

Editorial

Recent Advances in Organometallic Chemistry and Catalysis

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The use of organometallic compounds in organic chemistry is one of the cornerstones of the modern synthetic methodology for the activation and generation of new bonds in a molecule. Although the fundamental basis of their applications lies in stoichiometric transformations, the ability of transition metal complexes to catalyze organic reactions is one of the most powerful tools currently available for designing new synthetic routes. In fact, their use is so widespread that it is difficult to find today advanced syntheses of complex organic molecules or natural products that do not use these methods in some of the synthetic steps. Moreover, the strategies based on the use of metal catalysts have excellent potential to meet the current requirements of chemistry, which advocate the maximization of the global economy of the processes and environmental respect. The current availability of a huge number of efficient and selective processes, a direct consequence of the countless studies on the synthesis and reactivity of organometallic complexes that have been carried out for decades, has consolidated this research field, crossing the barrier that separates pure basic research from industrial applications. Seven contributions covering different aspects related to this topic are included in the present Special Issue.

N-Heterocyclic carbenes (NHCs) represent a privileged class of ligands due to the facile tuning of their electronic and steric properties, their ease of access and their particular bonding properties, becoming essential ligands today for the design of novel organometallic complexes [1,2]. Additionally, transition metal complexes with NHC ligands have found practical use in homogeneous catalysis since they usually display enhanced activity and stability in comparison with analogous systems featuring more classical organophosphine ligands [1–3]. In particular, the development of the second-generation Grubbs and Hoveyda–Grubbs catalysts, in which one phosphine ligand of the original ruthenium-carbenes is replaced by an NHC, represented a significant landmark in olefin metathesis since it allowed extension of the scope of this reaction that was far beyond the initial expectations [4]. Since then, countless studies have focused on the design of new NHC-containing ruthenium catalysts with tailored properties. In this Special Issue, Kajetanowicz, Grela and co-workers have contributed to the field with the preparation of new indenylidene- and Hoveyda–Grubbs-type ruthenium complexes with fluorene-based unsymmetrical NHC ligands capable of catalyzing efficiently challenging olefin metathesis processes, such as the self-metathesis of α -olefins [5].

The use of NHCs as ligands has also led to exciting developments in palladium-catalyzed cross-coupling reactions in the last two decades [6]. In this context, a breakthrough in the field was reported in 2006 by the group of Organ with the development of the so-called PEPPSI complexes (PEPPSI stands for pyridine-enhanced precatalyst preparation stabilization and initiation) [7], which rapidly found commercial success. In marked contrast to many alternative palladium catalysts, PEPPSI-type complexes are stable to air and moisture, relatively easy to synthesize and handle, and feature outstanding activities in different carbon–carbon and carbon–heteroatom cross-coupling reactions [8,9]. A work published in this issue demonstrated that Pd-PEPPSI complexes, and related Pd-NHC derivatives in which the pyridine ligand is replaced by triphenylphosphine, can find application not only in the field of homogeneous catalysis, but also in medicinal chemistry. Thus, the biological assays performed by Hamdi and co-workers indicated that these compounds



Citation: Cadierno, V. Recent Advances in Organometallic Chemistry and Catalysis. *Catalysts* **2021**, *11*, 646. <https://doi.org/10.3390/catal11050646>

Received: 27 April 2021
Accepted: 29 April 2021
Published: 19 May 2021

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are highly active against the breast cancer cell lines *MCF7* and *MDA-MB-231* [10]. In addition, some representatives also featured antibacterial, antileishmanial and antifungal activities. Given that Pd-PEPPSI complexes can be designed à la carte by modifying the NHC, pyridine and halide ligands, a fine tuning could lead in the future to the discovery of new metallodrugs for cancer therapy, a field at the forefront of current research [11,12].

On the other hand, since the pioneering report on the Na[AuCl₄]-catalyzed hydration of alkynes by Fukuda and Utimoto in 1991 [13], the use of gold-based catalysts in organic synthesis has exponentially expanded, representing one of the fastest growing fields in contemporary chemistry [14,15]. In particular, the superior effectiveness of gold as a π -bond activator compared to other transition metals has been widely exploited for the electrophilic activation of unsaturated carbon-carbon bonds (alkynes, alkenes, allenes, enynes, etc.) towards nucleophiles. In this context, the application of gold-based catalysts in hydrofunctionalization reactions of alkynes and allenes with carboxylic acids has been comprehensively reviewed by Cadierno in this Special Issue [16]. Both intra- and intermolecular processes, leading respectively to functionalized lactones and linear unsaturated esters, were discussed. The utility of these transformations was nicely illustrated by their involvement in the total synthesis of a number of naturally occurring products, as well as by the assembly of elaborated polycyclic compounds through cascade processes involving the initial cycloisomerization of an alkynoic acid. A second review article by the same author, dealing with the synthesis and catalytic transformations of β -haloenol esters, has also been included in this Special Issue [17]. In this particular class of compounds, the reactivities of the haloalkene and enol ester functionalities can be combined, making them versatile building blocks in synthetic organic chemistry. A comprehensive overview of the most recent approaches to β -haloenol esters, mainly based on the addition of carboxylic acids to readily available haloalkynes [18,19], was given by the author, along with the metal-catalyzed reactions in which these functionalized olefins participate as substrates. Regarding this last point, a number of palladium-catalyzed cross-coupling processes (Suzuki-Miyaura, Sonogashira, Mizoroki-Heck, Negishi and Kumada-Corriu reactions), allowing the easy construction of polysubstituted olefins, were properly discussed. Returning to the synthetic utility of gold, Michelet and co-workers recently reported an efficient and mild synthetic route for the preparation of functionalized bicyclo[3.2.1]oct-2-ene and bicyclo[3.3.1]nonadiene derivatives, which represent privileged scaffolds for natural products and biologically active molecules, via gold-catalyzed cycloisomerization of 1,6-cyclohexenylalkynes [20]. These studies are complemented in the present Special Issue with a work demonstrating that the cheaper Lewis acid InCl₃ can alternatively act as an effective catalyst for such cycloisomerization processes [21]. A critical comparison between the indium- and gold-based catalytic systems was made by the authors, and density functional theory (DFT) calculations on the corresponding key intermediates involved in the catalytic cycles were included in the manuscript.

The search for effective methods for catalyst separation and recycling is an important topic in the catalysis field. In this context, to overcome the intrinsic separation problems associated with homogeneous catalysts, intense research has been devoted in recent decades to immobilizing them on a diverse range of supports, such as inorganic solids, polymers or dendrimers [22]. Results by Luna and co-workers included in this issue have demonstrated the utility of the AlPO₄/Sepiolite (a porous clay with a large surface area) system as a support for the covalent immobilization of ruthenium hydrogenation catalysts [23]. The anchoring was easily achieved by functionalization of the inorganic solid surface with a tridentate *N*-donor ligand to which [RuCl(P^{*}P)]⁺ (P^{*}P = chiral or achiral diphosphine) units can be coordinated. The resulting heterogenized Ru(II) complexes were successfully employed in the hydrogenation of several carbonyl compounds and olefins, featuring a good activity, enantioselectivity (up to 99%) and reusability (up to 14 consecutive runs).

The issue is completed with an article by Martins and co-workers describing a catalytic system for the oxidation of cyclohexene to adipic acid [24]. The process presented is of interest from an industrial perspective since adipic acid, also referred to as hexanedioic

acid, is a commodity chemical produced worldwide in more than 3 million tons per year with primary use in the manufacture of the Nylon 6,6 polyamide, via its reaction with 1,6-hexanemethylenediamine. Almost all adipic acid produced nowadays in the world is generated from cyclohexane using the two-step process developed by DuPont in the 1940s, in which cyclohexane is initially oxidized by air to generate a mixture of cyclohexanol and cyclohexanone, which is subsequently oxidized with nitric acid [25]. In addition to the low conversions (4–8%), a major drawback concerns the nitric acid oxidation step in which the greenhouse gas N₂O is produced in large amounts (ca. 300 kg of N₂O per ton of adipic acid). Therefore, enormous research efforts have for some time been devoted to finding more sustainable pathways for the synthesis of adipic acid [26]. In its contribution, the group of Martins presents an N₂O-free procedure for the generation of adipic acid based on the direct oxidation of cyclohexene by aqueous H₂O₂ catalyzed by the iron(II) complex [FeCl₂{κ³-HC(pz)₃}] (pz = pyrazol-1-yl) under microwave irradiation. Under optimized conditions, adipic acid was selectively obtained in a 46% yield. In addition, the authors also demonstrated the recyclability of the iron catalyst (up to 5 consecutive runs without appreciable loss of activity and selectivity) by using room-temperature ionic liquids (ILs) as reaction media.

In summary, the collection of original research and review articles included in this Special Issue offers a broad view of different topics of interest in modern organometallic chemistry and catalysis.

As Guest Editor, I would like to express my gratitude to all the authors for their outstanding contributions, the anonymous reviewers for their excellent work, and all the staff of the Catalysts Editorial Office. I am especially grateful to the Managing Editor Ms. Adela Liao for her constant and exceptional help during the production of this Special Issue.

Funding: This research received no external funding.

Conflicts of Interest: The author declares no conflict of interest.

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