

Editorial

Metal Promoted Cyclocarbonylation Reactions in the Synthesis of Heterocycles

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Oxygen and nitrogen heterocycle systems are found in a vast number of natural substrates and biologically active molecules such as antimycotics, antibiotics, antitumors and antioxidants, in addition to pigments and fluorophores. Therefore, several procedures dedicated to the building of such heterocycles have been developed. Many of them are based on the cyclization of suitable substrates [1–3], multi-component reactions [4,5] and ring expansion processes [6,7]. In this field, metal-catalysed cyclocarbonylative reactions represent atom-economical and efficient methods for the synthesis of several functionalized compounds. Indeed, when the cyclization reaction is performed under CO pressure, the potentiality of the process is enhanced, since the formation of the ring takes place with the contemporary introduction of the carbonyl functional group. An improvement in the field of carbonylation reactions is represented by the substitution of the CO gas by surrogates, molecules which are able to generate the carbon monoxide inside the reaction vessel or may act as CO synthons [8–10].

The present Special Issue collected two research articles and three reviews focused mainly on the preparation of different heterocyclic compounds such as lactones, furans, epoxides, chromanes, chromanones, chromenones, indolinones, tetrahydroquinolines, quinolinones, lactams, benzoimidazoles and benzoxazoles via cyclocarbonylation reactions.

The first research article [11] concerns the selective monocarbonylation of epoxides into the corresponding lactones. The reactions were carried out in the presence of a chromium (III)-phthalocyanine derivative connected to a porous organic polymer. The catalyst was highly effective in promoting the ring expansion reaction and preliminary tests indicated that the catalyst can be reused without losing its catalytic activity.

The preparation of bicyclic lactones has been investigated in the second research article [12] as a key step for the total synthesis of Jaspine B, which has shown promising biological activity as an antitumor against several types of cancer cells. In order to avoid the use of dangerous carbon monoxide gas, the authors have developed a new protocol for Pd-catalysed carbonylation reactions based on the use of iron pentacarbonyl $\text{Fe}(\text{CO})_5$ as a CO surrogate. After the optimization of the reaction sequence under batch conditions, the carbonylation reactions were performed also in a flow reactor that provided the desired bicyclic lactones in comparable yields to standard batch conditions.

Metal-mediated cyclizations are important transformations in a natural product total synthesis. In the first review [13] of this Special Issue, the Co, Rh, and Pd catalysed Pauson–Khand reactions (PKR) published in the last five years have been summarized. In particular, their application to the synthesis of cyclopentenone and lactone-containing structures have been highlighted. In many examples, the carbonyl moiety has been inserted, employing metal carbonyl compounds as a masked CO source, through the transition metal decarbonylation to in situ generated CO ($\text{Co}_2(\text{CO})_8$, $\text{Mo}(\text{CO})_3(\text{DMF})_3$, $\text{Rh}(\text{CO})_2\text{Cl}$). The hetero-Pauson–Khand reaction has also been considered, since it represents a useful tool for the generation of bicyclic γ -butyrolactones and unsaturated lactams. The final part of the review is focused on the synthesis of natural macrocyclic compounds containing cyclopentenone motif.



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A different approach to the synthesis of carbonyl-containing oxygen and nitrogen heterocycles based on visible light photocatalytic radical carbonylation has been summarized in the second review [14] of this Special Issue. Acyl radicals serve as the key intermediates in these transformations and can be generated from the addition of alkyl or aryl radicals to carbon monoxide (CO), or from various acyl radical precursors such as aldehydes, carboxylic acids, anhydrides, acyl chlorides or α -keto acids. The discussion of the literature is organized based on the types of acyl radical precursors, and an exhaustive analysis of the transformations leading to the different heterocycles is reported, with particular attention to the mechanistic aspects.

The last review [15] is focused on the synthesis of heterocyclic rings of different sizes, nature and potentialities containing both a silyl and a carbonyl moiety. Intramolecular silylformylation and silylcarbocyclization reactions are the key step for the cyclocarbonylation to occur. The content of this review is divided into two sections: the first is dedicated to a detailed description of intramolecular silylformylation reactions with the corresponding synthesis of oxa- and aza-silacyclane, while the second is centred on the silylcarbocyclization of functionalized acetylenes. In each section, particular emphasis is given to the heterocycles which can be obtained, as well as a special look into used metal catalysts.

In summary, the contribution of the articles collected in this Special Issue will be stimulating for those authors working in the field of heterocycles synthesis and will provide a valuable guide to develop new innovative methodologies for cyclocarbonylative reactions performed under batch, flow and photoredox catalytic conditions, with particular attention to the use of CO surrogates or equivalent synthons.

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