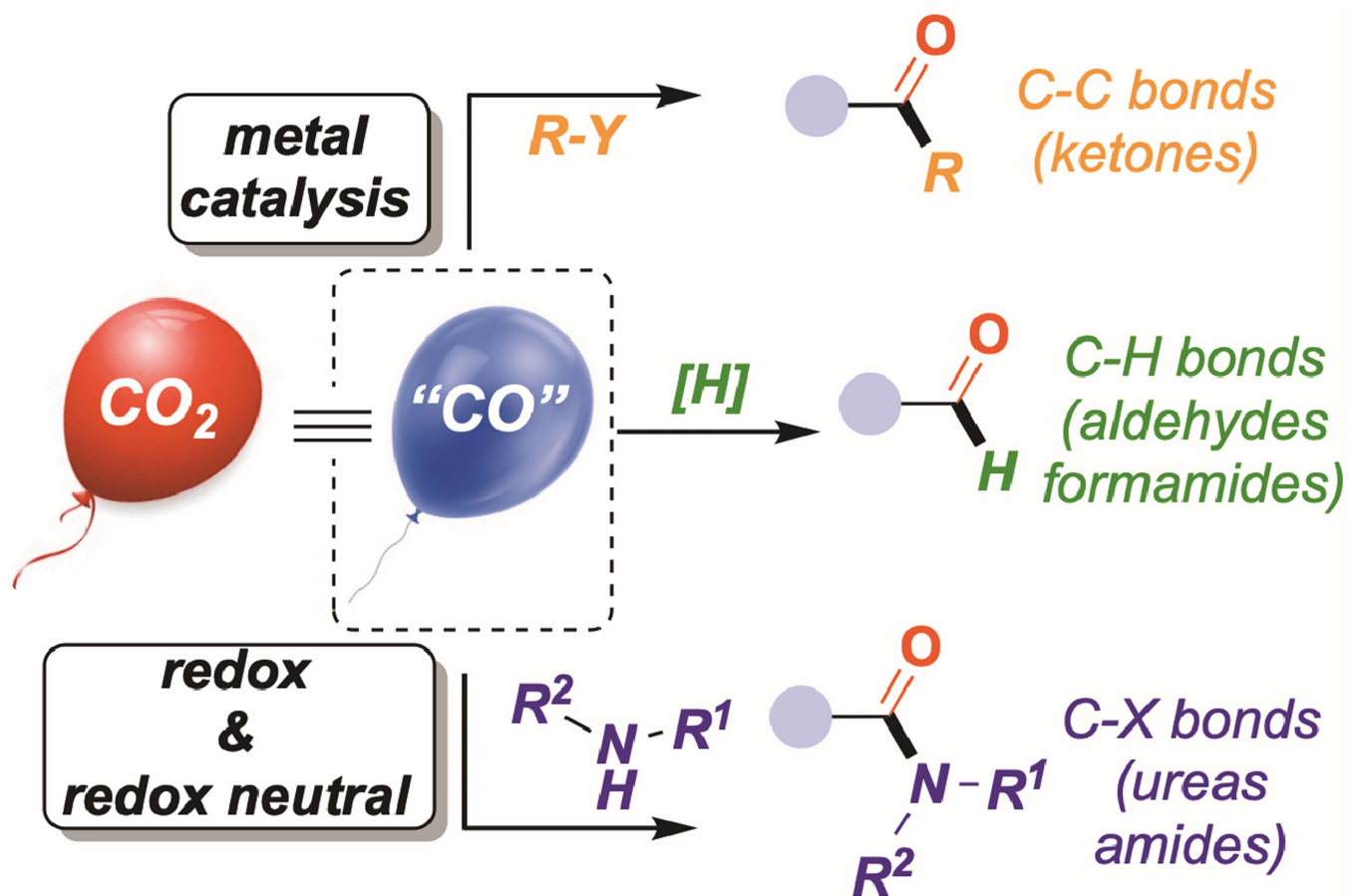


# Metal-Catalyzed Carbonylation Reactions with CO<sub>2</sub>: An Update

Riccardo Giovanelli,<sup>[a, b]</sup> Giulio Bertuzzi,<sup>\*[a, b]</sup> and Marco Bandini<sup>\*[a, b]</sup>

*Prof. Pier Giorgio Cozzi in occasion of his 60<sup>th</sup> birthday*



The utilization of CO<sub>2</sub> as an efficient and environmentally friendly chemical analogue of CO is becoming a solid reality in the chemical scenario. CO<sub>2</sub>-based carbonylations have started paralleling the more consolidated carboxylation procedures, opening new horizons and perspectives in the utilization of carbon dioxide as an organic C1-containing building block. The advent of efficient and site-selective metal-catalyzed protocols

for the fixation of CO<sub>2</sub> into organic scaffolds, under controlled reductive conditions, contributed substantially to the development of robust, efficient, and convenient protocols. In the present *Review* article, a collection of the most recent examples of metal-catalyzed CO<sub>2</sub>-based carbonylations is documented with a particular emphasis on mechanistic aspects.

## 1. Introduction

Aiming at always more sustainable, efficient, and economically advantageous processes, synthetic organic chemistry is nowadays facing an exponentially growth of interest in the usage of non-toxic, cheap, abundant raw materials. In addition, the valorization of common wastes is deemed extremely fruitful. In this scenario, CO<sub>2</sub> is the ultimate candidate to fulfill the above-mentioned goals, fitting all the parameters to be elected as the C1-synthone of the future. Indeed, the use of carbon-dioxide based carboxylation processes (i.e. introduction of a carboxylic acid moiety into the desired organic scaffold) is considered a very *hot topic* in modern organic synthesis, both on large and small-scale laboratory processes.<sup>[1]</sup> Despite the current daily discovery of new methodologies for the fixation/valorization of CO<sub>2</sub>,<sup>[2]</sup> the seek for an expanded portfolio on sustainable and site-selective carbon dioxide-based transformations is ubiquitous within the chemical community. These can either be realized by enhancing the reactivity of the organic scaffold towards CO<sub>2</sub> capture<sup>[3]</sup> or by emphasizing the chemical flexibility of the carboxylic carbon.

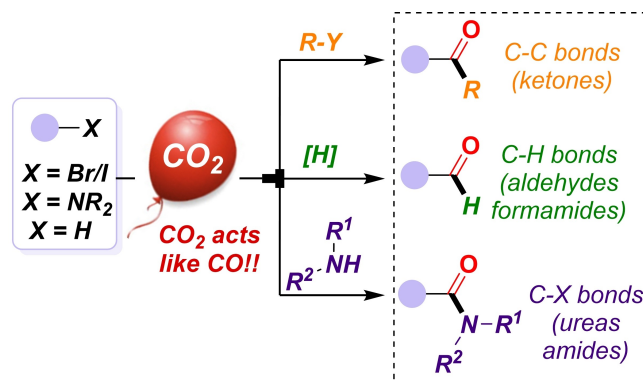
The latter strategy envisions the transformation of the trapped CO<sub>2</sub> into functional groups different from carboxylic acids, by creating a further bond, either with the terminal oxygen (preparation of esters and carbonates) or with the carbon atom with concomitant oxygen scavenging (CO<sub>2</sub>-based **carbonylation** event, Figure 1).

In the present *Review* article, we report a survey on the most recent advances on the usage of carbon dioxide as a **carbonylating** agent, implying the formation of two bonds at the CO<sub>2</sub> carbon atom and thus showing how much the reactivity of this kinetically inert and thermodynamically excessively stable moiety can be pushed further. In this topic, carbon dioxide is shown to be a valid alternative to commonly

employed carbonylating species such as carbon monoxide, phosgene, and its derivatives.<sup>[4]</sup> The former two species are highly toxic gases, which use, storage, and transportation poses serious issues in terms of cost and sustainability. In addition, CO is extremely flammable, and phosgene displays serious corrosivity problems. The use of phosgene surrogates, such as 1,1-carbonyldiimidazole, is a classical solution to the toxicity problems, however it results in enhanced chemical wastes, which disposal is usually troublesome or costly. Alternative strategies to introduce a carbonyl group into organic scaffolds are restricted to a narrow series of substrates (i.e. Vilsmeier-Haak formylation) or target compounds (i.e. lithiation-formylation with DMF). Given those premises, the use of CO<sub>2</sub> as a carbonylating species enhances its role as a highly convenient, non-toxic, traceless, general, and versatile C1-synthone.

Due the presence of two elegant literature surveys reported in late 2019,<sup>[5]</sup> we focused our attention on the last three years and particularly on the large volume of metal-catalyzed processes. The present account is organized based on the nature of the bonds formed at the central carbon atom: namely, one C–H bond (hydroformylation processes), C-heteroatom bonds (formation of amides, ureas and thiocarbamates) and two C–C bonds (synthesis of ketones). Formamides and ureas, common targets of the described methodologies, are arguably products of utmost importance on the industrial point of view, being useful monomers for polymer production and raw materials for fine industry such as pharmaceuticals, agrochemicals and plasticizers manufactory.<sup>[6]</sup>

This *Review* article is deliberately confined to a critical selection of key advancements in this *hot topic*, and it is not intended to be comprehensive and exhaustive as an encyclopedic coverage of all the examples present in literature.



**Figure 1.** Manifold strategies for CO<sub>2</sub>-based carbonylation reactions, as summarized in this *Review* article.

[a] R. Giovanelli, Dr. G. Bertuzzi, Prof. M. Bandini  
Dipartimento di Chimica "Giacomo Ciamician"  
Alma Mater Studiorum – Università di Bologna  
via P. Gobetti 85, 40129 Bologna (Italy)  
E-mail: giulio.bertuzzi2@unibo.it  
marco.bandini@unibo.it

[b] R. Giovanelli, Dr. G. Bertuzzi, Prof. M. Bandini  
Center for Chemical Catalysis – C3  
Alma Mater Studiorum – Università di Bologna  
via P. Gobetti 85, 40129 Bologna (Italy)

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Finally, we wish to emphasize that convenient strategies involving the CO<sub>2</sub>-overreduction, with carbon dioxide acting as methyl or methylene unit, will not be discussed in the present *Review* and the readers are kindly re-addressed to previously reported dedicated review articles.<sup>[7]</sup>

## 2. Formation of a C–H bond

In the field of the transformation of CO<sub>2</sub> into the formyl group (CHO), two main categories of compounds can be obtained, depending on the starting material undergoing the formylation process, namely formamides and aldehydes. The former is produced when the substrate contains a nucleophilic nitrogen (amines, amides, etc.), the latter arises mainly from alkene hydroformylation reactions. Both groups will be discussed in the following chapters of this *Review* article.

### 2.1. Hydroformylation of Amines

Hydroformylation of amines can be divided in two main sub-categories, depending on the reductant (*i.e.* hydride source) employed in the process: namely, silane- or molecular hydrogen-based methodologies. Regarding the applied catalytic systems, it is possible to find a variety of both noble- and non-noble metals being competent as active centers to promote the desired transformations. In the reported examples, first-row transition metals such as V, Mn, Fe, Co, Cu and Zn are employed in the majority of the cases,<sup>[8]</sup> when silanes are used as reductants, highlighting the attention of the synthetic community for the application of always cheaper and more abundant metals. Sustainability issues are also perused by means of supported and recyclable catalytic species or green and reusable solvents as well. On the other hand, while the use of hydrogen gas conveniently lowers the cost and chemical

wastes, expensive second- (or third-) row metal catalytic systems are commonly required (Ru-based catalysts in the present *Review* article).

#### 2.1.1. Silane-based strategies

Silanes (in most cases, phenylsilane, PhSiH<sub>3</sub>) are a powerful source of hydrogen in hydroformylation reactions with CO<sub>2</sub>, avoiding the use of highly flammable and explosive hydrogen gas. Additionally, the use of fully homogenous conditions commonly leads to improved reaction rates.

In 2019, Choi and co-workers developed a highly efficient protocol for the *N*-formylation of amines, amides and carbamates in the presence of a Zn(OAc)<sub>2</sub> – 1,10-phenanthroline (Phen) complex as the catalytic species and PhSiH<sub>3</sub>.<sup>[9]</sup> During the optimization studies the basicity of the counterion and the presence of a *N*-donor ligand were found to be pivotal parameters to obtain high yields (Scheme 1). Although the standard reaction conditions required 2 mol% Zn(OAc)<sub>2</sub> and 6 mol% ligand at room temperature for 4 h, Zn(II) loading could be lowered down to 0.0002 mol% by increasing the reaction temperature (150 °C, autoclave) and time (72 h). TONs up to 350000 were then recorded, proving the excellent thermostability of the catalytic complex.

The process also showed high flexibility, rendering formamides **2** when secondary or primary amines **1** were employed. However, by simply prolonging the reaction time, imides **3** could also be obtained via double CO<sub>2</sub> fixation. Primary amides **4** (R=H) reacted smoothly under unoptimized conditions, while secondary amides **4** (R≠H) and carbamates **5** required a solvent switch to toluene and higher temperatures (100 °C) to give the respective unsymmetrical imides **6** and formyl carbamates **7**. Mechanistically, the formation of a silicate ester **8** is proposed first; this undergoes acylic substitution with the *N*-nucleophile of choice. The role of Zn(OAc)<sub>2</sub> is believed to form a zinc-



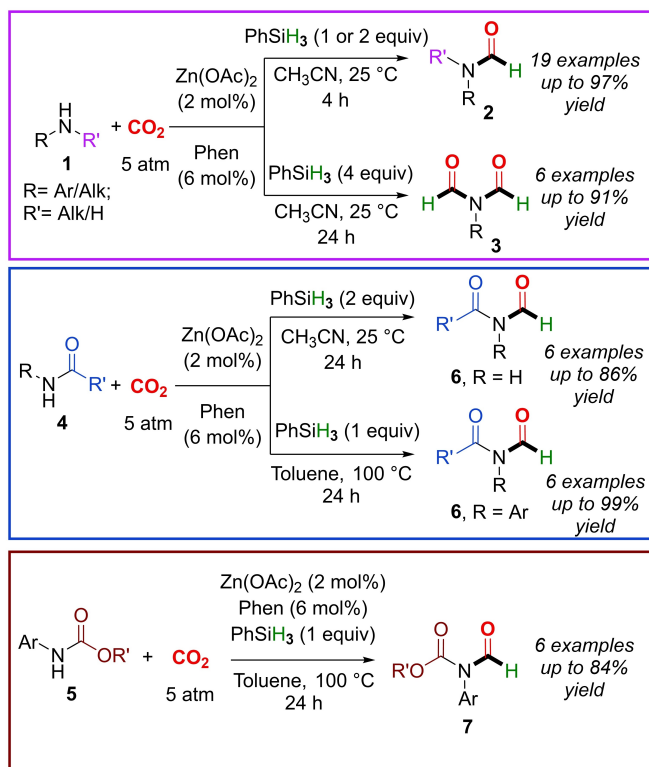
Riccardo Giovanelli got his BSc (2018) and his MSc (2021) in Chemistry at @UNIBO. Then, he entered the PhD program (II year) under the supervision of Prof. Marco Bandini. His research interests deal with the development of nickel catalyzed cross-couplings for carbon dioxide valorization and electrochemical tools applied to organic synthesis (eChem).



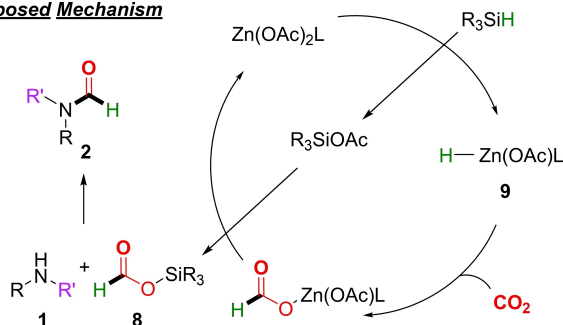
Giulio Bertuzzi received his PhD in Chemistry @ UNIBO in 2018. He worked as a post-doc at the University of Aarhus (DK) and is currently an Assistant Professor (RTDa) at the Department of Chemistry “Giacomo Ciamician”. His research interests involve the utilization of CO<sub>2</sub> in catalytic processes, Ni-catalyzed cross-electrophile couplings and electrosynthesis.



Marco Bandini (MB) got the PhD in Chemistry @ UNIBO in 2000 and after Postdoctoral periods in USA and UK became Associate (2012) and then Full Professor (2019) at the Department of Chemistry “Giacomo Ciamician”. He is also co-coordinator of the Center of Chemical Catalysis – C<sup>3</sup> @ UNIBO. Scientific interests focus on the development of sustainable synthetic methodologies by means of catalysis, enabling technologies and valorization of CO<sub>2</sub>. MB is also involved in scientific divulgation activities.



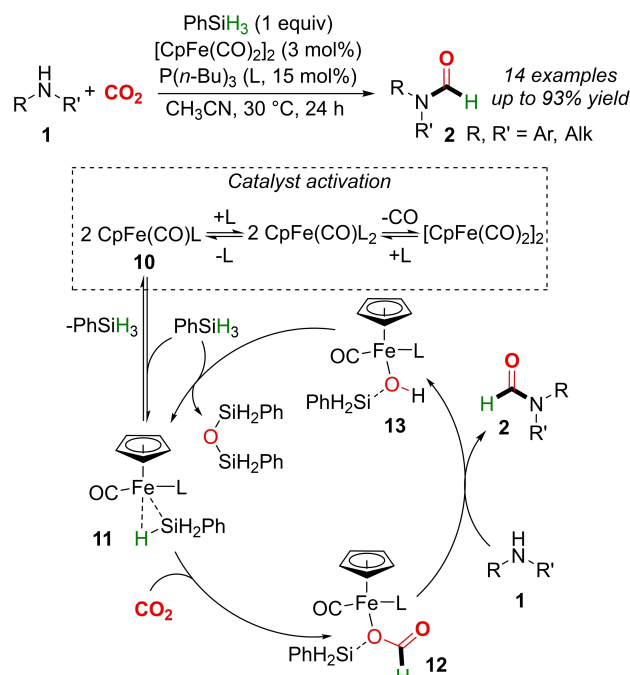
### Proposed Mechanism



**Scheme 1.** Zn-catalyzed hydroformylation of amines, amides and carbamates. The mechanism is exemplified with amines **1** as nucleophiles, giving formamides **2** as products.

hydride intermediate **9** responsible for the reduction of  $\text{CO}_2$ . Moreover, the activation of the N–H bond by proton abstraction from the basic counter anion (*i.e.*  $\text{AcO}^-$ ) is also invoked, especially with less nucleophilic, yet more acidic, **4** and **5** analogous.

In the same year, Xia and co-workers developed a Fe-catalyzed *N*-formylation of amines **1** with  $\text{CO}_2$  and phenylsilane ( $\text{PhSiH}_3$ ) as the reducing species, for the preparation of formamides **2** under mild conditions.<sup>[10]</sup> The catalytic system features high efficiency and tolerates a variety of substituted secondary amines. Importantly, the protocol could be selectively switched to a methylation reaction (further reduction of the CO unit) by simply increasing the equivalents of phenylsilane, the reaction temperature and time (Scheme 2). Mechanistically, the formation of a 17-electron species **10** by reaction of the pre-catalyst with tri-*n*-butylphosphine (L) is proposed. This

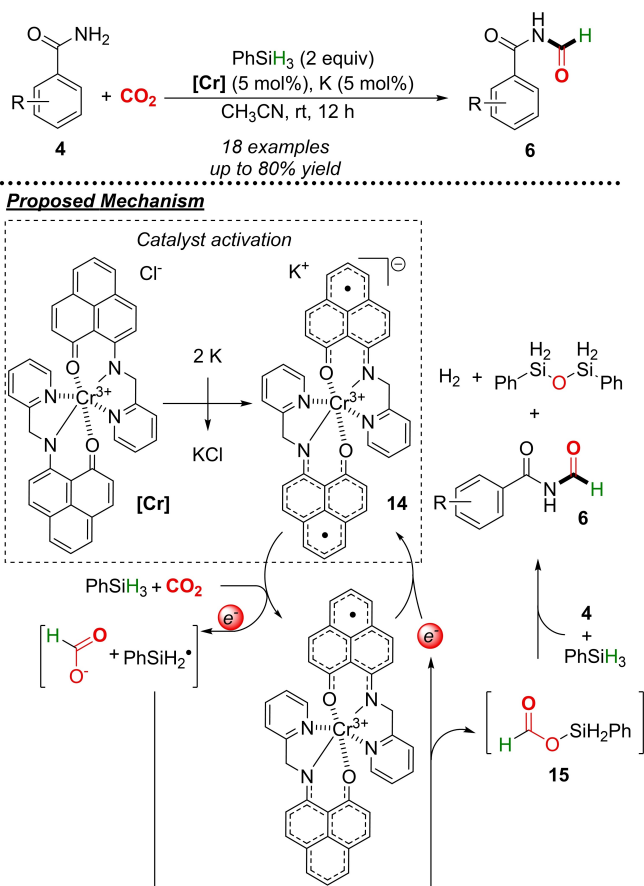


**Scheme 2.** Fe-catalyzed hydroformylation of amines.

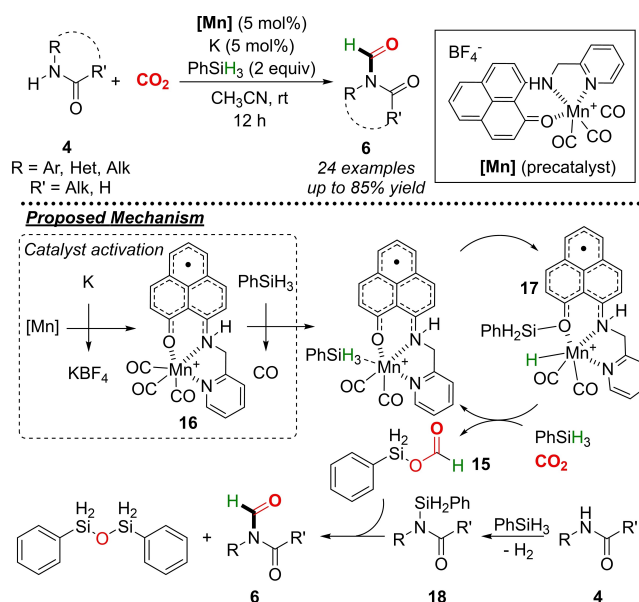
is responsible for the generation of  $\eta^2$ -silyl complex **11**, by addition with phenylsilane. Insertion of the Fe–hydride bond of **11** into  $\text{CO}_2$  renders Fe–formate **12**, being an electrophilic species able to undergo nucleophilic addition of **1** to render formamides **2**. Regeneration of the active species **11** from Fe–silyl complex **13** occurs by reaction with phenylsilane, rendering phenylsiloxane as the co-product.

In 2020, Mandal *et al.* reported the effectiveness of a Cr(III)-complex bearing a redox non-innocent phenalenyl (PLY) ligand as a catalyst for SET mediated hydroformylation of primary amides **4** with carbon dioxide and phenylsilane ( $\text{PhSiH}_3$ ) for the preparation of imides **6**.<sup>[11]</sup> The reaction proceeds under mild conditions in acetonitrile as solvent with elemental potassium as initial reductant and low  $\text{CO}_2$  pressure (Scheme 3). The authors propose a two-electron reduction (operated by potassium) of the precatalyst to generate a radical anion species **14** which, by single-electron activation of phenylsilane, can split the Si–H bond into a silyl radical and a hydride ion. Following previous studies by the same group,<sup>[12]</sup> the generated hydride is proposed to be stored in the redox active PLY backbone and subsequently transferred to the electrophilic center of  $\text{CO}_2$ , reducing it to the formate ion. This is then recombined with the silyl radical to generate a silyl formate **15** upon another SET event, responsible also for the regeneration of the active catalytic species **14**.

In 2023, the same group successfully employed a Mn(I) catalyst featuring a similar redox-active tridentate phenalenyl (PLY) ligand for the catalytic *N*-formylation of secondary amides and lactams **4** in the presence of phenylsilane ( $\text{PhSiH}_3$ ) and catalytic potassium metal (Scheme 4).<sup>[13]</sup> Remarkably, the protocol was found to be applicable to a wide range of secondary amides including bio-active derivatives and lactams, being



Scheme 3. Chromium-catalyzed hydroformylation of amides.



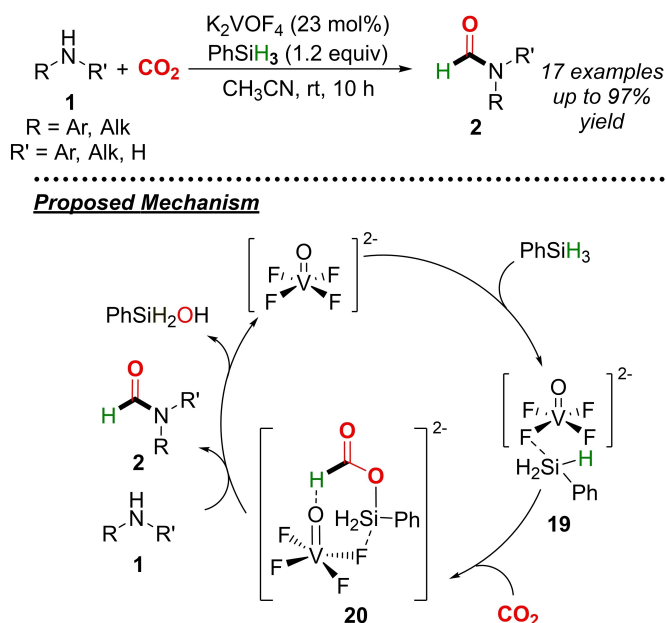
Scheme 4. Manganese-catalyzed hydroformylation of amides and lactams.

converted to the respective formylated adducts **6** in good yields. Mechanistically, a dual catalytic cycle is predicted to be involved in the process, where the catalyst is responsible for the formation of the two reactive intermediates undergoing the

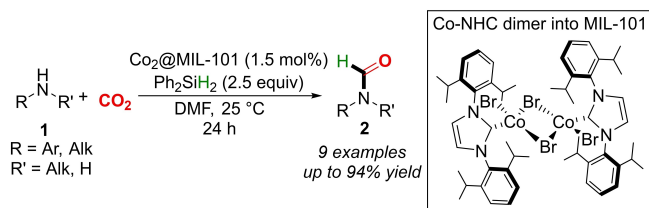
final amide-bond formation. The active Mn-complex (**16**), formed by a K-mediated reduction of the pre-catalyst, featuring a ligand-centered radical, promotes homolytic activation of the Si–H bond in PhSiH<sub>3</sub>, leading to the formation of an active silyl radical and a Mn–H complex. Subsequently, the metal-bound hydride **17** can be transferred to CO<sub>2</sub>, which in turn binds with the silyl moiety to produce a reactive silyl-formate intermediate **15** and regenerates the active catalyst. Simultaneously, amide **4** is activated by phenylsilane via the generation of a more nucleophilic *N*-silyl amide (**18**).

In 2021, phenylsilane (PhSiH<sub>3</sub>) was shown to promote the hydroformylation of amines **1** with CO<sub>2</sub> in combination with the catalysis of an oxalovanadate complex [K<sub>2</sub>V(O)F<sub>4</sub>].<sup>[14]</sup> A number of aromatic as well as aliphatic primary and secondary amines were transformed into the target formamides **2**, under very mild conditions (Scheme 5). Mechanistically, intermediate **19** is proposed to be first formed by interaction of the catalyst with phenylsilane. The activated Si–H then attacks carbon dioxide leading to the formation of the transient silyl formate intermediate **20**. The final product **2** is achieved by condensation of the latter species with **1** with the release of phenylsilanol. Owing to the excellent degree of recyclability of the catalyst, as showed by the authors, and the fact that the V–F bond is never cleaved during the catalytic cycle, the proposed strategy represents a valid heterogeneous fluoride-based activation of hydrosilanes in the benchmark reduction of CO<sub>2</sub>.

In 2022, Liu, Ma and co-workers employed a MOF-encapsulated binuclear Co–NHC (*N*-heterocyclic carbene) complex to realize the formylation of amines **1** towards formamides **2** with CO<sub>2</sub> and hydrosilanes (Ph<sub>2</sub>SiH<sub>2</sub>, Scheme 6).<sup>[15]</sup> The unique features of the catalytic system ensured the activity of an homogeneous catalyst and the reusability of a heterogeneous encapsulate system, ensuring even enhanced performance if compared to common homogenous catalysts. DFT calculations



Scheme 5. Vanadium-catalyzed hydroformylation of amines.

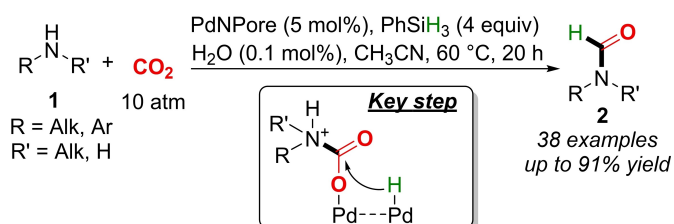


Scheme 6. MOF-encapsulated cobalt-catalyzed hydroformylation of amines.

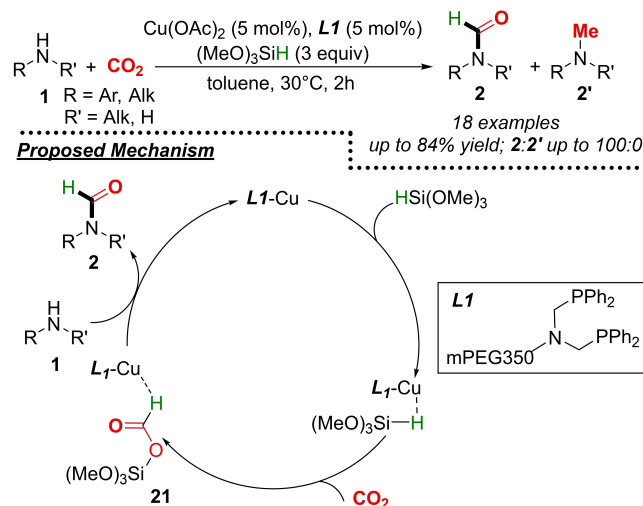
led to suggest the formation of a silyl formate pre-product, undergoing nucleophilic substitution with amines 1 and showed higher competence in the hydrosilylation step of the chosen binuclear complex, compared to a similar mononuclear Co-species.

Unsupported nanoporous Pd composites (PdNPore) were elected by Feng, Bao and co-workers to promote the catalytic transformation of amines 1 to formamides 2 with phenylsilane (PhSiH<sub>3</sub>) as hydrogen source (Scheme 7).<sup>[16]</sup> A large number of secondary and primary amines were productively reacted under the optimized conditions, requiring acetonitrile and water as solvents, at 60 °C and atmospheric CO<sub>2</sub> pressure. Interestingly, PdNPore proved higher reactivity than other dispersed Pd-sources such as Pd/C or Lindlar's catalyst and showed excellent recyclability (10 cycles with no appreciable loss in isolated yield). Mechanistically, the assistance of water in the adsorption of both hydrosilane and amine 1 to the Pd-surface was highlighted by the authors, as well as the formation of a Pd-formate species by a Pd-H insertion into an activated carbamate, generated by the reaction of CO<sub>2</sub> and 1. The final condensation of the amine and the Pd-formate yields the target product.

In addition, the catalytic conversion of CO<sub>2</sub> into formamides 2 with amines 1 and (MeO)<sub>3</sub>SiH was realized by Peng, Bai and co-workers in the presence of a Cu-(PNP) complex containing a PEG chain (L).<sup>[17]</sup> The process was found to tolerate both primary and secondary aliphatic as well as aromatic amines 1, including highly encumbered substrates. Careful optimization of reaction conditions allowed good selectivity, suppressing undesired over-reduction products (2') to be formed (Scheme 8). Extensive screening of the chosen ligand showed a beneficial effect of both the PNP structure and the PEG chain, and Cu was found to be superior to a variety of other transition metals in promoting the described transformation. Mechanistically, the Cu-catalyst promotes the hydrosilylation of CO<sub>2</sub> affording silyl formate 21



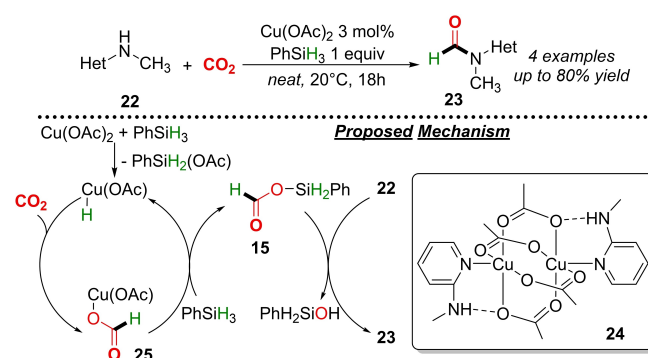
Scheme 7. Unsupported Pd-catalyzed hydroformylation of amines.



Scheme 8. Copper-catalyzed hydroformylation of amines.

which is the active species undergoing condensation with the desired amine 1. The formation of highly nucleophilic silylamine species was ruled out by the authors through dedicated experimental studies.

In 2023, the group of Ema realized the *N*-formylation of 2-(methylamino)pyridines 22 with CO<sub>2</sub> and phenylsilane (PhSiH<sub>3</sub>), catalyzed by Cu(OAc)<sub>2</sub> in a ligand- and solvent-free fashion (Scheme 9).<sup>[18]</sup> The obtained products, *N*-methyl-*N*-(2-pyridyl)formamides 23, also called Comins-Meyers-type formamides, could be directly subjected to Grignard reactions in THF for the one-pot synthesis of aldehydes and alcohols, demonstrating the obtained products as versatile formyl-group storages. A metal complex consisting of two copper centers bridged by four acetate ions and two molecules of 2-(methylamino) pyridine on both axial sites (24) was isolated from the reaction mixture, suggesting a substrate-improved solubility of the copper catalyst and an enhanced nucleophilicity of the acetate ion for the activation of phenylsilane. A catalytically active Cu-H species is proposed to promote hydrogen transfer to CO<sub>2</sub> for the production of a Cu-formate 25. Then, reaction with another molecule of phenylsilane, to form the key silyl



Scheme 9. Copper-catalyzed hydroformylation of heteroarylamines.

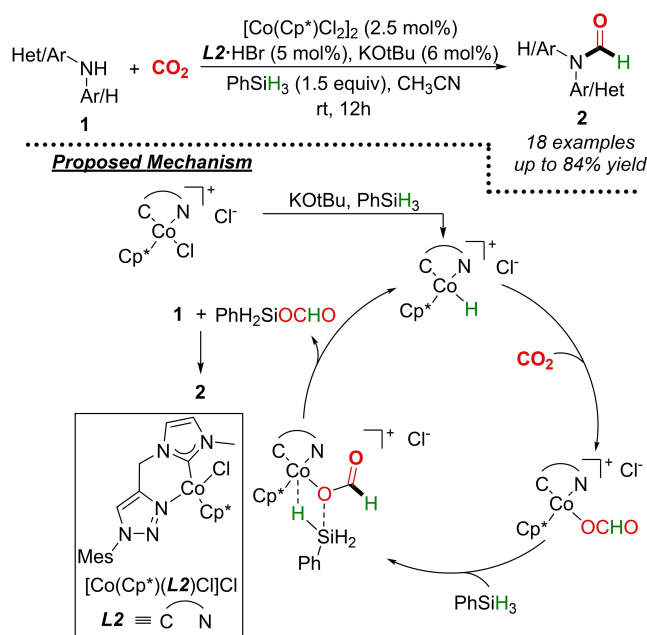
formate intermediate **15**, was postulated, directly affording *N,N*-disubstituted formamides **2**.

In 2023, Rit and co-workers realized the preparation of heteroditopic chelating NHC–Co(III) complexes, featuring variable triazole *N*-substituents, being competent catalysts for the reductive amination of CO<sub>2</sub> with anilines **1** in the presence of PhSiH<sub>3</sub> under mild conditions (Scheme 10).<sup>[19]</sup> The catalytic activity of the complexes was found to be tuned by the triazole *N*-substituents, arising from electronic perturbations of the ligand, rather than steric alterations. As already noted in the previous examples, control experiments suggested that the protocol proceeds via a Co–H promoted hydride transfer to CO<sub>2</sub>, formation of a silyl formate and final condensation to render the desired products **2**.

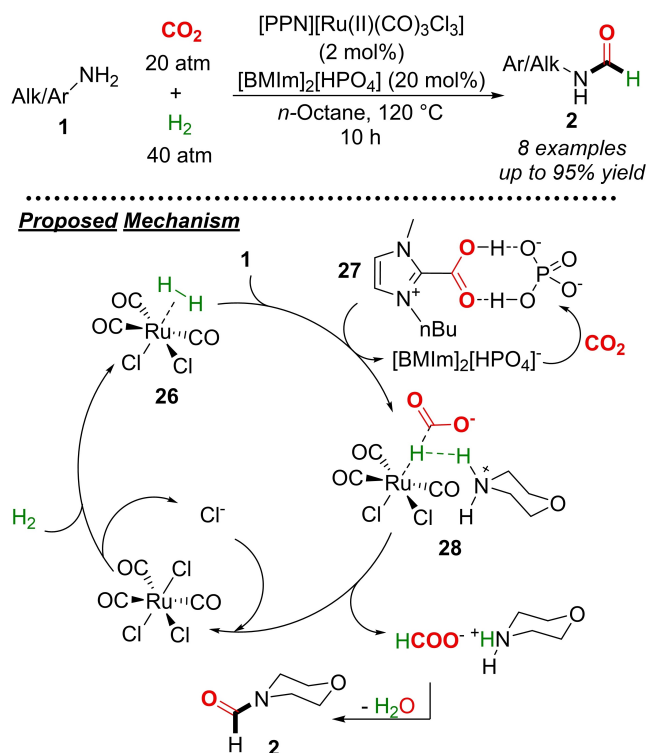
### 2.1.2. Hydrogen gas-based strategies

Another convenient way of providing hydride-sources in amine hydroformylations involves the usage of hydrogen gas (H<sub>2</sub>). Despite the high flammability issues, these methodologies avoid the use of expensive and highly corrosive hydrosilanes, with the additional advantage of enhanced atom economy (reaction co-products changing from siloxanes to water), in a more large-scale, industrial-oriented point of view.

The *N*-formylation reaction of amines **1** with CO<sub>2</sub> and H<sub>2</sub> was explored in 2021 by Hou and co-workers in the presence of a Ru catalyst ([PPN][Ru(CO)<sub>3</sub>Cl<sub>3</sub>]) (PPN, bis(triphenylphosphine)iminium) and the ionic liquid 1-butyl-3-methylimidazolium hydrogen phosphate ([Bmim]<sub>2</sub>[HPO<sub>4</sub>], Scheme 11).<sup>[20]</sup> The assistance of the ionic liquid improved the catalyst dispersion and CO<sub>2</sub> absorption, allowing the process to be run under very mild conditions, over a small range of



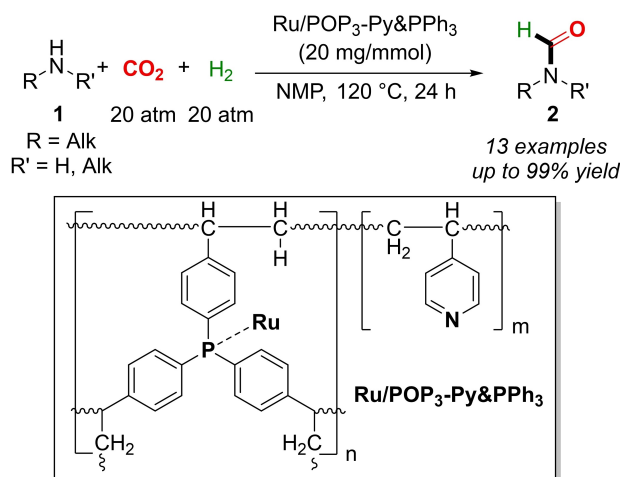
**Scheme 10.** Cobalt-catalyzed hydroformylation of amines (Mes = 1-(2,4,6-trimethyl)phenyl; Cp\* = pentamethylcyclopentadienyl).



**Scheme 11.** Ruthenium-catalyzed hydroformylation of amines. Morpholine is shown as an example of employed amine in the proposed mechanism.

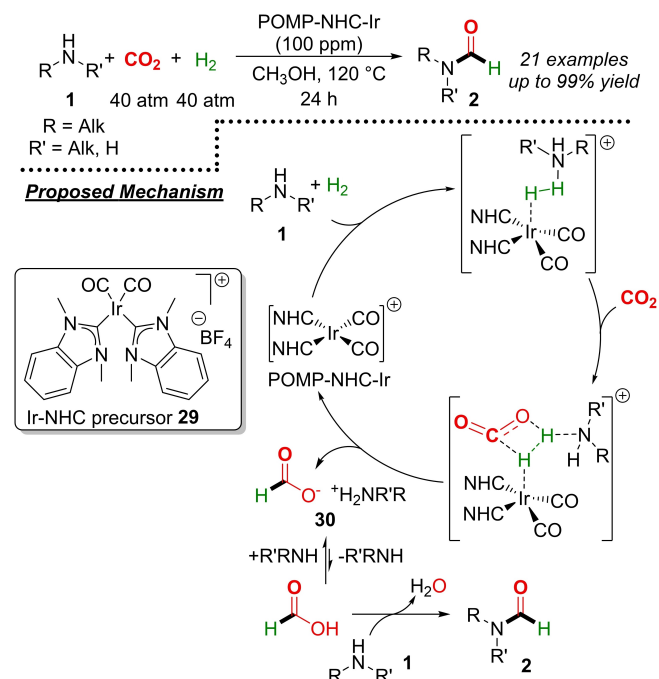
aliphatic and aromatic primary/secondary amines **1** and granted a good degree of reusability of the catalytic system. Experimental NMR studies and DFT calculations elucidated the role of ([Bmim]<sub>2</sub>[HPO<sub>4</sub>]), promoting the adsorption of CO<sub>2</sub> by a concerted action of both ions for the formation of a phosphorus carbonate adduct **27**, being the effective carbonylating species. Through DFT calculations, the formation of the Ru–H intermediate **26** occurs first, then the CO<sub>2</sub> molecule trapped in **27** is inserted directly into Ru–H bond to deliver complex **28**. After that, the free formate ion, dissociated from the Ru catalyst, undergoes condensation with **1** to form formamide **2** aided by the basicity of the ionic liquid.

In 2021, Jia and co-workers disclosed a dual catalytic system based on a Ru-catalyst supported on pyridine functionalized porous organic polymers (POPs-Py&PPh<sub>3</sub>), resulting from the polymerization of tris(4-vinylphenyl)phosphine and 4-vinylpyridine, for the convenient hydroformylation of amines **1** into formamides **2** with CO<sub>2</sub>/H<sub>2</sub> mixtures.<sup>[21]</sup> The POP supported Ru catalyst (Ru/POP<sub>3</sub>-Py&PPh<sub>3</sub>) shows excellent catalytic performance (TON up to 710), and the protocol, proceeding in NMP as solvent at high temperature and elevated CO<sub>2</sub> and H<sub>2</sub> pressure, is suitable for a variety of primary and secondary aliphatic amines **1** (Scheme 12). The authors verified that the optimal catalytic activity depends greatly on the ratio between pyridine and phosphine (*i.e.* Ru-sites) units in the copolymer, as well as on the porosity of the material, leading to the proposal that the synthesized system is a bifunctional catalyst, with the pyridine moieties contributing to CO<sub>2</sub> adsorption and activation. The heterogeneous catalyst could also easily be separated from the

Scheme 12. Ru/POP<sub>3</sub>-Py&PPh<sub>3</sub> catalyzed hydroformylation of amines.

reaction mixture and reutilized for eight consecutive cycles without appreciable loss in efficiency.

In the same year, Tu and coworkers reported on a series of porous organometallic polymers (POMP) that could be employed as highly efficient and recyclable catalysts for the hydroformylation of amines **1** to formamides **2** with hydrogen gas as reductant. The catalytic material was fabricated by the reaction of Ir-NHC precursor **29** with benzene and formaldehyde dimethyl acetal (Scheme 13).<sup>[22]</sup> The authors demonstrated that, in order to achieve high catalytic performances (20 ppm catalyst loading, TON up to 10<sup>6</sup>) the correct interplay between effects of specific surface area, iridium content, and CO<sub>2</sub> adsorption capability is of utmost importance.

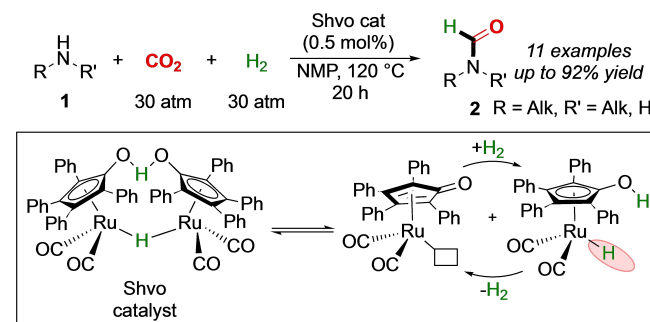


Scheme 13. Ir/POMP catalyzed hydroformylation of amines.

The solid catalysts could be easily separated from the reaction mixture and reused up to 12 times, maintaining the same level of excellent efficiency. The reaction machinery is proposed to start with the activation of H<sub>2</sub> by the catalytic metal center with a synergistic assistance of the amine substrate **1**, with the resultant quaternary ammonium salt acts as a hydride donor in the subsequent carbonylation with CO<sub>2</sub>, leading to the formation of formic acid adduct **30**. This further reacts with another HCOOH molecule via "proton-relay", leading to the formation of formamide product **2**. This mechanism, proceeding through a redox-neutral catalytic pathway, was supported by both experimental (time-dependent <sup>1</sup>H NMR analysis) and DFT calculations.

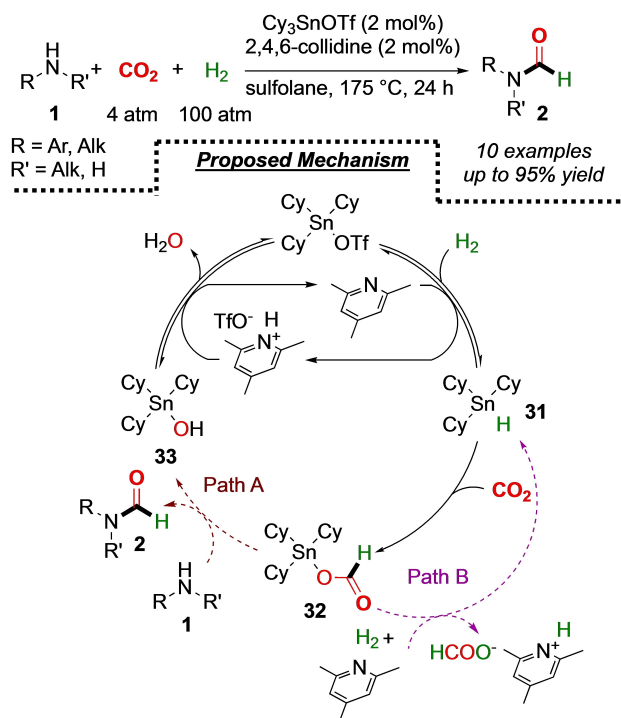
In 2023, the group of He conducted a study directed to the elucidation of the role of ionic liquids in the product distribution of the Shvo's catalyst in the reduction of CO<sub>2</sub> with H<sub>2</sub>.<sup>[23]</sup> Although the work is centered on the production of CO mediated by ionic liquids, the authors realized that, under ionic liquid-free conditions the *N*-formylation of amines **1** occurred, as the result of a product switch to formic acid. Aliphatic secondary amines as well as primary aliphatic and benzylic amines were converted to the corresponding formamides **2** with excellent yields. On the other hand, the protocol showed a significant loss in efficiency when hindered secondary amines were employed (Scheme 14).

In 2023, the group of Hulla reported a selective amine **1** hydroformylation via CO<sub>2</sub> hydrogenation (H<sub>2</sub> gas), catalyzed by trialkyl tin triflates Cy<sub>3</sub>SnOTf.<sup>[24]</sup> The protocol displays excellent tolerability of potentially reducible functional groups such as alkenes, amides, esters, and carboxylic acids and displays high catalyst activity (TON > 300) and good yields (Scheme 15). Furthermore, the authors verified that increasing the steric bulkiness of the alkyl substituents is beneficial in preventing catalyst decomposition through self-disproportionation. Mechanistically, trialkyltin triflates can act as Lewis acids, forming a frustrated Lewis pair (FLP) with **1** and/or 2,4,6-collidine, used as auxiliary base. FLP activation of molecular hydrogen leads to the *in situ* formation of a trialkyltin hydride (**31**) displaying excellent reactivity and selectivity towards CO<sub>2</sub> hydrogenation to tin formate **32**. The final formamide product **2** may be formed either by direct formate transfer from **32** to the amine **1** or by formate transfer to 2,4,6-collidine acting as a Lewis base and subsequent formylation of the amine **1**. In the first case, a



Scheme 14. Shvo catalyst-promoted hydroformylation of amines.





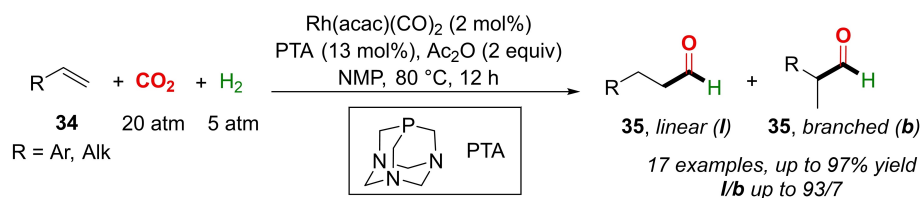
Scheme 15. Tin-catalyzed hydroformylation of amines.

tin hydroxide (33) is formed and the original trialkyltin triflate is generated by reaction with 2,4,6-collidinium triflate. In the second, through the assistance of another molecule of H<sub>2</sub>, direct regeneration of active tin hydride 31 is proposed.

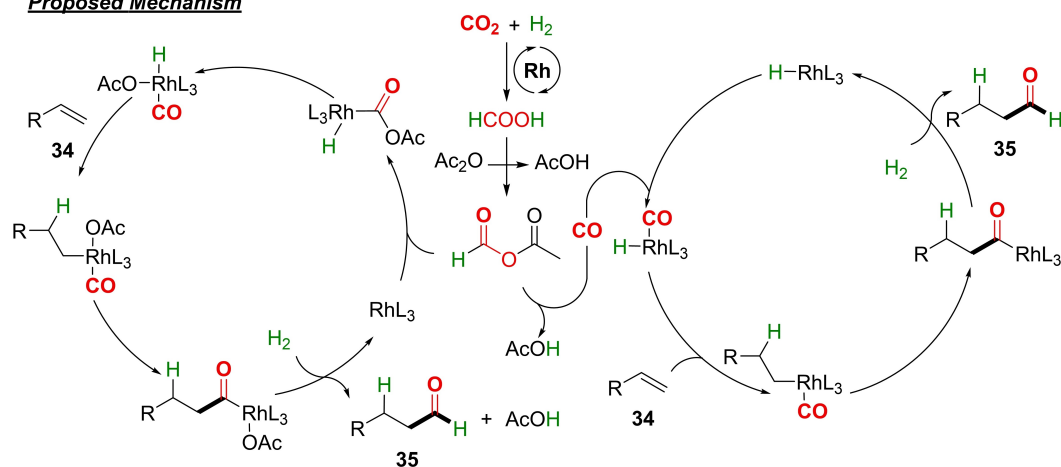
## 2.2. Hydroformylation of Alkenes

In the field of alkene hydroformylation reactions, a recent report (2021) by Sun and co-workers showed a highly efficient and selective rhodium-catalyzed hydroformylation of alkenes **24** using CO<sub>2</sub>/H<sub>2</sub> mixtures as a syngas surrogate in the presence of Ac<sub>2</sub>O as an activator.<sup>[25]</sup> The chemo- as well as regioselectivity of the reaction were optimized by careful choice of the reaction conditions: the most important parameter was found to be the PTA ligand (PTA: 1,3,5-triaza-7-phosphaadamantane), responsible for a negligible amount of hydrogenated, as well as isomerized byproducts and affecting a high linear to branched selectivity (Scheme 16). The process was found to be less reliant (and thus, quite robust) on other parameters, such as temperature, Rh-source and CO<sub>2</sub> or H<sub>2</sub> partial pressures. A variety of terminal aliphatic alkenes **34** were productively transformed in the respective linear aldehydes **35** in high yields. Interestingly, a regioselectivity switch was observed in the case of styrenes, rendering the branched aldehyde, predominantly. Mechanistically, the authors proposed a CO<sub>2</sub> hydrogenation by Rh/PTA to produce HCOOH, decomposing to CO with the assistance of Ac<sub>2</sub>O, through the formation of a mixed anhydride, namely HCOOAc. In the presence of H<sub>2</sub> and *in situ* generated CO, a Rh/PTA-catalyzed conventional hydroformylation process is then invoked (Scheme 16, bottom right). Alternatively, HCOOAc was also considered as a plausible C1-source, especially at early stages of the reaction sequence, when the CO concentration is still lower with respect to HCOOAc (Scheme 16, bottom left).

In 2023, the group of Sadeghzadeh developed a Ru-catalyzed hydroformylation of alkenes **34** using CO<sub>2</sub>/H<sub>2</sub> gas mixture under mild conditions.<sup>[26]</sup> The high dispersion of Ru-nanoparticles, for which enhanced reactivity is observed, is due



### Proposed Mechanism

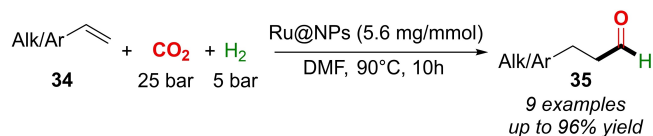


Scheme 16. Rhodium-catalyzed hydroformylation of alkenes.

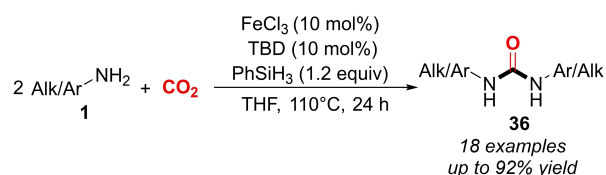
to the usage of an ionic liquid (constituted by the imidazole-4-carboxylic and the 1,2-dibromoethane framework) encapsulating the Ru catalyst. The hydroformylation process took place in an autoclave reactor using 25 bar carbon dioxide and 5 bar of hydrogen pressure (90 °C, DMF), and tolerated a variety of styrenes, as well as aliphatic alkenes, including ethylene (Scheme 17). Interestingly, the catalytic system could be easily separated from the reaction mixture and reutilized for ten consecutive runs without any loss of activity.

### 3. Formation of C–X bonds

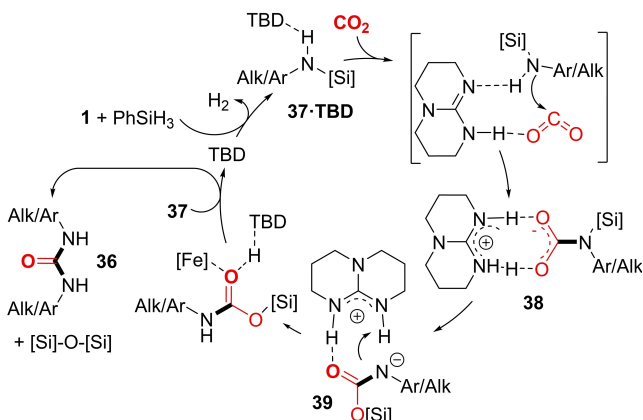
Differently from hydroformylation reactions, where the type of catalyst was depending mostly on the type of reductant employed, in the formation of C–N, C–O and C–S bonds the type of metal catalyst employed varies greatly, depending on both type of product and starting material. For example, in the formation of ureas, metals displaying good Lewis acidity such as Fe, V and Zn are preferred, while in redox-active protocols (*i.e.* synthesis of quinazolinones starting from iodoanilines), Pd-catalyzed strategies are usually utilized.



Scheme 17. Ruthenium-catalyzed hydroformylation of alkenes.



#### Proposed Mechanism



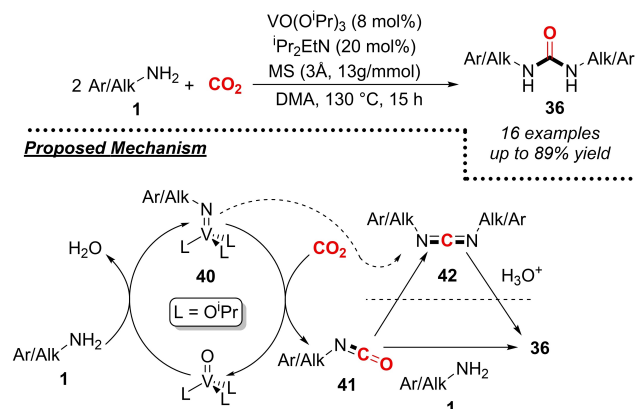
Scheme 18. Iron-catalyzed carbonylation of amines toward ureas.

### 3.1. Formation of Ureas

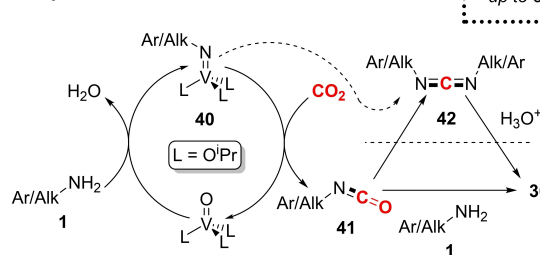
In 2020, Zhao, You and co-workers developed a novel methodology for the direct preparation of symmetrical ureas **26** starting from amines **1** and carbon dioxide.<sup>[27]</sup> The use of TBD and FeCl<sub>3</sub> as catalysts, together with phenylsilane, avoided the pre-synthesis of unstable silylamines (Scheme 18). The reaction is proposed to proceed by an initial cross-dehydrocoupling between PhSiH<sub>3</sub> and amine **1** to give silylamine **37**, carboxylation of which, under the aid of TBD, renders *N*-silylcarbamates **38**. Subsequently, after Si-migration and H-shift, *O*-silylcarbamate **39** is generated. Fe-coordination to this electrophilic species promotes the addition of a second equivalent of silylamine **37** to give final product **36** and phenyldisiloxane. The process was found to be productive by employing either anilines (ranging from very electron-rich to electron poor ones) or aliphatic amines, and tolerant to functional groups such as indoles and carboxylates.

Vanadium-based catalysts are among the most employed ones for double amination protocols of CO<sub>2</sub> towards the preparation of symmetrical ureas **36**, from amines **1**, as demonstrated recently by the group of Moriuchi.<sup>[28]</sup> In 2021 they realized the titled transformation by employing VO(OiPr)<sub>3</sub>, a commercially available oxovanadium(V) compound, at ambient pressure of CO<sub>2</sub> (Scheme 19). A key feature of the process is the *in situ* catalytic generation and transformation of imidovanadium(V) complexes **40** from VO(OiPr)<sub>3</sub> and amines **1**. The mechanism proceeds then through the formation of an isocyanate intermediate (**41**), arising from the reaction of **40** with carbon dioxide. This is believed to generate the target product either directly, by a second addition of amine **1**, or through the intermediacy of a carbodiimide (**42**), as the result of the reaction with imidovanadium(V) complex **40**, after acidic hydrolysis. The reaction, proceeding in the presence of DIPEA as a base and 3 Å MS as dehydrating agents. High tolerance towards aliphatic amines (even highly encumbered ones) was ascertained and asymmetric ureas were readily accessible using secondary and primary amines. However, anilines could be scarcely employed in the present transformation.

Shortly after, the same group documented a new variant of the protocol starting from silylamines **43** and air-stable NH<sub>4</sub>VO<sub>3</sub>.



#### Proposed Mechanism

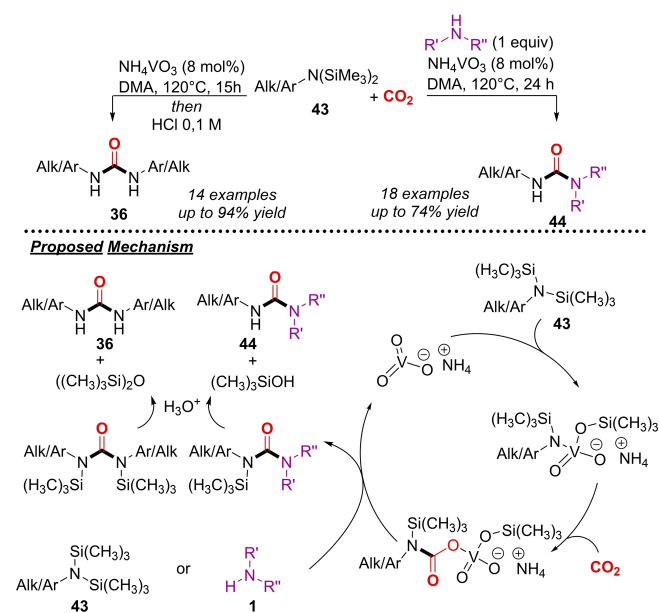


Scheme 19. Vanadium-catalyzed carbonylation of amines toward ureas.

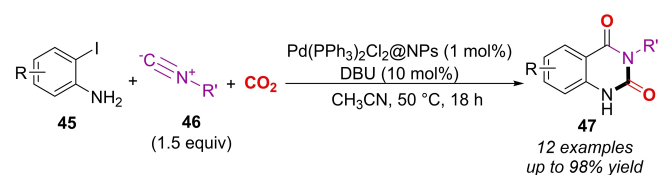
Here, both symmetrical **36** and unsymmetrical **44** (with the employment of a primary silylamine and a secondary amine) ureas were obtained in high yields (Scheme 20).<sup>[29]</sup> Importantly, electron-rich, as well as electron-poor, silylanilines were found suitable precursors. Despite efficiency, unsymmetrical ureas **44** were always obtained together with large amounts of the symmetrical analogues, derived by the double amination of CO<sub>2</sub> with the primary (silyl)amine. However, on a subsequent report, a slight modification of the reaction conditions enabled the obtainment of **44**, predominantly.<sup>[30]</sup> Importantly, the amount of NH<sub>4</sub>VO<sub>3</sub> catalyst and the concentration of the reactants were found to affect the product distribution greatly, while the portion-wise addition of the primary silylamine **43** did not improve the formation of unsymmetrical **44**.

### 3.2. Formation of Quinazolinones

The preparation of quinazoline-2,4-diones **47** is nowadays becoming a benchmark platform for the evaluation of methodologies directed to the fixation of CO<sub>2</sub> into organic scaffolds. Following the first report by Beller *et al.* in 2017,<sup>[31]</sup> which employed 2-haloanilines **45** and isocyanides **46** as starting platforms, recent progresses have been reached by the groups of Cheng and Tang.<sup>[32]</sup> In particular, the reaction of 2-iodoani-



**Scheme 20.** Extension of the vanadium-catalyzed amine carbonylation protocol toward ureas.

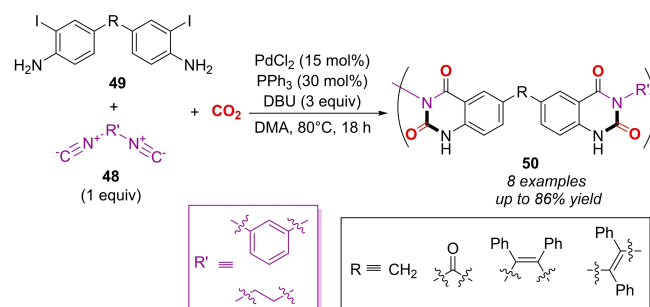


**Scheme 21.** Palladium-catalyzed preparation of quinazolinones.

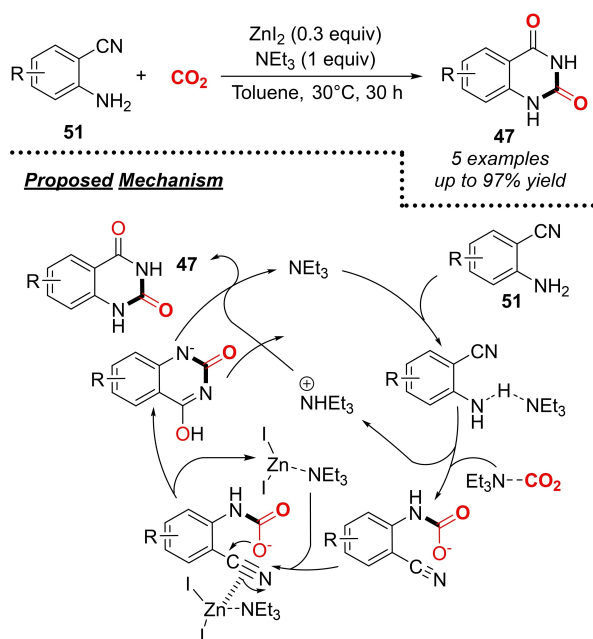
lines **45** and tert-butyliisocyanide within a metal (Pd)-organic framework (MOF) “microreactor”, was reported. Herein, dispersed (PPh<sub>3</sub>)<sub>2</sub>PdCl<sub>2</sub> was utilized as a single-molecular catalyst (Scheme 21). Remarkably, “quasi-homogeneous” conditions were realized to convert CO<sub>2</sub> into quinazolinones **47** under mild conditions with promising yields. MIL-101 (Cr) was used as a MOF microreactor due to its high stability, highly porous structure and cage-type pores with a suitable size for the permeation of PPh<sub>3</sub> ligands. Additionally, the microreactor strategy restricted the leakage of the *in situ* assembled complex (PPh<sub>3</sub>)<sub>2</sub>PdCl<sub>2</sub> following the “ship in a bottle” principle. Compared to the present process, displaying high yields for a range of 2-iodoanilines **45**, reported homogeneous catalytic systems required 10 times more Pd content, and higher temperatures, and pressures of CO<sub>2</sub>. Finally, good recyclability of the heterogeneous promoters was recorded as well. As a matter of fact, the recovered catalyst was reused in up to five consecutive cycles with no appreciable reactivity loss.

In 2019, the group of Quin and Tang exploited the transformation of diisocyanides **48** and bis(2-iodoanilines) **49** for a facile and efficient CO<sub>2</sub>-based multicomponent polymerization.<sup>[33]</sup> The catalytic system, namely PdCl<sub>2</sub> and triphenylphosphine in the presence of excess DBU (DMA, CO<sub>2</sub> 1 atm) furnished a soluble polymeric architecture **50** with a weight-average molecular weight (Mw) of up to 8700 (yields up to 86%, Scheme 22). Some properties of the synthesized polymers were also investigated, such as their capability to self-assemble into spheres (200 – 1000 nm size) due to the hydrogen bonding interactions of the amide groups, and their photoluminescence towards a selective detection of [Au<sup>3+</sup>] ions.

Quinazoline-2,4-diones **47** can alternatively be easily prepared by double amination of CO<sub>2</sub> with 2-aminobenzonitriles **51**. Following seminal examples, mainly run under simple base-catalysis, the group of Deng (2019) disclosed that ZnI<sub>2</sub>, in the presence of excess Et<sub>3</sub>N, could catalyze the titled transformation at room temperature and low CO<sub>2</sub> pressure recording high yields, avoiding expensive and highly reactive bases such as TBD and DBU (Scheme 23).<sup>[34]</sup> Mechanistic studies indicated that the ZnI<sub>2</sub>/Et<sub>3</sub>N complex can effectively activate the CN bond in **51** and further promote the reaction under milder conditions (it was otherwise proved that Et<sub>3</sub>N alone is able to promote the reaction in low yields under more forcing conditions).<sup>[35]</sup> A small series of electron-rich as well as electron-poor 2-aminobenzoni-



**Scheme 22.** Palladium-catalyzed synthesis of polymeric quinazolinones.



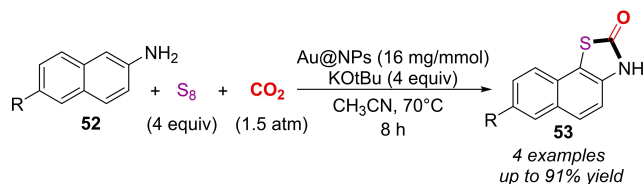
**Scheme 23.** Zinc-catalyzed preparation of quinazolinones through double C–N bond forming event.

triles **51** were subjected to the optimized reaction conditions obtaining the target products **47** in very high yields.

### 3.3. Formation of One C–N and One C-chalcogen Bond

Stemming away from ureas and urea-containing heterocycles, the realization of two C-heteroatom bonds in  $\text{CO}_2$ -based carbonylation reactions can be exploited to prepare thiazolidine-2-ones **53** in high yields, from anilines **52** and elemental sulfur, as disclosed by Wei and Wang in 2021 (Scheme 24).<sup>[36]</sup> The authors proposed a  $\text{C}(\text{sp}^2)\text{--H}$  bond functionalization mechanism promoted by a  $\text{Au@Cellulose/DFNS}$  adduct in the presence of  $\text{tBuOK}$ . Outer layer analysis of the synthesized catalyst showed the functionalization of cellulose and Au in the mesopores silica surface. Under optimal conditions, the heterogeneity and recyclability of the catalytic material were tested with excellent results.

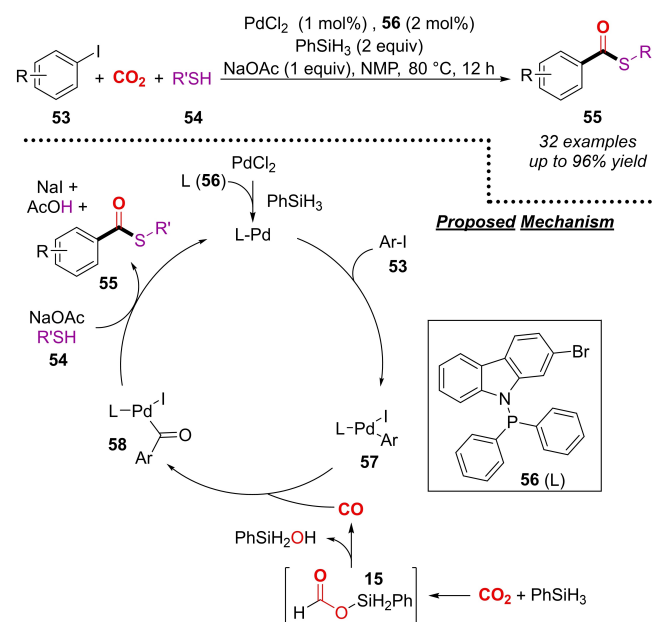
Expanding on the field of C–S bonds formation with carbon dioxide, very recently (2023), Li and co-workers developed a Pd-catalyzed formation of thioesters **55** from aryl iodides **53** and thiols **54**.<sup>[37]</sup> The reaction proceeds in the presence of  $\text{PdCl}_2$ , P–N ligand **56**,  $\text{NaOAc}$  as a base, phenylsilane as the reductant



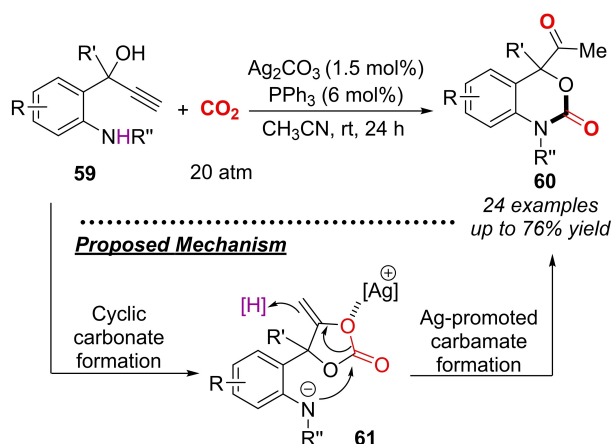
**Scheme 24.** Gold-catalyzed preparation of thiazolidine-2-ones.

(Scheme 25). Carbazole-based ligand **56** proved superior reactivity compared to common mono- or bi-dentate phosphines. A wide range of aryl iodides, ranging from very electron-poor to highly electron-rich ones, were tolerated. Importantly, the reaction showed exquisite selectivity for iodoarenes, while bromo substitutions were fully compatible with the present reaction conditions. Both aliphatic and aromatic thiols could be employed in the transformation. Mechanistically, the *in situ* formation of CO from  $\text{CO}_2$  was invoked (via silyl formate intermediate **15**), as pointed out by dedicated experiments. Then, after phosphine- and silane-mediated reduction of  $[\text{Pd}(\text{II})]$  to  $[\text{Pd}(0)]$  and oxidative addition with **53** (formation of intermediate **57**), insertion of CO provides the acyl palladium species **58**. This undergoes nucleophilic substitution by thiols **54** to generate the desired thioester products **55** and concomitant the regeneration of the catalytically active  $[\text{Pd}(0)]$  species.

In 2023 the group of Kleij developed an Ag-catalyzed cascade process to access benzoxazine-2-ones **60** from alkynylanilines **59** and  $\text{CO}_2$ .<sup>[38]</sup> Under the optimized reaction conditions, involving the use of  $\text{Ag}_2\text{CO}_3/\text{PPh}_3$  as the catalyst in ACN (room temperature to  $60^\circ\text{C}$ ) the reaction scope was found to be broad and highly functional group tolerant (Scheme 26). Interestingly, also less nucleophilic amido groups were efficiently utilized, recording similar reactivity. Moreover, the synthesized products **60** were shown to undergo a range of productive functionalizations, showing the importance and flexibility of the targeted moiety. Mechanistically, the Ag-promoted formation of carbonate **61** was proposed to occur, via a standard Lewis-acid catalyzed nucleophilic  $\text{CO}_2$  capture by the hydroxy group followed by electrophilic capture by the activated alkyne. Then, ring-opening of **61** by the amino group leads to the formation of the target compound **60** having a ketone and a carbamate functional group. Interestingly, even though the final product still comprises two oxygens



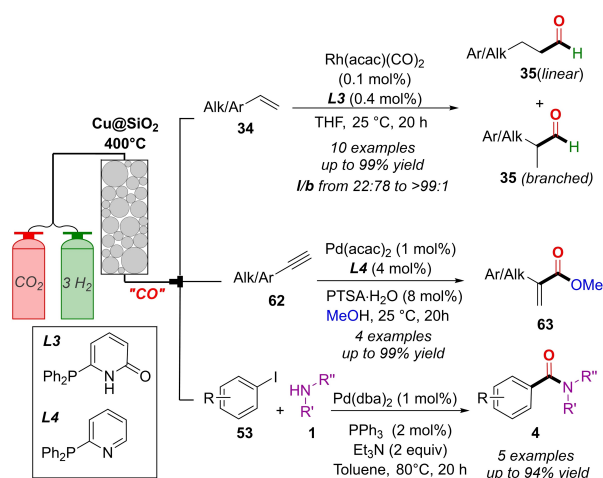
**Scheme 25.** Palladium-catalyzed preparation of thioesters.



Scheme 26. Silver-catalyzed preparation of benzoxazinones.

(carbamate unit) at the CO<sub>2</sub>-deriving carbon atom, the process can still be classified as a carbonylation event. Indeed, one oxygen of this carbamate derives from the hydroxy group of **61** and thus a “formal” scavenging of the C–O bond occurred in CO<sub>2</sub> over reaction course.

In 2022, Beller *et al.* developed a methodology for the realization of multiple carbonylation reactions with carbon dioxide and hydrogen as a safe alternative to *syngas*, where CO is generated “on demand” and immediately utilized.<sup>[39]</sup> A heterogeneous Cu-catalyst, constituted by uniformly dispersed Cu(I) centers (Cu@SiO<sub>2</sub>-PHM, prepared by a hydrothermal method) was optimized for the production of CO-enriched gas mixtures from CO<sub>2</sub>. The generated carbon monoxide was used in Rh-catalyzed hydroformylation reactions of alkenes **34** towards aldehydes **35**, Pd-catalyzed alkoxy-carbonylations of alkynes **62** for the preparation of esters **63**, and Pd-catalyzed amino-carbonylations of aryl iodides **53** with amines **1** for the preparation of amides **4** (Scheme 27). All the reported transformation occurred smoothly in high yield and selectivity, with broad functional group tolerance. The experimental set-up

Scheme 27. Multiple carbonylation reactions using CO<sub>2</sub>-H<sub>2</sub> mixtures as *syngas* alternative.

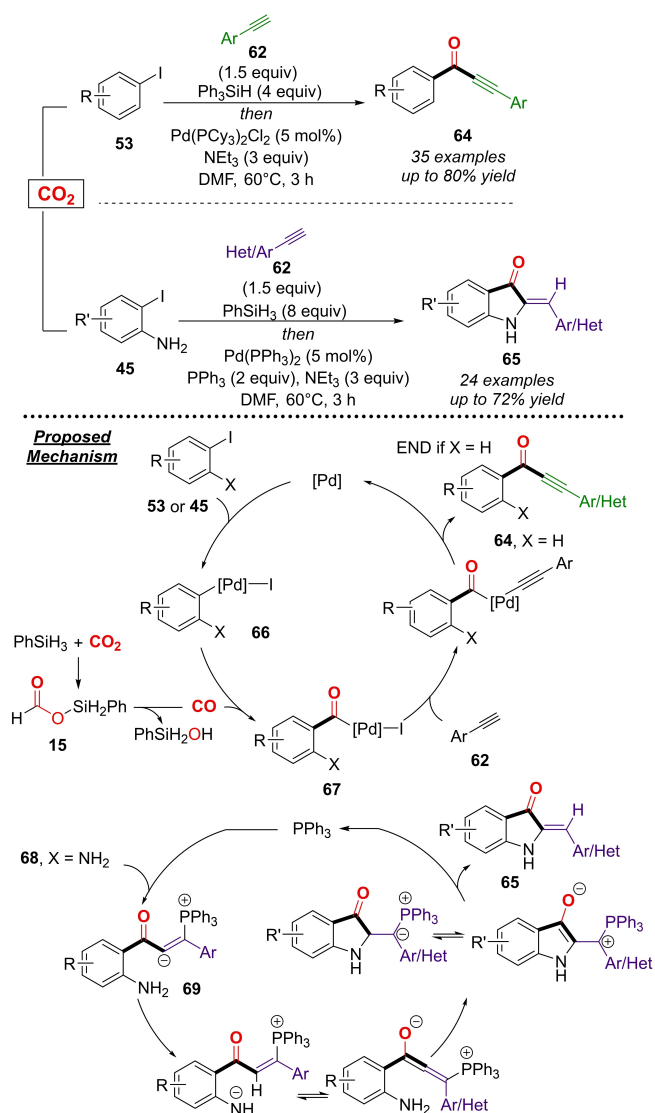
consisted in a continuous-flow reactor where immobilized Cu-catalyst operates the desired H<sub>2</sub>-promoted reduction of CO<sub>2</sub> to CO; importantly, the produced gas mixture could be directly utilized in the following metal-catalyzed cross-coupling reactions without the need of gas purification systems.

#### 4. Formation of Two C–C bonds: Synthesis of Ketones

In the field of carbonylation process with CO<sub>2</sub>, the formation of two C–C bonds for the preparation of ketones is arguably one of the most fascinating, yet challenging transformations.<sup>[40]</sup> The majority of the processes disclosed so far employ the *in situ* (or *ex situ*) reduction of CO<sub>2</sub> to CO (or equally reactive silylformate species) and subsequent application in metal-catalyzed carbonylation reactions. This approach represents a smart, safe, and environmentally friendly way to tackle standard CO chemistry without the need to store and manipulate highly toxic and flammable carbon monoxide sources. On the catalyst point of view, Pd-catalysis is employed almost exclusively, with the carbonylative event taking place between the oxidative addition and transmetalation of standard Pd-catalyzed transformations such as Sonogashira or Suzuki cross-couplings.

In 2021 the group of Qi and Jiang, disclosed a one-pot protocol for a Pd-catalyzed carbonylative Sonogashira coupling, using CO<sub>2</sub> as the carbonyl source (Scheme 28).<sup>[41]</sup> The methodology required phenylsilane as the reducing agent, triethylamine as the base and simple phosphines (such as PPh<sub>3</sub> and PCy<sub>3</sub>) as ligands. Under optimal conditions a vast range of functionalized alkynes **64** and 2-alkylideneoxindoles **65** were accessible, starting from alkynes **62** and aryl iodides **53** or 2-iodoaniline **45**, respectively. Mechanistically, the reduction of CO<sub>2</sub> operated by PhSiH<sub>3</sub> is proposed to occur first (*via* silylformate **15**), with generation of CO (and PhSiH<sub>2</sub>OH). The so-formed carbon monoxide is proposed to insert in the (*σ*-aryl)palladium species **66** (formation of intermediate **67**), generated *via* oxidative addition of [Pd(0)] on the aryl iodide **53**. Subsequently, a base assisted Sonogashira coupling give rise to products **64** or intermediate **68**. The latter can, by reaction with PPh<sub>3</sub>, produce intermediate **69** followed by isomerization and intramolecular cyclization to **65**. Importantly, thanks to a judicious optimization of the reaction conditions, the CO-producing (silane mediated reduction of carbon dioxide) and the CO-consuming (carbonylative Sonogashira coupling) events could be conducted simultaneously in the same reaction vessel, preventing the requirement of a double-chamber apparatus.

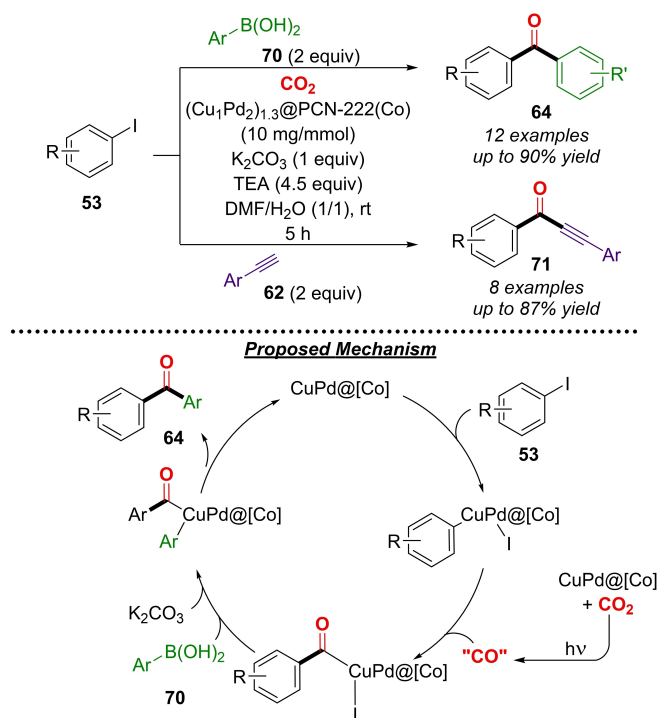
In 2021, Guo, Zhang and co-workers developed ultrafine Cu–Pd nanoclusters (Cu–Pd NCs) integrated in a MOF light-absorbing cobalt single-site catalyst (PCN-222(Co), a metal-organic framework consisting in the self-assembly of Coporphyrin complexes and Zr<sub>6</sub> clusters) for the construction of a composite multi-catalytic system for the realization of carbonylation reactions of a number of aryl iodides **43** with either arylboronic acids **70** or alkynes **62** upon visible light irradiation.<sup>[42]</sup>



**Scheme 28.** Palladium-catalyzed preparation of alkynyl ketones and alkyldene oxindoles.

The process consists of an initial  $\text{CO}_2$ -to- $\text{CO}$  photoconversion, enabled by Co-porphyrin complexes, followed by Pd-mediated carbonylation and final Suzuki or Sonogashira cross-coupling reaction for the preparation of alkynyl ketones **64** or benzophenones **71** with excellent functional group compatibility and high yields (Scheme 29). The observed high catalytic performance could be attributed to the synergistic interaction of the different components. Light absorption of the Co-porphyrin photosensitizer was demonstrated to promote the conversion of  $\text{CO}_2$  to  $\text{CO}$  at the single Co sites; then, the carbonylation reaction on the reduced Cu–Pd NCs could directly employ the *in situ* generated carbon monoxide to trigger the carbonylative cross-coupling event.

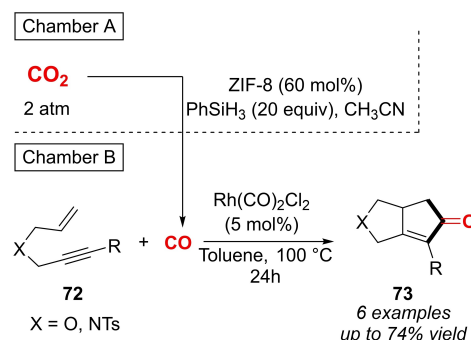
In 2022, Dyson and co-workers exploited the double-chamber method for the *ex situ* production of  $\text{CO}$  from  $\text{CO}_2$  and subsequent application in the Pauson-Khand cyclization.<sup>[43]</sup> The reduction of  $\text{CO}_2$  to carbon monoxide was efficiently catalyzed by a zeolitic Zn imidazolite framework (ZIF-8), which showed



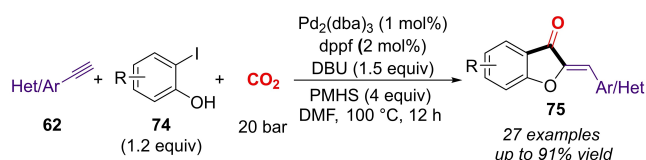
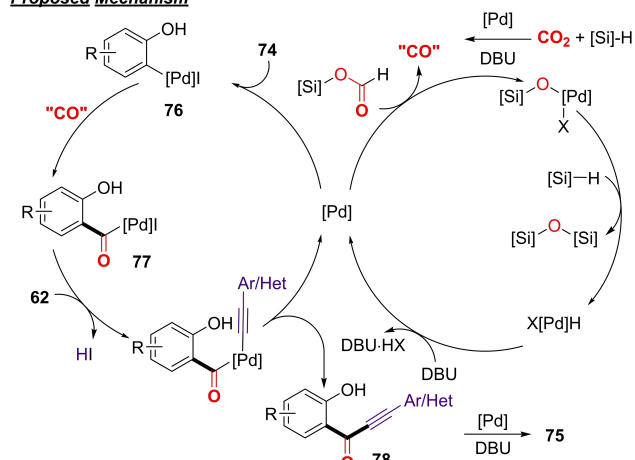
**Scheme 29.** Photocatalytic synthesis of benzophenones and alkynyl ketones. The Mechanism is exemplified for the Suzuki coupling only.

pivotal basic sites (imidazoles) as well as acidic sites (Zn metal centers), as demonstrated by the authors in dedicated control experiments. The Pauson-Khand reaction of ene-yne **72** towards cyclic ketones **73** was effectively catalyzed by  $\text{Rh}(\text{CO})_2\text{Cl}_2$ , which required a two-chamber method due to the incompatibility of ZIF-8 and  $\text{PhSiH}_3$  with the Rh catalyst (Scheme 30).

In 2023, the group of Huang demonstrated that, a palladium-catalyzed carbonylation reaction of terminal aromatic alkynes **62** and 2-iodophenols **74** can serve for an efficient preparation of aurones (namely 2-alkylidene-benzofuran-3-ones) **75** by using  $\text{CO}_2$  as carbonyl source with poly(methylhydrosiloxane) (PMHS) – as reductant.<sup>[44]</sup> The reaction, being optimized with *dppf* as the ligand and *DBU* as the base (DMF at  $100^\circ\text{C}$ ) tolerates a variety of substituted phenylacetylenes **62** as well as differently decorated 2-iodophenols **74** (Scheme 31).



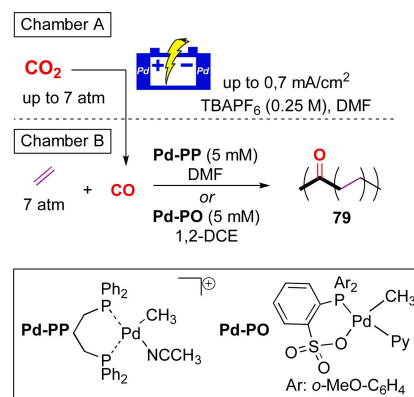
**Scheme 30.** Double-chamber  $\text{CO}_2$ -based Pauson-Khand cyclizations.

**Proposed Mechanism**

**Scheme 31.** Palladium-catalyzed preparation of aurones via a three-component cascade reaction

Control experiments revealed that the effective carbonylating agent is derived by a silylformate species, formed by action of PMHS on CO<sub>2</sub>. This undergoes insertion into the C(sp<sup>2</sup>)-Pd bond of intermediate **76** (formed by oxidative addition of [Pd(0)] on the starting material **74**) to give an acyl-palladium intermediate (**77**), finally performing the Sonogashira coupling (intermediate **78**). Analogously to the mechanism reported in Scheme 23, intermediate **78** undergoes intramolecular cyclization to the final aurone products **75**.

In 2023, the groups of Miller, Wang and Liu, developed an integrated electrochemical and organometallic catalytic process for the synthesis of CO<sub>2</sub>-derived polyketones **79**.<sup>[45]</sup> Key aspect was the design of a unique reactor to solve the incompatibility of the reaction conditions required for the CO producing (electrochemical CO<sub>2</sub> reduction) and consuming (CO-ethylene co-polymerization) events. A distinct optimization of the two reaction stages led first to the identification of the optimal parameters for each step. In particular, high Faradaic efficiency for the production of CO from CO<sub>2</sub> were recorded in DMF on Pd-foil electrodes, while for the co-polymerization events two Pd-catalysts, namely **Pd-PP** and **Pd-PO** (Scheme 32) were identified. Under these conditions, alternating or non-alternating co-polymers could be realized, respectively. Importantly, regio-regular alternating polyketones **79** showed a wt% of CO<sub>2</sub>-derived material as high as 50%, while non-alternating ones were less reliant on CO<sub>2</sub>-derived mass. To integrate the two processes, a vial-in-a-vial approach was adopted. Given the gaseous nature of CO, the electrocatalytic and the polymerization mixtures were physically separated, under a shared headspace in a high-pressure reactor (7 bar CO<sub>2</sub> and 7 bar C<sub>2</sub>H<sub>4</sub>). Interestingly, in the presence of **Pd-PP**, perfectly alternating polyketones **79** were always obtained, irrespectively to the



**Scheme 32.** Palladium-catalyzed synthesis of polyketones.

current intensity (directly proportional to the CO pressure) applied in the electrocatalytic vessel. On the contrary, **Pd-PO** catalyst showed a pressure dependent reaction outcome, with alternating **79** being produced at elevated currents (resulting in higher CO partial pressure) and non-alternating **79** at lower currents (resulting in low CO partial pressure).

## 5. Summary and Outlook

In the present *Review* article, the most recent advances of metal-catalyzed employment of CO<sub>2</sub> in **carbonylation** processes have been summarized. From an accurate analysis of the reported material, a general trend regarding the direction of the research in this *hot topic* can be estimated. The catalytic systems employed are usually strictly depending on the type of starting material or reductant necessary for the desired transformation. For example, in the field of amine hydroformylation, first-row transition metals are usually preferred with the use of silanes, while hydrogen gas requires Ru-based catalysts. On the other hand, when CO<sub>2</sub>-based carbonylations actually rely on the *in situ* formation of CO, carbonylative cross-coupling methodologies are usually encountered, with Pd being the most employed active metal center. The presence of many protocols involving the utilization of supported catalysts with optimal recyclability, the usage of ionic liquids or environmentally benign solvents and reductants, reveal a certain advancement of CO<sub>2</sub>-based **carbonylations**. Nonetheless, we still foresee further extension for the chemical space of **carbonylative** CO<sub>2</sub>-based fixations. For example, the formation of two different C-C bonds towards the preparation of ketones still represents a challenging transformation, for which a general solution still needs to be found. It is however easily foreseeable that, given the large interest of the synthetic community in this field, a vast number of novel methodologies as well as important improvements of the existing ones will be developed and disclosed in due course.

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## Conflict of Interests

The authors declare no conflict of interest.

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