

# PROTAGONISTS IN CHEMISTRY



Professor Gerard van Koten

This special issue is dedicated in honor of Professor Gerard van Koten, born in Haarlem, The Netherlands on September 13, 1942. He studied Chemistry at the Utrecht University and obtained a B.Sc. and a M.Sc. degree in 1964 and 1967, respectively. He went on to earn a doctorate degree (Summa Cum Laude) in chemistry at the Institute for organic Chemistry (TNO) in 1974 working with Professor G.J.M. van der Kerk, a pioneer in the field of organometallic chemistry in The Netherlands. After working at TNO as head of the 'Transition metal chemistry and catalysis' group he moved in 1977 to the University of Amsterdam where he was appointed Senior Lecturer at

the Inorganic Chemistry Department and, in 1984, Full Professor in the field of organometallic chemistry. He became a Full Professor in Organic chemistry at Utrecht University in 1986 with special emphasis on metal-mediated organic synthesis and organometallic chemistry. In addition, he remained part-time Professor at the University of Amsterdam until 1994. In 1991, he became head of the Organic Chemistry and Catalysis group, which under his creativity and enthusiasm was awarded twice the maximum score (four times Excellent) in the National Audit for research in chemistry in The Netherlands. From 1995–1999, he was Dean of the Faculty of Chemistry. At present,

he is Dean of the Faculty of Science (2005) as well as University Professor (2004) at Utrecht University.

Van Koten's research started in the field of organocopper chemistry and he can be considered as one of the pioneers in the design, synthesis, and application of organometallic pincer complexes. Over the years his research efforts have evolved around metal-mediated synthesis as a central theme. Nowadays, his research interests comprise the study of fundamental processes in organometallic chemistry, the application of organometallic complexes as catalysts for homogeneous catalysis, in particular for fine-chemical synthesis, and as materials with special physicochemical properties (molecular wires and switches). The preparation and use of the first examples of homogeneous metallodendrimer catalysts demonstrate his interest for supramolecular systems with (organometallic) catalytically active functionalities.

The availability and flexibility of various synthetic routes to organometallic compounds such as pincer-metal complexes are important conditions for the incorporation of organometallic fragments in supramolecular (nanosize) materials. Thus far, only routes involving highly reactive reagents (organolithium or Grignard reagents) or substrates (e.g., pincer-iodides) had been available for the synthesis of pincer-metal containing materials or catalysts. These routes are often incompatible with the presence of other reactive groups or substituents in the supramolecular material. Recently, the Van Koten group found various mild routes for the synthesis of pincer-metal complexes of which a new transcyclometalation (TCM) reaction and the electrophilic substitution of a trimethylsilyl group are the most important and unprecedented ones. These routes paved the way to the selective synthesis of metallodendrimers and shape-persistent analogues containing from 4 up to 36 metal sites per molecule.

An important new research area in the field of homogeneous catalysis is the development of catalytic processes, which combine the advantages of homogeneous (high activity/selectivity, mild reaction conditions, reproducibility, good catalyst description) and heterogeneous catalysis (easy catalyst recovery, low catalyst quantities, high total turnover number). Finding a way to integrate the advantages of homogeneous and heterogeneous catalysis into one chemical process is therefore interesting, both from an environmental and commercial point of view. Development of such systems and applying them industrially will lead to green commercial processes. Van Koten and his co-workers have addressed the separation of the catalyst from product solutions by functionalization of (in)soluble polymer backbones with catalytic entities in combination with the use of continuous nanofiltration in a membrane reactor. This approach enables recycling of the catalyst, thereby increasing the total turnover number of the catalytic process. As polymeric supports, various types of dendritic molecules (symmetric or hyperbranched carbosilanes) have been used which were functionalized either at the periphery with

pincer-metal units or in the core with a single pincer-metal unit. Redox catalysis of the Kharasch addition of C-Cl bonds across alkenes by carbosilane-multi(pincer-nickel) dendritic catalysts was studied. Various new aspects of the use of these nanosize (1.5–3.5 nm) metal catalysts were discovered by the Van Koten group including their use in a membrane reactor involving continuous separation of the catalyst by nanofiltration. A new type of multi-metal catalyst was developed consisting of a rigid hexa(aryl)benzene core "decorated" at the periphery by 3–12 pincer-metal catalysts, the so-called cartwheel catalysts. Important advantages of these catalysts are their facile synthesis, comprising a limited number of reaction steps, their relatively large size to molecular weight ratio, and their shape-persistent molecular structure. The latest generation showed complete retention in a nanofiltration membrane reactor. Application of this catalyst under continuous reaction conditions increased the total turnover number by a factor over 40 and holds great promise for application in fine chemical synthesis. The expertise gathered in these studies has been used for the development of a new methodology, compatible with the use of reactive organometallic reagents, for the use of carbosilane dendrimers as soluble supports in organic synthesis. Generations (libraries) of low molecular weight organic molecules could be generated. In combination with nanofiltration techniques, separation and recycling of the dendrimers was realized.

The study of the structure/activity relationship of organocopper intermediates in copper-catalyzed organic synthesis is of importance to enhance the selectivity and applicability of these cheap metal catalysts. The longstanding expertise of Van Koten in the synthesis of these often highly sensitive organometallic compounds led to the isolation and characterization of the first examples of higher-order cuprates, the determination of the aggregation state of these reagents in solution as well as the elucidation of the influence of the solvent on the nature of the aggregates in solution. Furthermore, an enantiopure aminoarenethiolate copper catalyst was developed for use in organic synthesis involving Grignard reagents. These organocopper reagents are supramolecular assemblies of which the composition in solution depends on the nature of all ingredients, i.e., copper catalyst, organometallic reagent, substrate, solvent, additives and ligands. The kinetic intermediate from which product formation occurs is formed by a self-assembly process. This process, which is of crucial importance for the selectivity of the copper-catalyzed organic reaction, has been studied using time-resolved EXAFS and in situ IR spectroscopy.

The availability of *para*-functionalized pincer-metal compounds provided the Van Koten group with the possibility to study the use of this scaffold in the synthesis of functional materials. For example, both in solution and in the solid-state *para*-OH substituted NCN-pincer Pt-Cl complexes form one-dimensional polymers by non-covalent hydrogen bonding via (OH...Cl) bridges. Also, *para* C-C coupled pincer metal cations undergo reversible

2-electron switching with concomitant change of the angle between the aryl groups about the central C–C bond, resulting in an on-off switching of the Ru–Ru interaction. New synthetic routes were developed which allowed the introduction of useful *para*-substituents, e.g., amino acids or peptides, using standard organic chemistry with the  $\sigma$ -metal–carbon bond to the NCN-system already in place. This approach led to new peptide labels containing NCN–metal systems that are now studied as biomarkers and biosensors.

The reversible binding of sulfur dioxide to the platinum center of NCN-pincer Pt–Cl was also a research topic that was intensively investigated by Van Koten. This binding is accompanied by a strong color change from colorless to bright orange. A metallodendritic sensor material for sulfur dioxide gas detection was developed. These sensors were found to be highly selective for sulfur dioxide and are sensitive to submillimolar to molar gas quantities. Their response is tunable by electronic and steric modifications of the NCN-pincer ligand array. Most exciting was the observation that a controlled and fully reversible crystalline-state reaction of gaseous sulfur dioxide with crystalline NCN-pincer–platinum halides was possible without destroying the crystalline state. This process, including repetitive expansion–reduction sequences of the crystal lattice, modifies the structures of the molecules without affecting the supramolecular crystallinity. This allows the study of their properties as gas-storage devices and as optoelectrical switches.

Entering the field of chemical biology more recently, Van Koten pioneered a strategy for the regioselective introduction of organometallic complexes into the active site of the lipase cutinase. Cutinase was treated with pincer organometallic phosphonate esters and the new metal-complex/protein hybrids were identified as containing

exactly one organometallic unit per protein. The pincer ligand allows the introduction of a variety of transition metals and provides a unique method to merge organometallics with the properties found in biology. In addition, a covalent attachment of organometallic pincer complexes to enzymes is achieved preventing metal leaching from these hybrids.

Gerard van Koten has been promotor for nearly 60 PhD students and acted as referent for 18 PhD theses. His scientific output resulted in almost 750 publications and 25 patents. By ISI he has been identified as being among the world's top 100 most highly cited researchers. He has been visiting professor in Strasbourg (France), Salt Lake City (US), Sassari (Italy), Heidelberg and Dortmund (Germany), Fribourg and Lausanne (Switzerland), and North West Pacific Inorganic Chemistry Lecturer (1999, Canada/US). He has been appointed lifetime member of the Royal Academy of Arts and Sciences (KNAW) and is presently chairman of the Academy Committee for Chemistry. He has been scientific director for the Netherlands Institute for Catalysis Research (NIOK) and chairman of the European Cooperation in the field of Scientific and Technical Research (COST) of the European Union. In 2002, he was appointed by the Minister of Education, Culture and Science as chairman of the committee responsible for the renewal of the Chemistry Education Programme for the secondary school. He was/is board member of various scientific journals amongst others *Organometallics*, *Journal of Organometallic Chemistry*, *Advanced Synthesis and Catalysis*, and *Chemistry – A European Journal*.

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