cyclodextrins: Emergence Opens up a Whole New World of Wonders

	Parallelsession I (Ir. Haakzaal) Chair: Romano Orru	**Parallelsession II (Tarthorstzaal)** Chair: Tom Wennekes
10:45	**Jordy Saya (VU)** HFIP as a Novel Acid Component in the Passerini Reaction: One-Pot Access to β-Amino Alcohols	**Marta Artola (UL)** Rational Design of Mechanism-based Retaining Glycosidase Inhibitors
11:05	**Luuk Steemers (UvA)** Terephthalic acid derivatives as covalent templates for the synthesis of mechanically interlocked molecules	**Johan Pijnenborg (RU)** New chemical tools to modulate sialic acid expression and signaling
11:25	**Nabil Tahiri (RUG)** Total synthesis of Mycolic Acids from Myco-bacterium tuberculosis for structure elucidation	**Dennis Wander (UL)** Doxorubicin and Aclarubicin: Shuffling Glycans for Improved Cytotoxic Agents

11:45 **Lunch in Terraszaal (ALV@12:15 in Tarthorstzaal)**

13:15 **Keith Woerpel (New York University, USA, Sponsored by Mettler-Toledo)**
Stereoselective Addition Reactions to Carbon Electrophiles: Conformational Analysis, Stereoelectronic Effects, and Reactivity

	Parallelsession III (Ir. Haakzaal) Chair: Mark Borst	**Parallelsession IV (Tarthorstzaal)** Chair: Kim Bonger
14:15	**Hidde Elferink (RU)** Glycosylations Caught in the Act	**Can Araman (UL)** Amyloid-like behavior of citrullinated myelin oligodendrocyte protein (MOG) derived epitope peptides lead to enhanced antigen presentation in multiple sclerosis
14:35	**John Braun (VU)** Intramolecular Tsuji-Trost Cascade Cyclization to Fused Vinylcyclopropanes	**Niek van der Zouwen (RUG)** In Situ Combinatorial Synthesis and Screening of Chemical Probes
14:55	**Stella Verkhnyatskaya (RUG)** Fucosylated Cyclodextrins as Novel Antiadhesives	**Jorick Bruins (WUR)** Inducible, selective labelling of antibodies via enzymatic oxidation of tyrosine to 1,2-quinones

15:15 **Coffee in Terraszaal**

15:45 **Annemieke Madder (Ghent University, BE, Sponsored by Elsevier)**
Furan-based Click and Photo-click Reactions for the Study and Targeting of Protein and Nucleic Acid Interactions

16:45 **Laura Kiessling (MIT, USA, Sponsored by Screening Devices)**
Glycans as Cellular IDs

17:45 **Announcement of 2017 winner "The KNCV – Dr. H.J. Backer Organic Chemistry Award"**

18:00 **Dinner (registration necessary)**

Programme Friday April 6th 2018

9:15 **Coffee in Terraszaal**

9:45 **David Spring (University of Cambridge, UK, Sponsored by ChemConnection part of Ardena)**
Enriching Chemical Space to Drug Undruggable Targets

	Parallelsession V (Ir. Haakzaal) Chair: Gino van Strijdonck	Parallelsession VI (Tarthorstzaal) Chair: Leendert van den Bos
10:45	**Pia Kröger (UT)** Versatile Single Chain Polymeric Nanoparticles via Thiol-Michael Addition	**Reinder de Vries (RUG)** Bio-orthogonal Chemical Modification of Peptide Antibiotics
11:05	**Jaime Mateos (RUG)** Regio- and Stereoselective Synthesis of Borylated 1,4-Dienes by Cu/Pd Dual Catalysis	**Mark de Geus (UL)** Chemical Control over T-Cell Activation In Vivo Using Deprotection of Trans-cyclooctene-modified Epitopes
11:25	**Sybrin Schröder (UL)** Activity-based protein profiling of exo- and endo-xylanases in Aspergillus secretomes	**Seino Jonkees (UU)** Macrocyclic peptide inhibitors of carbohydrate-active enzymes

11:45 **Lunch in Terraszaal**

13:00 **Roeland Nolte (Radboud University, NL)**
Encoding polymers with information. A supramolecular approach

	Parallelsession VII (Ir. Haakzaal) Chair: Romano Orru	Parallelsession VIII (Tarthorstzaal) Chair: Tom Wennekes
13:45	**Flip Holtrop (UvA)** Van der Waals forces in frustrated Lewis pair chemistry	**Digvijay Gahtory (WUR)** New click on the block: Strain-promoted cycloaddition of cyclopropenes with o-quinones
14:05	**Shuqin Cao (UT)** Supramolecular Chemistry Inside Protein Cages	**Victor Somovilla (UU)** Fluoroproline in MUC1 antigen opens a new via in the development of enhanced cancer diagnostic tools

14:25 **Coffee in Terraszaal**

15:00 **Rachel O'Reilly (University of Birmingham, UK, Sponsored by Buchi)**
Semi-crystalline polymers for controlled self-assembly

16:00 **MG Finn (Georgia Institute of Technology, USA, Sponsored by Mercachem-Syncom)**
Click, Carry, and Release: Building and Transporting Molecular Function

17:00 **Closing followed by drinks @ Down Under bar**

Our sponsors:

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Materials Beyond Cyclodextrins: Emergence Opens up a Whole New World of Wonders

Sir Fraser Stoddart

Northwestern University, USA stoddart@northwestern.edu

During the past decade, members of the Stoddart research group have made two momentous discoveries in the area of carbohydrate materials, each having the potential to become a 'disruptive technology' for environmentally friendly products and sustainable processes. The two materials, both of which incorporate cyclic sugars known as cyclodextrins (CDs), are readily available from starch, and are inexpensive and environmentally benign. Promising as these materials are for technologies ranging from food processing to gold mining, they also constitute exquisite examples of molecular self-assembly processes, aided and abetted by molecular recognition where: (i) the four-fold γ-CD molecular symmetry with eight glucose units orchestrates the spontaneous formation of the first edible metal-organic frameworks (MOFs) containing alkali metal (M+) cations, and (ii) the selective second-sphere coordination of potassium tetrabromoaurate (KAuBr4) by α-CD, with its six glucose units, leads to the selective bulk separation of the gold salt by precipitation, even in the presence of other precious metals. The secret behind the CD-MOF formation is the simultaneous coordination of M+ ions to both primary and secondary γ-CD toroidal faces, promoting the assembly of (γ-CD)6 cubes linked in an infinite 3D network. The CD-MOFs also serve as chiral stationary phases for the chromatographic separation of flavors and fragrances, as well as separating aromatic compounds such as xylene isomeric mixtures. It was found that when the anion, accompanying the M+ cations, is AuBr4−, a 3D channel-like superstructure results, wherein gold-containing anions are interspersed along the CD units. Mixing of dilute aqueous solution of KAuBr4− and α-CD produces a precipitate, revealed by x-ray diffraction as a superstructure embodying a perfect lock-and-key component match that drives the precipitation of the gold-bearing adduct. Transmission electron microscopy showed that the precipitate is composed of high- aspect ratio nanowires having lengths in the tens of micrometers range. This discovery heralds a potential game-changer for recovering elemental gold from ores to electronic waste.

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Stereoselective Addition Reactions to Carbon Electrophiles: Conformational Analysis, Stereoelectronic Effects, and Reactivity

Keith Woerpel

Department of Chemistry, New York University, 100 Washington Square East, New York, New York 10003 USA, kwoerpel@nyu.edu

Because oxygen-stabilized carbocations (oxocarbenium ions) are important intermediates in both synthetic chemistry and glycobiology, a deeper understanding of their structures and reactivities would benefit both fields. Our research demonstrates that electronic effects exert powerful influences on the conformational preferences of these cations. When the oxocarbenium ion is substituted with alkoxy groups, axially substituted conformers are generally favored because of stabilizing electrostatic attractions between the partially negatively charged substituents and the cationic carbon atom. Nearby electron-donating groups that can engage in neighboring-group participation may or may not be involved in bond-forming reactions depending upon the substrate. A number of the phenomena observed with oxocarbenium ions can also be applied to understand selectivities (or lack thereof) in reactions of carbonyl compounds.

Sponsored by Elsevier-Reaxys

Furan-based Click and Photo-click Reactions for the Study and Targeting of Protein and Nucleic Acid Interactions

Willem Vannecke, Eirini Antonatou, Lieselot Carette, Nathalie De Laet, Kurt Hoogewijs, Joke Elskens, Eva Marina Llamas Garcinuño, Christophe Ampe, Marleen Van Troys and Annemieke Madder

annemieke.madder@ugent.be Organic and Biomimetic Chemistry Research group, Department of Organic and Macromolecular Chemistry, Ghent University, Krijgslaan 281, S4, 9000 Ghent, Belgium,

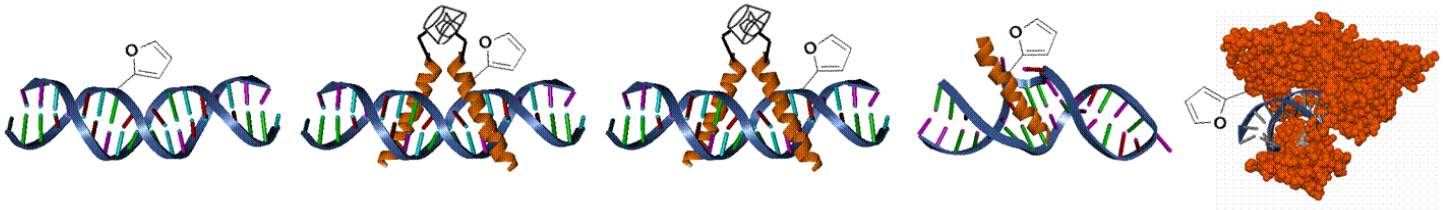
Mapping transient protein-protein and protein-nucleic acid interactions is key to understanding tumor biology and especially ligand-receptor interactions are frontline events in tumor cell response. Chemical crosslinking is well-established for investigating such interactions. Traditionally, photo-crosslinking is used but is associated with problems of selectivity and UV-toxicity in a biological context. Within OBCR, we have recently developed a highly selective and efficient furan-oxidation mediated crosslink technology which is applicable to peptide-protein, peptide-nucleic acid and nucleic acid interstrand crosslink scenarios.

We developed furan-modified oligonucleotide probes which can be used for efficient and selective crosslinking to natural nucleic acid targets as well as protein targets. We have shown that furan activation requires an oxidation trigger,[1] allowing spatiotemporal control of the crosslinking event. As the cross-link reaction showed to be highly proximity sensitive, mapping of interaction surfaces is within reach.

We further investigated singlet oxygen ($^1O_2$) mediated furan-based peptide labeling in physiological aqueous solutions. Furan-containing peptides were subjected to standard oxidative conditions (air, light, photosensitiser) so that the reactive electrophilic species were generated. These reactive intermediates were intercepted by *α*-effect nucleophiles to form stable conjugates. Incorporation of nucleophilic fluorophores through a cascade reaction sequence, led to the efficient construction of site-selectively labeled fluorescent peptides.[2]

Furthermore, in the context of peptide ligand-receptor interactions, we have described, in live cells under normal growth conditions, selective crosslinking of a furan-modified peptide ligand to its membrane receptor with zero toxicity, high efficiency and spatio-specificity. We show for multiple cell lines spontaneous oxidation of the furan moiety with concurrent selective crosslink formation. We propose that reactive oxygen species produced by NADPH oxidases form the cellular source establishing furan oxidation.[3]

Finally, most recently we have shown furan-oxidation mediated protein-protein crosslinking and the latest results in that context will be discussed.



[1] a) Stevens & Madder, Nucleic Acids Research **2009**, 1555; b) Op de Beeck & Madder, JACS **2011**, 133, 796; c) Op de Beeck & Madder, JACS **2012**, 10737; [2] a) Deceuninck, A.; Madder, A. *Chemical Communications* **2009**, 340-342; b) Antonatou, E.; Hoogewijs, K; Baudot, A.; Kalaitzakis, D.; Vassilikogiannakis, G.; Madder, A. *Chem. Eur J.* **2016**, 8457-8461; [3] a) Vannecke, Van Troys, Ampe & Madder, ACS Chemical Biology **2017**, 2191; b) EP10196898.0.; c) EP 15176415.6.

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Glycans as Cellular IDs

Laura Kiessling

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MIT Department of Chemistry, USA

As animals living amongst microbes, we need to distinguish between microorganisms that are generally benign (commensal), beneficial (mutualist/symbiont), or pathogenic. As microbial hosts, we must have mechanisms to influence which microbes stay and which must go. To this end, we are focusing on a prominent feature of the cell's exterior—the carbohydrate coat. From humans to fungi to bacteria, virtually all cells on Earth possess a carbohydrate coat. One important role of this coat is to serve as an identification card (ID). We have been examining the role of carbohydrate-binding proteins, lectins, in influencing our microbiota and in immune defense. This seminar will focus on an understanding of the basis of carbohydrate-protein interactions and how they are used to influence microbes. We envision that our findings can lead to alternative methods to combat pathogens, rapid approaches to ID microbiota, and new strategies regulate microbiome composition to promote human health.

Sponsored by ChemConnection (part of Ardena)

Enriching Chemical Space to Drug Undruggable Targets

David Spring

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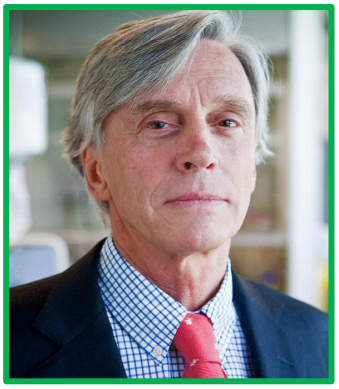
University of Cambridge, Department of Chemistry, UK

The pharmaceutical industry is an enormously successful business sector. However, the current challenges facing the industry are unprecedented. Foremost among these challenges are the industry's diminishing revenue forecasts due to the decreasing number of new chemical entity (NCE) approvals. A high attrition rate of clinical candidates (ca. 93-96%) is prevalent throughout the industry. Pharma's recent dramatic restructuring is largely due to this high attrition rate. My talk aims to highlight some of the underlying factors of this. Namely, (1) the relative lack of structural diversity and (2) the relative lack of targets exploited in drug discovery. The talk will include recent research within my laboratory aimed at addressing these issues.

Encoding polymers with information.

A supramolecular approach



Roeland J.M. Nolte

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The amount of information trafficking internet nowadays is enormous and will increase further in the near future. It can be expected that in the next decennia the current technologies to store and process data will no longer suffice and that other strategies to handle information will have to be developed. One approach is to explore chemical routes, which nature has also followed during evolution: our brain can store and handle very large amounts of data and process them in a way silicon-based computers cannot do. Although brain-like chemical computers are still far beyond reach, it is of interest to explore how atom and molecule-based systems that can write, read, and store information might be designed and constructed.
In this lecture I will discuss our efforts to develop a new technology to write, store, and read information, i.e. on a single polymer chain with the help of "molecular machines" that are inspired by the hypothetical device (Turing machine) proposed by the British mathematician Alan Turing in 1936 as the general basis for the operation of a computer. We are following two approaches. In the first one we try to construct molecular machines based on clamp-shaped proteins, modified with porphyrin catalysts, that can bind to DNA and move along it while modifying the DNA chain in a controlled fashion. In the second approach we use synthetic machines that are derived from chiral porphyrin cages, which bind to synthetic polymers (e.g. polybutadiene) and glide along it while encoding it with chiral epoxide functions, i.e. (*R,R*)-epoxide (digit 0) and (*S,S*)-epoxide (digit 1). This encoding process, which is in progress, will be controlled by light.

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Semi-crystalline polymers for controlled self-assembly

Rachel O'Reilly

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School of Chemistry, University of Birmingham

Crystallization-driven self-assembly (CDSA) is a novel tool in the solution polymer self-assembly toolbox and has been utilized to create an impressive range of hierarchical block copolymer structures. Unlike in conventional solution self-assembly, where the range of morphologies obtained are determined by varying the relative block composition of each block, in polymers assembled via CDSA, the formation of micelles with low interfacial curvature is favored. However, despite advances in CDSA there are relatively few examples where the aggregate morphology can be readily controlled to form nanostructures whose size can be controlled in 2 dimensions. Our group has pioneered research in the area of CDSA of poly(L-lactide) (PLLA)-based block copolymers. PLLA is a semi-crystalline polymer that is interestingly biocompatible as well as derived from renewable resources. To date, we have focused on the self-assembly of polyacrylates-b-PLLA polymerized via ROP and RAFT, where cylindrical morphologies have been obtained with varying block compositions. However, we were interested in using CDSA to develop fully biocompatible, degradable high aspect ratio nanostructures for utilization in nanomedicine applications. A number of reports indicate that elongated morphologies clearly outperform their spherical analogies in terms of escape from phagocytosis and firm binding to the target tissue. Indeed, it has been reported that particle shape (specifically the local particle shape at the point of initial contact) and not size plays a dominant role in phagocytosis. In this work we present the CDSA of a range of block copolymers (including PLLA and PCL) which form a range of self-assembled nanostructures including 2D nanostructures. Using these we have further explored the design rules for the synthesis of such 2D nanomaterials and demonstrated their epitaxial growth, which highlights their potential as biocompatible nanomaterials.

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Click, Carry, and Release: Building and Transporting Molecular Function

MG Finn

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The efficient formation of bonds in complex environments is an important enabling technology for chemical biology, medicinal chemistry, and materials science. We have focused recently on three ligation reactions that meet click chemistry standard, two allowing for controlled molecular fragmentation as well: copper-catalyzed azide-alkyne cycloaddition, oxanorbornadiene conjugate addition and retro-Diels-Alder fragmentation, and reversible substitution aided by anchimeric assistance. Each fills a different niche for functional materials development. The CuAAC reaction cements connections using unobtrusive functional groups. Oxanorbornadiene linkages allow for the control of disconnection over more than six orders of magnitude in rate. Our anchimeric assistance-based reagents provide easy access to a new and effective class of antimicrobial polycationic materials. The fundamentals of these reactions will be described and illustrated with applications to the modification of biomolecules, the creation of degradable materials, and drug delivery.

The KNCV - Dr. H.J. Backer Organic Chemistry Award

The KNCV- Dr. H.J. Backer Organic Chemistry Award is presented each year to the author of the best Ph.D. thesis in organic chemistry in the Netherlands in a given year. The award was created by four alumni of the University of Groningen who are currently all full professors in The Netherlands: profs. E.J.R. Sudhölter, E.W. Meijer, B.L. Feringa and H. Hiemstra. The award is named after professor H.J. Backer who held a chair in organic chemistry at the University of Groningen from 1916 until his retirement. Prof. Backer was known for his exceptional dedication to his students, he died in 1959. The award is funded from the Backer-fund, which was created from professor Backer's inheritance and is co-sponsored by the Organic Chemistry Division of the Royal Netherlands Chemical Society (KNCV), and currently amounts to € 2500,-.

Previous recipients (Ph.D. supervisors and university between brackets):

1986 Leo Jenneskens (Prof. Bickelhaupt, VUA)
1987 Leo Rupert (Prof. Engberts, RUG)
1988 Henk Oevering (Prof. Verhoeven, UvA)
1989 Ellen van den Berg (Prof. Lugtenburg, RUL)
1990 Sjoerd Harder (Prof, Brandsma, UU)
1991 Fred van der Steen (Prof. van Koten, UU)
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2001 Leonard J. Prins (Prof. Reinhoudt, UT)
2002 Vincent de Groot (Prof. Nolte, KUN)
2003 Xue-Mei Li (Prof. Reinhoudt, UT)
2004 Sander Kluwer (Prof. Elsevier, UvA)
2005 Dennis Vriezema (Prof. Nolte, RU)
2006 Rienk Eelkema (Prof. Feringa, RUG)
2007 Robin Bon (Prof. Orru, VU)
2008 Hans de Boer (Prof. Feringa, RUG)
2009 Martin Witte (Prof. Overkleeft, UL)
2010 Wim Noorduin (Prof. Vlieg, RU)
2011 Dennis Waalboer (Prof. Rutjes, RU)
2012 Marthe Walvoort (Prof. Overkleeft, UL)
2013 Danny Geerdink (Prof. Minnaard, RUG)
2014 Lianne Willems (Prof. Overkleeft, UL)
2015 Massimo Giannerini (Prof. Feringa, RUG)
2016 Mu-Chieh Chang (Prof. Otten, RUG) → 2017?

About the symposium organizer:

The Organic Chemistry Division (SOC; Sectie Organische Chemie) of the Royal Netherlands Chemical Society (KNCV) was established in 1925 and represents one of the biggest divisions of the KNCV. Our aim is to foster and stimulate the knowledge on the field of organic chemistry and represent the general interests of both students and professionals working within this field in the Netherlands. The division organizes two regular meetings per year, one organized by a university and the other by a company. In addition, every even year there is the 'International Wageningen Organic Chemistry Symposium' featuring internationally renowned scientists.

Division members receive:

- Information concerning activities & meetings organized by the division
- Free admission or with a significantly reduced fee to these meetings
- Access to an extended network of organic chemists and employers
- Possibility to apply for an international fellowship (for students that have been a member for at least one year). Each year, five 500 euro fellowships will be available.

Want to join our division (KNCV membership not necessary) or more information? Surf to: www.kncv.nl/SOC

For both members & non-member organic chemists in the Netherlands; join our LinkedIn group: KNCV Organic Chemistry Division (SOC)

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