Catalytic challenges and strategies for the carbonylation of σ-bonds

Tawfiq Nasr Allah†, Louise Ponsard†, Emmanuel Nicolas and Thibault Cantat*[a]

The carbene character of carbon monoxide offers the possibility to utilize this C_1-building block for the carbonylation of a variety of organic substrates by insertion of CO into σ-bonds. Although presenting an ideal atom economy this route requires the design and utilization of reactive catalysts able to activate strong C–O, C–N, and C–H bonds in the presence of carbon monoxide. This perspective article adresses, in the context of sustainable chemistry, the challenges and strategies facing the catalytic carbonylation of σ-bonds and presents the key advances in the field over the last decades, for the carbonylation polar and apolar substrates, such as the conversion of alcohols to formates and esters and the carbonylation of amines to amides.

1 Introduction

The chemical industry is heavily dependent on oil-based resources, the latter being required for the synthesis of 87% of chemicals in 2016.[1] To reduce this need and engage into a circular economy pathway, which would ultimately lead to its carbon-neutrality, it would be attractive to synthesize chemicals directly from CO_2. Nevertheless, the direct use of CO_2 for the production of functionalized chemicals remains limited in industry: its use as a C_1 building block for the production of chemicals has been well developed for the production of urea (81 Mt in 2016), salicylic acid (70 kt/y), and more recently for the production of cyclic and polymeric carbonates (130 k/y).[2] These transformations implicate the functionalization of CO_2, but only chemicals containing a carbon at the +IV oxidation state have been industrially synthesized so far. Accessing other chemicals directly from CO_2 would require synchronizing reduction and functionalization, which is an active field of research but is difficult to control. An interesting intermediate would be carbon monoxide (CO) that can provide access to functionalized chemicals at a more reduced oxidation state, +II, closer to the average oxidation state of most industrial chemicals.

Carbon monoxide (CO) is a colourless gas that already finds many uses in the chemical industry, despite its high toxicity.[3] For instance, the Mond process for the purification of nickel, the oxo process for the production of aldehydes from alkenes, or Fischer-Tropsch process for the synthesis of alkanes from syngas (mixtures of CO and H_2) have been industrialized over the past century, and are used on a megaton scale throughout the world.[4] Nevertheless, the CO produced for these applications derives mainly from fossil resources, through methane steam reforming or dry reforming.[5]

A promising route based on renewable carbon sources through biomass gasification enables the production of CO or syngas.[6] This pathway could enlarge to the gasification of carbon waste streams such as mixtures of plastics or chemicals that cannot be separated.[7] The deoxygenation of biomass by decarbonylation for the production of high value substrates generates a highly concentrated flow of CO.[8]

Moreover, CO_2 conversion to CO is a highly active field of research, which could provide for a more sustainable source of CO in the near future.[9] In particular, large amounts of CO_2 (41 Mt/yr) are produced upon anaerobic digestion of biomass which produces a gas stream with ca. 65% methane and 35% CO_2.[10] Its conversion into CO is well-known through reverse water-gas shit (RWGS), and, examples of electroreduction or photoreduction of CO_2 have been developed in the past decade.[11] Electroreduction would especially be of interest, and if one considers the few main processes that use CO (consuming approximately 55 Mt/year for the production of methanol, butanal, acetic acid and phosgene),[12] a full shift of its production from fossil resources to CO_2 electroreduction would consume approximately 2-3% of the global electric production, which is comparable to the world aluminum or chlorine production.[13]

CO can thus be considered as a key intermediate for the production of chemicals from CO_2 and alternative carbon sources. The wide usage of CO for the synthesis of organic chemicals can be attributed to its specific chemical properties. CO indeed displays a carbenic character, with its HOMO and LUMO being both centred on the carbon atom. Its use for the insertion of a C=O group into covalent bonds is thus favoured compared to using CO_2, where a C–O bond will need cleaving.

[a] *Dr T. Nasr Allah, L Ponsard, Dr E. Nicolas, Dr T. Cantat*
Université Paris-Saclay, CEA, CNRS, NIMBE, CEA Saclay 91191 Gif-sur-Yvette cedex, France
E–mail: thibault.cantat@cea.fr.
† These authors contributed equally

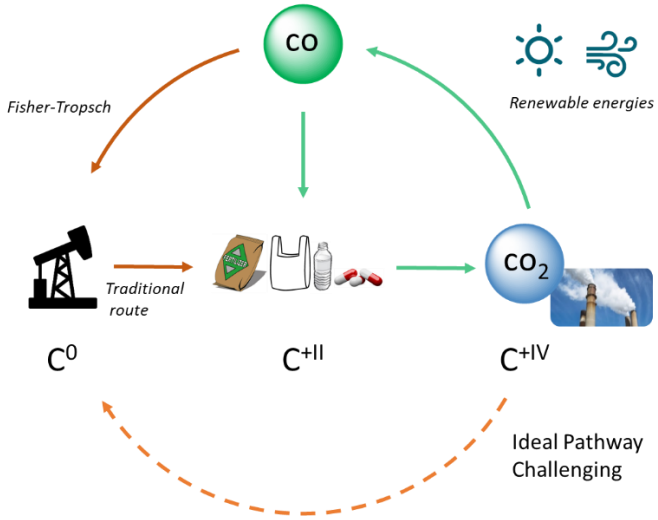
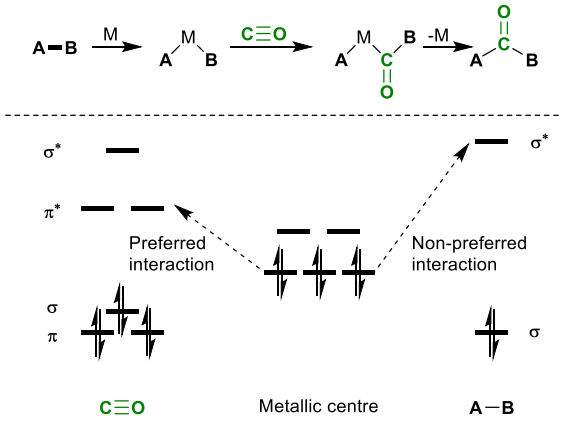


Figure 1: Principle of the use of CO as a C_1 intermediate from CO_2.

Carbonylative cross-coupling reactions have been successfully developed and implemented in organic chemistry, to prepare carbonyl functional groups via the metal-catalyzed coupling of a nucleophile with an electrophile, under an atmosphere of CO. This topic has been widely reviewed over the last years.[14] This synthetic route is however hampered by the formation of stoichiometric amounts of by-products, in the form of inorganic salts that derive from the utilization of the two partners. In contrast, the direct insertion of a C=O group in a σ-bond of an organic molecule is a highly desirable reaction that would avoid the use of strong, usually toxic, oxidants for the synthesis of various C=O containing compounds. In an atom-economy perspective, this method provides the most efficient pathway for the synthesis of various carbonylated derivatives. To this end, the ideal catalytic carbonylation sequence would rely on three steps (Scheme 1, top): the activation of a σ bond, insertion of CO in one metal-ligand bond, prior to an elimination step that provides the carbonylated product. In this scenario, the challenge mainly relies on the selective activation of a σ bond. The presence of low-lying π* orbitals in CO, constrains the utilization of strongly reducing metal ion, which could activate strong σ bonds by oxidative addition processes by accessing the σ* orbital of the substrate (Scheme 1, bottom). In addition, the presence of several σ* orbitals in the substrate, corresponding to different σ bonds, may lead to selectivity issues. To tackle the challenges associated with the carbonylation of σ bonds, catalytic strategies must hence be designed.

In this perspective, we discuss the existing literature relative to the carbonylation of σ-bonds, demonstrating with relevant examples how it is an efficient way to synthesize carbonylated compounds such as esters, ketones, or amides. The chosen examples will highlight the different catalytic strategies engaged to activate the σ-bond, enabling subsequent carbonylation, with a particular focus on mechanisms. First, the carbonylation of polar bonds, more easily activated, is described, starting with O–H and C–O bonds, with an emphasis on an industrially relevant substrate: methanol. Second, existing methods for the carbonylation of N–H and C–N bonds, and related carbon-halogen bonds, is presented. Finally, we review the carbonylation of apolar bonds, starting with dihalogens and H_2, to conclude with the last progresses in the field of the carbonylation of C–C and C–H bonds.



Scheme 1: Top: Ideal carbonylation sequence; Bottom: Preferred orbital interactions between a metal centre and a substrate (A-B), in the presence of CO.

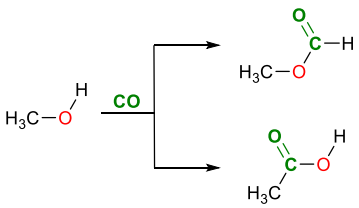
2 Carbonylation of polar substrates

2.1 Activation strategies for the carbonylation of polar σ-bonds

The catalytic carbonylation of polar σ-bonds is the preferred method to reach carbonyl-containing compounds with good atom economy. To unlock the potential of this approach, strategies have been developed that involve the use of various additives. For instance, Lewis acids can coordinate to the oxygen atom of a C–O bond, to facilitate its activation. Alternatively, the *in situ* conversion of strong C–O bonds to a weaker C–I bond is a successful route for the carbonylation of alcohols and ethers, as exemplified in the Monsanto and Cativa processes for the production of acetic acid from methanol (*vide infra*).

2.2 Carbonylation of methanol

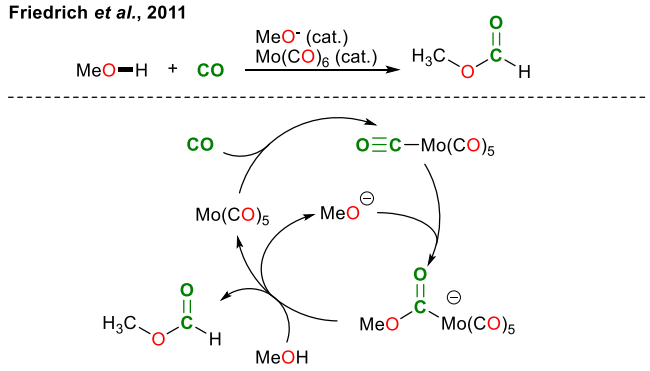
While methanol is currently produced from methane through syngas, this C_1 compound can also be produced from biomass or CO_2 hydrogenation.[12c] In a methanol economy, it is expected to serve as a vector for energy storage, as a liquid fuel for transport and as a feedstock for the downstream production of chemicals.[15] Its carbonylation can lead to two different compounds that are used in industrial processes: methyl formate results from the carbonylation of the O–H bond, while acetic acid is formed upon insertion of CO into the C–O bond (Scheme 2).



Scheme 2: Carbonylation of methanol to methyl formate or acetic acid

Carbonylation of the O–H bond of methanol

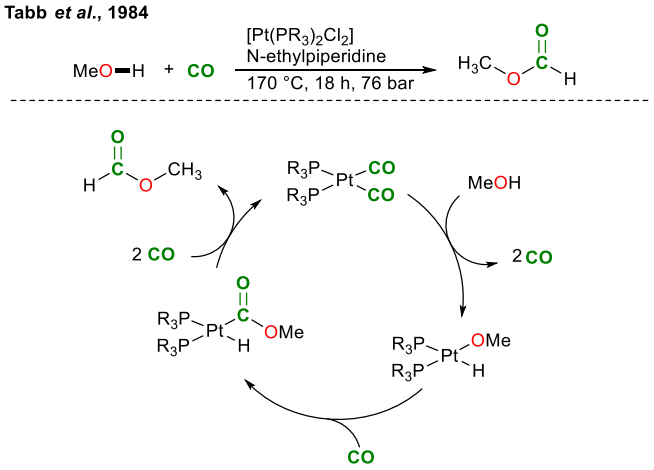
The insertion of carbon monoxide into the O–H bond of methanol leads to methyl formate, a starting material to formic acid, formamide and dimethylformamide.[16] BASF reported in 1926 the first example of a carbonylation of an O–H bond, using sodium methoxide as a catalyst. Efficient carbonylation was observed after a few hours at 80 °C, under 200 bar of CO.[17] It has been shown that the ionization potential of the alkali cation influences the formation of the alkoxide anion and therefore the rate of the reaction, which increased with the size of the alkali ion (Li < Na < K).[18] The catalytic sequence involves the nucleophilic attack of an electron-rich alkoxide onto the carbon atom of CO to form the corresponding acyl anion. The latter is a strong Brønsted base, able to deprotonate methanol to yield methyl formate and regenerate the methoxide catalyst. The chain length of the alcohol and the degree of substitution close to the hydroxyl group have a strong influence on the rate of the reaction: this is confirmed by the poor reactivity of benzyl alcohol, a weaker nucleophile than methanol. Interestingly, the carbonylation of the O–H bond is one of the only examples which does not require any co-catalyst to activate the σ-bond, and is easily cleaved by a strong Brønsted base. Nevertheless, the assistance of a metal carbonyl, such as $W(CO)_6$,[19] $Ru_3(CO)_{12}$,[20] or $Mo(CO)_6$,[21] improves the reaction rate by enhancing the electrophilicity of the CO carbon atom and facilitating the outer sphere nucleophilic attack of the alkoxide anion (Scheme 3).



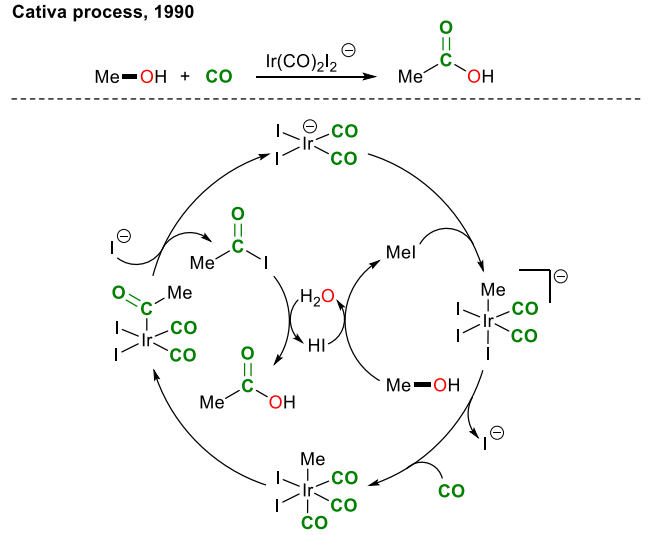
Scheme 3: Catalytic carbonylation of the O–H bond of methanol, assisted by a low valent metal-carbonyl complex ($Mo(CO)_6$)

Tabb *et al.* reported in 1984 the selective carbonylation of methanol into methyl formate, using a platinum-based catalyst, at 170 °C under 76 bar. This catalytic system proceeds *via* a completely different mechanism (Scheme 4),[22] which was studied based on in-situ IR spectroscopy and supported by previous results from the literature.[23] After its in-situ synthesis, the Pt^0 complex $[Pt(CO)_2(PR_3)_2]$ was shown to activate MeOH through an oxidative addition in the O–H bond, to form $[Pt(H)(OMe)(PR_3)_2]$. In that case, an oxidative addition of the metallic centre into the O–H bond was in fact observed, resulting in an inner-sphere mechanism in contrast with the outer sphere nucleophilic attack previously described. The platinum complex $[Pt(H)(C(O)OMe)(PR_3)_2]$ is then formed by insertion under CO pressure. Finally, reductive elimination of methyl formate regenerates the catalyst.[24]

In both types of mechanism reported for the carbonylation of an O–H bond, assistance of a co-catalyst is not required. Indeed, the cleavage of this bond can be easily performed under mild conditions.



Scheme 4: Platinum catalyzed carbonylation of methanol to methyl formate



Scheme 5: The Cativa process for the carbonylation of methanol

Carbonylation of the C–O bond of the methanol

The carbonylation of the C–O bond of methanol leads to acetic acid, used as a solvent or starting material for various industrial fine chemicals, such as vinyl acetate or acetic anhydride.[12b] In 2012, 90% of the global production of acetic acid (ca. 8 Mt/y) was achieved through methanol carbonylation. The direct carbonylation of a σ C–O bond has, to the best of our knowledge, never been observed despite its lower bond dissociation energy (BDE=377 vs. 437 $kJ.mol^{-1}$ for C–O *vs* O–H bonds in MeOH),[25] the activation of the O–H bond being usually kinetically favoured. To circumvent this issue, it is necessary to convert the alcohol to its corresponding iodide, thereby replacing the C–O bond by a weaker C–I bond (BDE=232 $kJ.mol^{-}$

[1]). The latter can be carbonylated through a classical catalytic sequence of oxidative addition / migratory insertion in a metal carbon bond / reductive elimination of the acyl iodide.[16b]

The first catalytic process for the carbonylation of methanol was reported by BASF in 1955, using harsh conditions (680 bar CO, 250 °C) despite the use of cobalt[26] or nickel[27] combined with an iodide source as catalyst, leading to the 90%-selective formation of acetic acid. In the following decades, Rh[28] and Ir[29] have been reported as alternative efficient catalysts. The most used catalytic processes, with Rh (Monsanto process) and Ir (Cativa process) exploit very similar mechanisms and both use iodide promoters.[30] The Monsanto process developed in the late sixties typically runs at 150-200 °C, under 30-60 bar CO, but has been gradually replaced in the late nineties by the energetically less demanding Cativa process that runs at 20-25 bar and 200 °C, using a more stable Ir complex. The mechanism for the Cativa process is an excellent example of the C–O/C–I replacement that helps the carbonylation reaction. First, hydrogen iodide, additive of the reaction, reacts with methanol to form water and methyl iodide. The latter then reacts with $[Ir(CO)_2I_2]^-$ to yield a methyl complex. This complex undergoes a ligand substitution, from iodide to carbonyl, to generate $[Ir(Me)(CO)_3I_2]$, which further evolves to an acyl complex $[Ir(C(O)Me)(CO)_2I_2]$ through a migratory insertion step, constituting the rate determining step, in contrast with the Monsanto process, that is limited by the oxidative addition of methyl iodide to the rhodium centre. Addition/elimination of an iodide on the acyl moiety regenerates the starting catalyst and acetyl iodide, which is hydrolysed to acetic acid, completing the carbonylation sequence.[31] Following this process, methanol is converted to methyl iodide, which is actually carbonylated, taking advantage of its enhanced reactivity with the iridium catalyst (Scheme 5). The addition of a promoter such as a ruthenium salt has been reported to convert the ionic methyl complex $[Ir(Me)(CO)_2I_3]^-$ to the neutral species $[Ir(Me)(CO)_3I_2]$ for which the migration of the methyl is faster.[32]

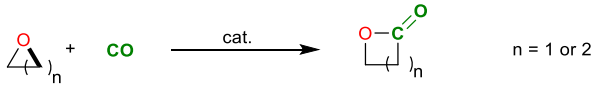
Carbonylation of the C–O bond of higher alcohols

As for methanol, higher alcohols, such as ethanol, are easily produced from biomass, by sugar or starch fermentation (1st generation) or by hydrolysis and fermentation of lignocellulosic material (2nd generation).[33] The production of carboxylic acids by bio-based alcohols carbonylation would then constitute a sustainable and atom-economic pathway. The carbonylation of higher alcohols was explored with a rhodium-based catalyst assisted by hydrogen iodide. Nevertheless, high temperatures are required and the rate of the reaction decreases significantly with a growing chain, where ethanol and propanol were carbonylated 21 and 45 times slower than methanol respectively, effectively preventing the carbonylation of more complex substrates.[34] This observation is consistent with the relative speeds of oxidative addition of the alkyl iodides on rhodium. The development of more reactive, but also acid-free, catalytic systems able to proceed in mild conditions is thus required to extend the scope to longer chain and functionalized alcohols. In parallel, strategies for the carbonylation of activated C–O bonds in milder conditions were developed.

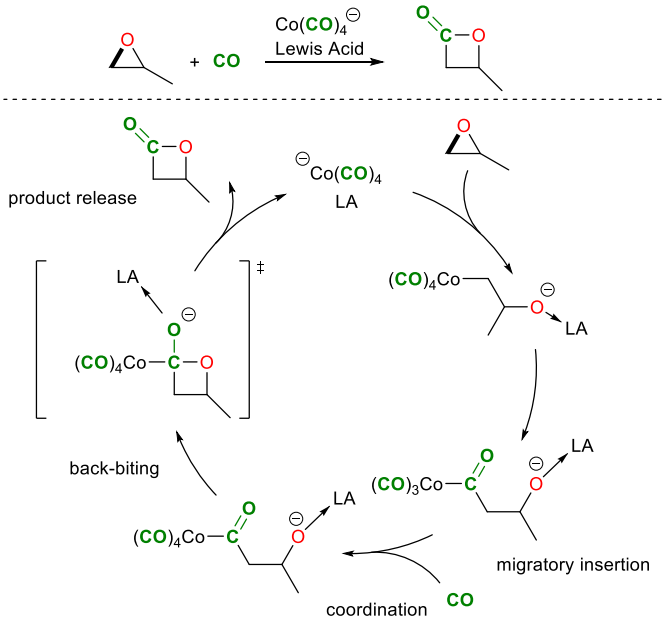
2.3 Carbonylation of activated C–O bonds

Carbonylation of strained cyclic ethers

The direct carbonylation of an endocyclic C–O bond through ring-expansion leads to the corresponding lactone, a class of chemicals commonly used as monomers for the production of biodegradable polyesters.[35] Although the release of the cyclic strain, induced upon insertion of a C=O moiety in the C–O bond, facilitates the reaction, an activation of the σ-bond by a Lewis acid is required.



Scheme 6: Synthesis of lactones by carbonylation of C–O bonds in cyclic ethers



LA = Lewis Acid (BF_3 - Et_2O, Tetraphenylporhyrin Chromium, Phthalocyanine Aluminium, etc)

Scheme 7: Mechanism for the cobalt-catalyzed carbonylation of epoxides

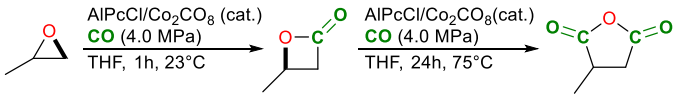
The direct carbonylation of an epoxide through ring-expansion leads to a four-membered lactone, which is an important monomer and a precursor to acrylic acid.[36] Most catalytic systems for this transformation are based on the combination of cobaltate carbonyl $[Co(CO)_4]^-$, with a Lewis acid that is required to activate the σ-bond and allow the opening of the epoxide. Only few Lewis acids have been described. The group of Alper reported the first example with boron trifluoride, yet high CO pressure was required (60 bar of CO).[37] Over the last two decades, the group of Coates has reported that the use of organometallic Lewis acids allows mild reaction conditions, with the possibility to carry out the carbonylation of propylene oxide at 22 °C, with 1 bar CO. The Lewis acid plays a key role in the catalytic cycle, where it improves the kinetics and the selectivity of the reaction, by preventing β-hydride eliminations (leading to acetone, product of the Meinwald rearrangement) and polymerization of the epoxide to polyethers. The best catalyst

reported involved [salphCr][Co(CO)$_4$]. It is able to convert propylene oxide to β-butyrolactone with more than 98% yield under 1 bar of CO.[38]

The same strategy can be applied for the carbonylation of oxetane. The first example has been reported by Alper *et al.* using cobalt carbonyl catalyst assisted by ruthenium carbonyl at 190 °C and 60 atm for 2 days in 1,2-dimethoxyethane to afford γ-butyrolactone.[39] A few years later, Coates *et al.* demonstrated the activity of the [salphAl][Co(CO)$_4$] complex already known for epoxide carbonylation with slightly different reaction conditions (14 bar of CO, 80 °C, 24 h in toluene).[40] Thanks to the activation of the σ-bond by a Lewis Acid, the carbonylation of oxetane proceeds easily under milder conditions. Nevertheless, the carbonylation of larger rings requires harsher conditions or stronger activation: the carbonylation of tetrahydrofuran has been reported to be catalyzed by Co(Ac)$_2$ at 200 °C, under 200 atm of CO/H$_2$ or with the Monsanto catalytic systems (Rh, source of iodine, 230 °C, 130 bar of CO).[41]

Carbonylation of strained cyclic esters

Yoon *et al.*, 2019



Scheme 8: Double carbonylation of epoxide to methylsuccinic anhydride

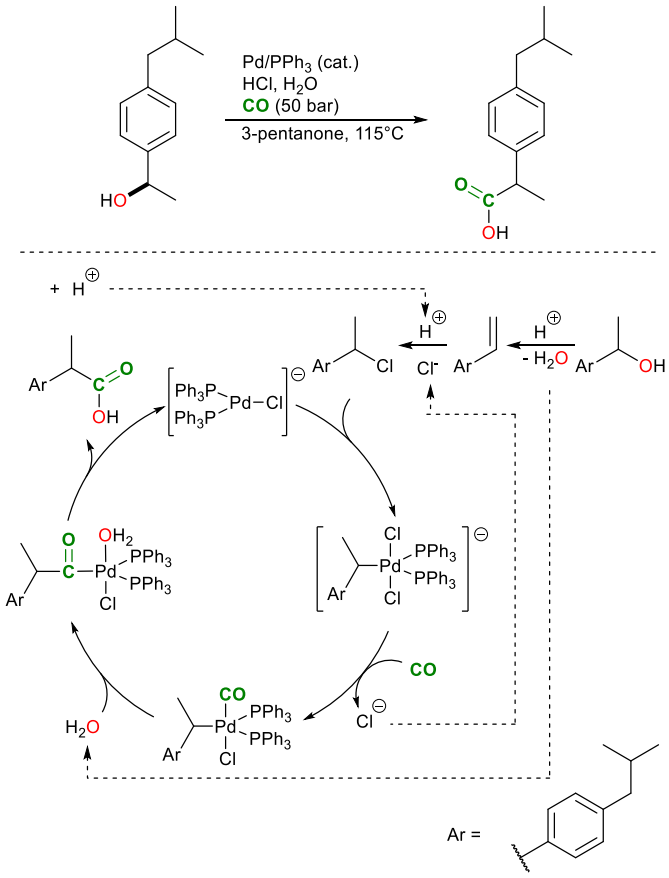
The carbonylation of lactones is a direct pathway for the formation of cyclic anhydrides, widely used as monomers for the production of polyester by copolymerization.[42] This reaction is performed using similar catalytic systems as used for the carbonylation of epoxides, with only slightly different conditions.[40, 43] The C–O bond cleavage of the lactone requires indeed a higher energy than the one of epoxides due to its lower ring strain. For instance, Yoon *et al.* reported very recently that a cobalt carbonyl catalyst associated with an aluminum phthalocyanine co-catalyst could perform the single carbonylation of propylene oxide to the corresponding lactone at room temperature within one hour. When the reaction medium was then heated at 75 °C for 24h, the insertion of a second C=O moiety was observed, leading to formation of methyl succinic anhydride.[44] (Scheme 8)

The carbonylation of β-lactone proceeds *via* similar mechanistic pathway as the carbonylation of epoxides. The carbonylation of lactones with >5 membered rings has however not been observed. In these cases, the cleavage of the other C–O bond in the molecule is favoured, leading to polymerization rather than carbonylation.[45]

Carbonylation of benzylic and allylic C–O bonds

Benzylic and allylic C–O σ-bonds are intrinsically more active than phenyl or alkyl ones because the heterolytic cleavage of the C–O bond generates a stabilized benzylic or allylic cation. Nonetheless, their carbonylation still requires an external activation. Yamamoto et al. described in 1997 the carbonylation of benzylic C–O bond with Pd/PPh$_3$ based catalyst.[46] Despite the already activated C–O bond, the reaction requires not only 90 bar of CO at 90 °C for 44 hours in an aqueous system, but also the use of hydriodic acid. The catalysis proceeds according to a mechanism similar to the Monsanto process, with the intermediate formation of benzyl iodide (*vide supra*, Scheme 5).[47] The carbonylation of 5-hydroxymethylfurfural (HMF) to the corresponding acid was reported by the group of Sheldon, at 70 °C under 5 bar, in the presence of sulphuric acid and a palladium catalyst in water.[48] Interestingly, the carbonylation of the benzylic C–O bond of 1-(4-isobutylphenyl)ethanol has been developed as this results in the formation of 2-(4-isobutylphenyl)propionic acid, also known as ibuprofen (Scheme 9).[49]

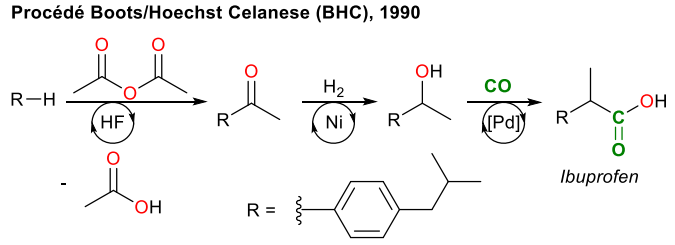
Kim *et al.*, 1999



Scheme 9: Palladium catalysed carbonylation of benzylalcohols *via* the *in situ* formation of a C–Cl bond

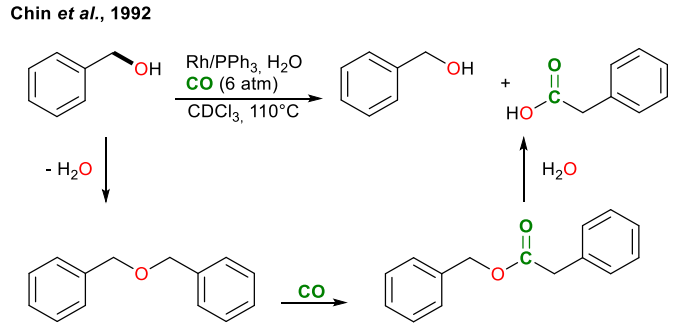
The carbonylation proceeds with a low valent Pd(PPh$_3$)$_2$Cl$^-$ catalyst in acidic conditions, under 50 bar of CO. The acid catalyses the dehydration of the alcohol to form an alkene that can be further converted to benzyl chloride by addition of HCl. The C–OH moiety is thus converted to a C–Cl bond that will actually be carbonylated. The Pd^0 active species then performs an oxidative addition on the benzyl chloride. The coordination of CO with concomitant abstraction of the Cl$^-$ anion followed by migratory insertion with coordination of H$_2$O leads to the acyl intermediate. After reductive elimination and deprotonation steps, the carboxylic acid is obtained and the Brønsted acid regenerated.[49-50]

The atom efficiency of ibuprofen synthesis increased from 40 to 77 % with the development of this reaction. Indeed, the process developed in 1969 (Boots Process) included 6 steps in particular including a carbene precursor that serves to introduce a single methylene group, generating stoichiometric amounts of reagents. In 1980, a new process (BHC Process, Scheme 10) with a very high atom economy was developed, including hydrogenation and carbonylation steps. Recycling the by-product of the first step, namely acetic acid coming from an acetylation would lead to an atom efficiency of 100 %.[51]



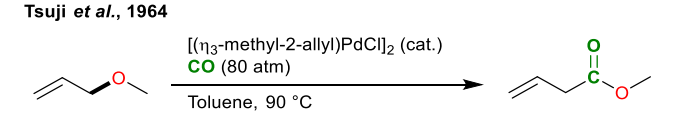
Scheme 10 : Synthesis of Ibuprofen using the highly atom-economic BHC process

An iodide-free catalyst based on Rh/PPh_3 has been described by Chin *et al.* for the carbonylation of benzyl alcohol.[52] The authors suggest that the alcohol is dehydrated, forming the benzyl ether, that is carbonylated into the corresponding ester. The latter is then hydrolysed to relase the benzyl formate and an equivalent of starting material (Scheme 11).

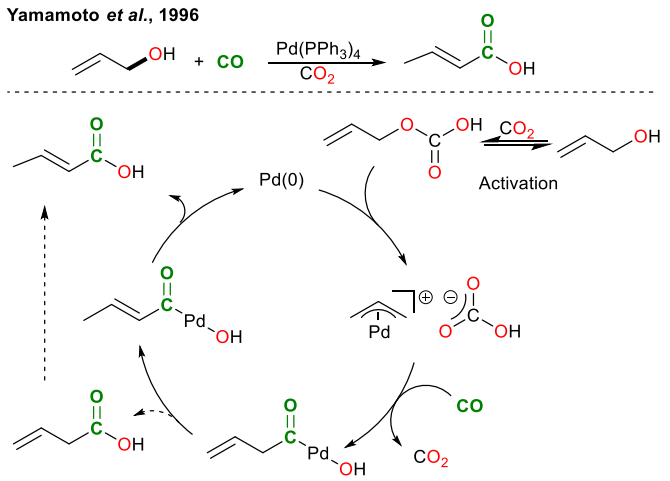


Scheme 11: An iodide-free catalytic system for the carbonylation of benzyl alcohol

In 1964, Tsuji *et al*. reported the carbonylation of allylic compounds, in particular allylic alcohols, esters and ethers, using Pd-based catalysts. The isomerisation of the carbonylated product demonstrated that the reaction proceeds through a π-allylpalladium intermediate that can be easily carbonylated. Nevertheless, the π-allylpalladium intermediate is then quenched by the alcohol used as solvent.[53] The formal carbonylation of allylic methyl ether has later been reported at 90 °C and 80 atm of CO in CCl_4 or toluene with $[(\eta^3\text{-methyl-2-allyl})PdCl]_2$ as precursor.[54] (Scheme 12)

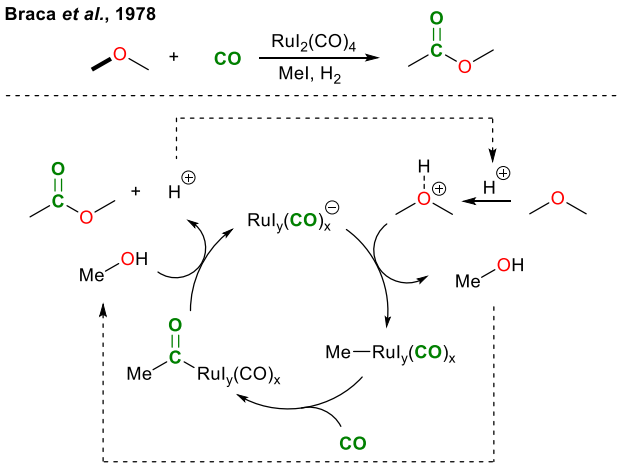


Scheme 12: Catalytic carbonylation of the C–O bond in allylmethylether



Scheme 13: Mechanism of the CO_2-assisted carbonylation of allylic alcohols

In 1996, Yamamoto *et al*. reported the Pd-catalysed carbonylation of the C–O bond of allylic alcohols promoted by CO_2.[55] The allylic ester is obtained in high yield and good selectivity under 50 atm of CO_2 and 50 atm of CO, at 110 °C in DMF. Interestingly, at the same temperature, only traces of the product are observed with 80 atm of CO in the absence of CO_2.[55] According to the authors, CO_2 promotes the C–O bond cleavage by formation of an intermediate carbonate species able to undergo a facile oxidative addition to π-allylpalladium bicarbonate complexes, as shown by *Tsuji et al.* in 1984 with the decarboxylation/carbonylation of allylic carbonates (Scheme 13).[56]



Scheme 14: Acid-assisted carbonylation of DME

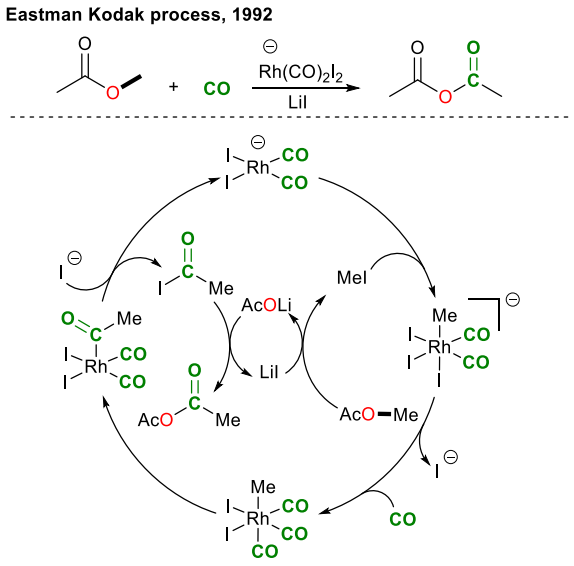
2.4 Carbonylation of unactivated C–O bonds

The C–O bonds are ubiquitous in biomass and especially in the very abundant lignocellulose.[57] In the perspective of fossil resources substitution, the activation of these bonds by carbonylation constitutes a challenge for the degradation of lignin and its conversion to bio-based chemicals. Moreover, the synthesis of esters from unactivated ethers through direct carbonylation could be an atom-economic way to reach these industrially relevant compounds.[58] The main challenge resides

however in the activation of the starting ethers, which feature extremely inert C–O bonds.

Carbonylation of dimethyl ether (DME)

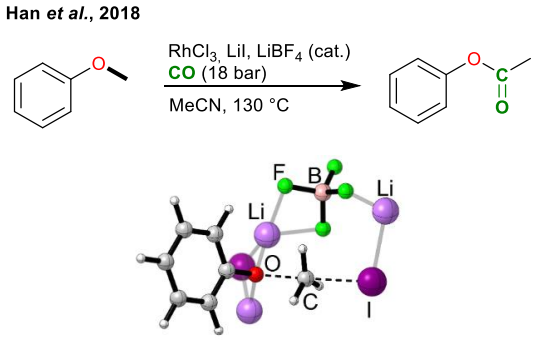
The carbonylation of DME to methyl acetate can be performed using similar catalytic systems as those used in the first examples for the carbonylation of the C–O bond of methanol. Indeed, the first examples on the carbonylation of DME utilized Ni and I_2, NiI_2 or FeI_2 at about 200 °C and 100-270 bar CO to reach low yields of 10-50%.[41a, 59] In 1978, Braca *et al*. reported a ruthenium catalytic system with iodide and hydrogen promoters, both required for catalytic activity (Scheme 14).[60] The authors suggest an acidic activation of the ether followed by a transfer of the methyl group on the ruthenium centre, the acid being generated through hydrogenolysis of MeI. After carbonylation of the ruthenium alkyl complex, the acyl group is transferred to methanol, releasing methyl acetate and a proton. Although the mechanism proposed by the authors do not rationalize the role of iodine in the catalytic cycle, one may suggest a mechanism similar to the one described for the Monsanto and Cativa processes or the Eastman-Kodak process (see below Scheme 15). DME could react with an iodide source to form methyl iodide, which would undergo an oxidative addition on the metallic centre and is further carbonylated to generate the acyl iodide. The latter is then converted to methyl acetate through reaction with methanolate and regenerate the iodide source.



Scheme 15: Rhodium catalysed carbonylation of methyl acetate

Nevertheless, the dimethyl ether being gaseous at room temperature, heterogeneous catalysis, and gas phase reactions are preferred for the carbonylation of DME to methyl acetate.[61] Methyl acetate can be carbonylated further to generate acetic anhydride, a chemical widely used in industrial chemistry for acetylation reactions or as a dehydration agent.[62] This reaction is catalyzed by rhodium complexes assisted by alkyliodide promotors (Eastman Kodak Process).[63] The mechanistic pathway is very the similar to the Cativa process, the only difference being that the reaction rate significantly increases upon using LiI instead of HI.[64] Kinetic experiments demonstrated that the lithium cation plays a key role in the two reactions involved in the second catalytic cycle. Both the formation of methyl iodide from lithium iodide and methyl acetate, and the formation of the acetic anhydride from the acetate and the acyl iodide are highly favoured in presence of an alkali cation, and especially lithium.[32]

Example of carbonylation of an aryl methyl ether



Scheme 16: C-O bond carbonylation of Phenyl methyl ester. Top: reaction conditions. Bottom: Assistance of LiI and $LiBF_4$ in the O–Me activation.

A significant part of the C–O bonds contained in lignin are aryl-alkyl-ethers and more specifically aryl-methyl-ether bonds.[57] The direct carbonylation represents an appealing method for the synthesis of valuable chemicals. Very recently, the group of Han reported the carbonylation of an aromatic ether bond, using a rhodium catalyst assisted by lithium iodide and lithium tetrafluoroborate (Scheme 16, top).[65] The rhodium based complexes, assisted by iodide salts, are known to be active in carbonylation reactions, as shown in the Monsanto process. Han *et al.* demonstrated that the joint assistance of LiI and $LiBF_4$ allows the activation of the Me–O bond in the aromatic ether by reducing the energy barrier for C–O bond cleavage for producing CH_3I (Scheme 16, bottom). This elegant example have previously been used for the carbonylation of methoxy groups in lignin to produce high purity acetic acid from pure CO or from CO_2 produced *in-situ* by RWGS.[66]

To the best of our knowledge, no other example of the carbonylation of an unactivated ether has been reported so far.

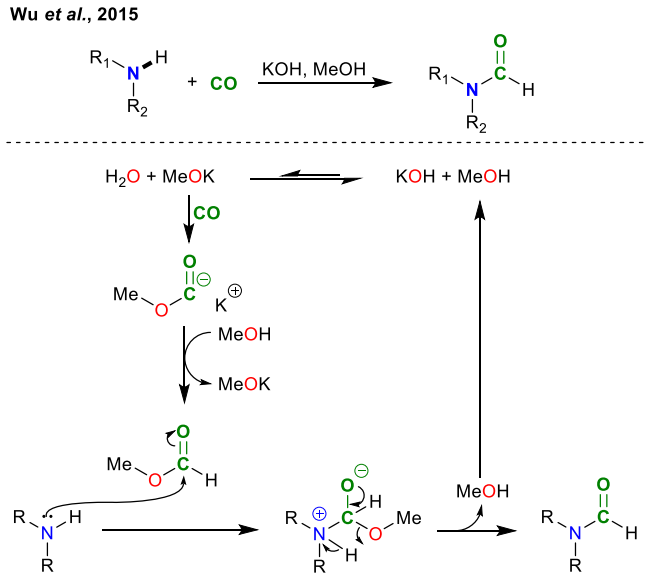
Conclusion on the carbonylation of C–O bond

The carbonylation of C–O bonds has been widely studied over the last century and is used nowadays at industrial scale. Various strategies depending on the nature of the σ bond have been developed to face the challenge of their carbonylation. The carbonylation of O–Me bonds is generally performed using rhodium catalysts together with an iodide source, palladium-based catalysts are effective for the allylic and benzylic substrates, and cobalt catalysts assisted by a Lewis acid are preferred for the carbonylation of cyclic substrates. Reactions are however usually involving high pressures and temperatures, and further development is needed in order to be able to carbonylate more sensitive and polyfunctionalized substrates such as lactic acid, and to use less demanding conditions. A deep understanding of the mechanisms involved and of the

requirements for an optimization of the catalytic systems will allow discovery of new reactivities working in mild conditions.

2.5 Carbonylation of N–H bonds

Using CO as a formylating agent is the most efficient way to synthesize formamides from readily available primary or secondary amines. In 1966, Hirota *et al.* demonstrated that copper salts catalyse the carbonylation of alkylamines, under 60 bar CO at 140 °C.[67] Moreover, many others metals have shown to be efficient in this reaction, including Rh,[68] Fe,[69] Ni,[70] Zn[71] and Ru.[72]



Scheme 17: Mechanism of KOH/MeOH catalyzed carbonylation of amines.

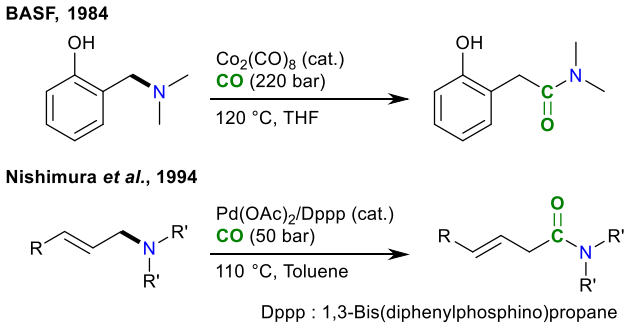
Transition metal-free catalysts are also efficient for the carbonylation of primary and secondary amines. For example, the use of NaOMe has been described in several patents dealing with the carbonylation of dimethylamine to dimethylformamide (DMF).[73] The use of heterocyclic carbenes and ionic liquids based on imidazolium salt has also been considered.[74] In 2015, Wu *et al.* developed a new catalytic system using inorganic bases (KOH, NaOH, Na_2CO_3, K_2CO_3) as catalysts for the carbonylation of a significant number of substrates under 10 bar of CO at 110°C.[75] The mechanism actually involves the previously presented carbonylation of methanol to methyl formate, with the latter product undergoing an amidification reaction that liberates MeOH and the formamide.

2.6 Carbonylation of activated C–N bonds

Carbonylation of benzylic and allylic C–N bonds

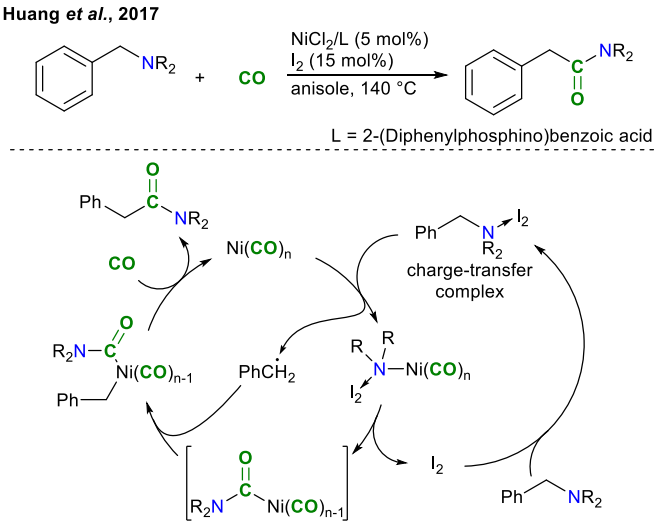
The carbonylation reaction of acyclic amines was first developed on activated amines. Indeed, in 1984, a BASF patent described the selective carbonylation of the benzylic position of the 2-((dimethylamino)methyl)phenol to yield 2-(2-hydroxyphenyl)-acetamide (Scheme 18).[76] [$Co_2(CO)_8$] was used as a catalyst under 220 bar of CO and 120°C.

In the same way, Nishimura showed that allyl amines can be carbonylated into α,β-unsaturated amides by using palladium complexes supported by phosphines under 50 bar of CO at 110 °C.[77] (Scheme 18) The optimization of the reaction conditions led to the development of an efficient strategy for allyl amines carbonylation under only 10 bar of CO and at 120 °C, using [Pd(XantPhos)Cl_2] as a catalyst.[78] A mechanistic study from the group of Nishimura showed the implication of a π–allyl palladium intermediate that facilitates the C–N bond activation.[77b] Nevertheless, only the linear product is accessible by this reaction.



Scheme 18: Benzylic and Allylic C–N bond carbonylation

More recently, Huang *et al.* developed an elegant carbonylation of benzylamines with nickel catalyst and iodine (Scheme 19).[79] Although the mechanism is not fully understood, the authors proposed that iodine activates the benzylamine, through the formation of an intermediate charge-transfer complex. The electron-transfer to iodine facilitates the cleavage of the C–N bond by the Ni-complex forming a radical-containing complex. After migratory insertion and further reaction of the benzyl radical on the Ni-center, a reductive elimination step delivered the amide and regenerated the Ni-catalyst.



Scheme 19: Benzylamine carbonylation through formation of a charge-transfer complex

Carbonylation of aziridines

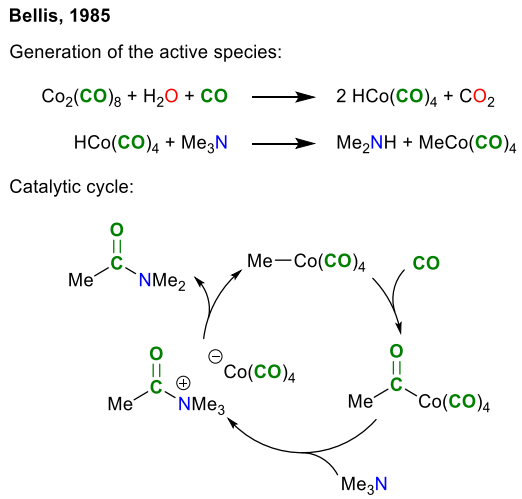
The direct formation of lactams from cyclic amines such as aziridines, azetidines, pyrrolidines and related compounds occurs with much more ease. Indeed, the direct carbonylation of such compounds has been observed under mild conditions in

the sole presence of cobalt carbonyl or other carbonyl complexes.[80] For example, the carbonylation of *N*-methyl-2-phenylazetidine was catalyzed by $[Co_2(CO)_8]$ under 3.5 bar of CO at 90 °C, when the carbonylation of the corresponding oxetane required the joint use of of an activator (salen Al complex) and harsher conditions (14 bar CO).[40]

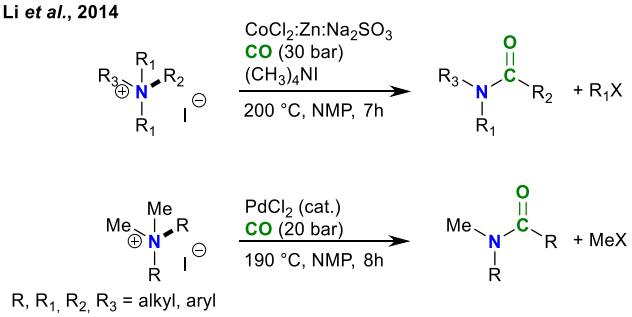
2.7 Carbonylation of alkyl and aryl amines

Although the catalytic carbonylation of several C–N bonds are known when the amines are activated, only few methods have been described starting from tertiary non-activated amines.[81] This observation can be rationalized by the fact that the carbonylation of a tertiary amine requires the breaking of a C–N bond to insert CO. However, the C–N bonds in allylic and benzylic molecules are more reactive than in simple alkylamines, this is explained by comparing their respective BDEs: while the BDE of the benzyl–$N(CH_3)_2$ linkage is about 255 kJ.mol^{-1}, it reaches 272 kJ.mol^{-1} for CH_3–$N(CH_3)$Ph. In 1968, a Shell patent showed that $[Co_2(CO)_8]$ can catalyse the carbonylation of trimethylamine (TMA) to DMF under harsh conditions (T>150 °C, P(CO) > 85 bar and 1 eq of water).[82] In 1984, Bellis optimized the previous Shell process for TMA carbonylation, by using catalytic amounts of water under harsh condition (i.e 0.5-2.0 mol of water per mol of $[Co_2(CO)_8]$, T> 250 °C, P(CO) > 85 bar), however at the cost of an increased reaction temperature.[83] The use of water as promotor of the reaction is explained by the supposed *in situ* formation of $[HCo(CO)_4]$ (pKA = 8.3).[84] This hydride cobalt carbonyl complex might indeed react as a weak acid and promote the activation of the C–N bond by protonating the amine, to form $[Co(CH_3)(CO)_4]$ (Scheme 20).

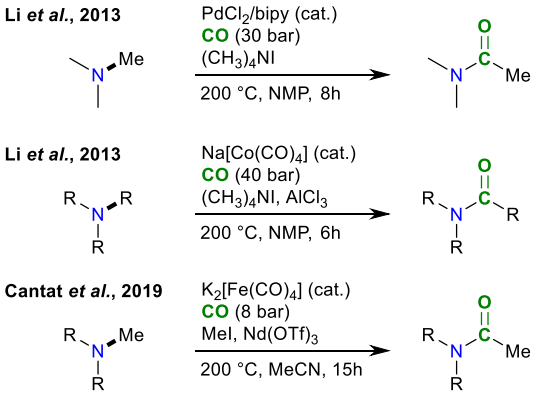
A similar strategy has been demonstrated in 2014 for the carbonylation of amines, when Li's group developed a carbonylation process using quaternary ammonium compounds in the presence of *in situ* prepared nucleophilic catalysts based on Pd^0 and Co^{-I}.[85] These reactions were performed under a CO pressure over 30 bar, for most examples, and high temperatures (> 190 °C). Finally, the scope of the reaction remained limited to a few examples. Co and Pd catalysts have subsequently been used for the carbonylation of tertiary amines such as trimethylamine. The use of $PdCl_2$ coordinated by 2,2'-bipyridine assisted by an ammonium iodide salt as iodide source made it possible to obtain good yields of dimethylacetamide.[86] Li's group also described the catalytic carbonylation of trimethylamine with $Na[Co(CO)_4]$, in presence of a iodinated ammonium combined with a Lewis acid as promotor (Scheme 22), which can be extended to the carbonylation of some tertiary, aromatic and aliphatic tertiary amines.[87] This synthetic route greatly improves the atom-economy of the carbonylation reaction of tertiary amines. Very recently, our group used the dianion $K_2[Fe(CO)_4]$ to perform the carbonylation of various amines at low pressure (8 bar), in the presence of MeI as an activating agent and $Nd(OTf)_3$ as a co-catalyst.[88] The requirement of an iodide promotor indicates that the catalyst does not directly activates the C–N bond, but that the latter is converted to a more reactive C–I bond.



Scheme 20: Proposed mechanism for the carbonylation of amines with low valent cobalt carbonyl complexes



Scheme 21: Carbonylation of alkylammonium salts as described by the group of Li



Scheme 22: Iodide promoted, Pd, Co and Fe-catalyzed, carbonylation of alkylamines

Conclusion on the carbonylation of C–N bonds

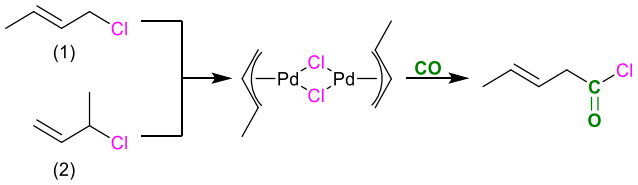
The traditional routes for the synthesis of amides generally involve chlorinating or coupling agents that are responsible of the generation of by-products and, in turn, a low atom efficiency. The direct synthesis of amides through carbonylation of the corresponding amines is atom-economic and would allow for an easy generation of amide functionalities. Activation of the C–N bond by an external additive is often required; the main strategies reported so far implicate iodide salts promoting the formation of an ammonium intermediate that is more easily

carbonylated. Nevertheless, the development of new activation strategies would enlarge the scope of the substrates, especially aiming at directly reacting with the C–N bond in amines. In this perspective, one may explore bio-mimetic pathways, taking inspiration from the Wood-Ljungdahl synthesis of acetic acid, in which cobalamine promotes the carbonylation of a methyl-folate intermediate by direct activation of a C–N bond.[89]

2.8 Carbonylation of C–X bonds (X=F, Cl, Br, I)

The synthesis of acyl halides is usually performed from the corresponding carboxylic acids, which are halogenated with toxic reagents such as phosgene, thionyl chloride, or phosphorus tri- or pentachloride. Their direct formation by carbonylation of the corresponding organic halide would significantly increase the atom efficiency of their synthesis. The challenge in this alternative pathway is two-fold: the catalysts used need to be able to activate σ C–X bonds, but the newly formed acyl halide must not react with other species present in the reaction medium.

Carbonylation of allylic C–X bonds



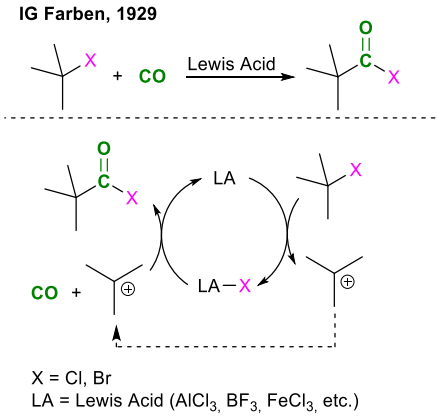
Scheme 23: Carbonylation of allyl chlorides with palladium complexes

The activation of allylic carbon-halogen bonds is made possible by the use of nucleophilic catalysts through an S_N2 mechanism or an oxidative addition. The favourable thermodynamics of the oxidative addition of the Pd catalyst leading to the formation of a stable π-allyl intermediate facilitate the C–Cl bond cleavage (Scheme 23). This was demonstrated by Whitfield *et al.* who described the formation of a π-allyl intermediate upon carbonylation of the 1-chlorobut-2-ene (1) or the 3-chlorobut-1-ene (2) to pent-3-enoyle, limiting the scope of this reaction.[90]

Carbonylation of aliphatic C–X bonds

First results demonstrating the feasibility of the carbonylation of alkylhalide derivatives were obtained with *tert*-butyl chloride.[91] The synthesis of the pivaloyl halide was possible in the presence of a stoichiometric amount of a Lewis acid (i.e. $AlCl_3$, BF_3, $FeCl_3$) or a Brønsted acid (RSO_3H) under a high CO pressure (> 200 bar). The reaction mechanism begins with the abstraction of the halogen atom *via* a heterolytic cleavage of the C-X bond according to an S_N1 type mechanism leading to the formation of a stabilized tertiary carbocation (Scheme 24).

CO then reacts with the carbocation to generate an acylium intermediate, which is trapped by the halide anion to yield the corresponding acyl halide. The C–X activation step is reminiscent of the Koch reaction, that is used to produce carboxylic acids from alkenes and carbon monoxide at industrial scale (150000 t/year in 2003).[92] This strategy has been used catalytically for the synthesis of a haloacetyl halides *via* the reaction between CO (900 bar), carbon tetrachloride and 10 mol% of $AlCl_3$ at 200 °C.[91] However, the reaction requires harsh reaction conditions and affords only low yields and a low selectivity. The carbonylation of primary and secondary alkyl halides has been described to occur in the presence of strong Lewis acids such as $AlCl_3$, under 50 bar of CO at 50 °C.[93]



Scheme 24: Lewis Acid catalyzed carbonylation of tertiary alkyl halides

Conclusion on the carbonylation of C–X bonds

Acyl halides are common starting materials in organic synthesis. Their production from the corresponding halide by carbonylation significantly reduces the amount of by-products generated by the use of chlorinated agent. Nevertheless, very few examples of direct carbonylation of C–X bonds are reported in the literature, and they require both harsh conditions and stoichiometric amounts of Lewis acids. They are moreover mostly limited to tertiary alkyl halides as substrates. The carbonylation of halides in mild conditions with a catalytic system would improve the atom-economy of the synthesis of organic compounds. An interesting route would be to use the knowledge gathered in the carbonylation of C–O and C–N bonds that often uses C–I as reactive intermediates, and transfer it to synthesis of acyl halides. The main challenge lies however in the intrinsic reactivity of the acyl halides, which must be controlled in order to synthesize them form such routes.

2.9 Perspectives in the carbonylation of polar bonds

The carbonylation of polar bonds is an active field of research, for which a number of reactions are used at industrial scale. Most catalytic strategies rely however on the use of Lewis acid co-catalysts that are required to activate the σ bond, or iodide sources utilized to generate a more reactive intermediate. The latter strategy suffers from major drawbacks, including a low functional group tolerance, and the use of variable amounts of additives, which have to be recycled or disposed of at the end of the process. New activation pathways need to be found, to widen the scope of reactive substrates without resorting to co-catalysts. Moreover, activation of highly stable bonds such as those in ethers remain a challenge, but their carbonylation would lead to greener and atom-economic routes towards complex, high-value chemicals.

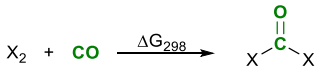
3 Carbonylation of non-polar substrates

3.1 Challenges in the activation of non-polar substrates

The carbonylation of polar substrates through transition metal catalysis is a challenge due to selectivity issues and inherent moderate reactivity of some substrates such as amines. Still, these can be overcome using various promotors as shown above. The carbonylation of non-polar substrates is, however, a long-standing challenge. Indeed, the lack of reactivity and the ubiquity of a number of non-polar bonds in a molecule, such as C–H or C–C bonds, poses unsolved efficiency and selectivity issues. In addition, the stability of such inert bonds may present thermodynamic limitation, as the inherent exotherm of the carbonylation reaction can be low, and in some cases disfavoured (*vide infra*). High pressures or temperatures will then be required in order to shift the thermodynamics of the reaction towards a productive carbonylation.

3.2 Dihalogens

Table 1: Exergonicity of the carbonylation of dihalogens

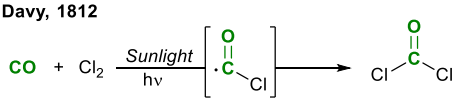


Dihalogen X_2	ΔG_{298} (kJ.mol^{-1})
F_2	-487.3
Cl_2	-68.7
Br_2	+6.1
I_2	+68.3

Data taken from ref [94]

The carbonyl halide (*i.e.* $C(O)X_2$) derivatives constitute a class of important compounds, frequently used in halogenation and acylation reactions. The change in Gibbs free energies (ΔG_{298}) associated with the carbonylation of dihalogens is however favourable for F_2 and Cl_2 while the reaction is endergonic for Br_2 and I_2 (Table 1), preventing the synthesis of $C(O)Br_2$ and $C(O)I_2$, the latter being known to spontaneously decarbonylate at room temperature.[94] The first carbonylation of a dihalogen was reported by Davy in 1812, who described the photochemical synthesis of phosgene by exposing a mixture of CO and Cl_2 to the sun (Scheme 25).[95] The involvement of a radical mechanism was confirmed in 1965 by a trapping experiment of the radical [COCl].[96]

Davy, 1812



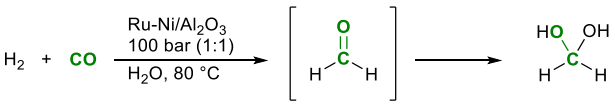
Scheme 25: Carbonylation of Cl_2 by exposition of a mixture of CO and Cl_2 to the sun.

The carbonylation of F_2 to form carbonyl difluoride was performed using a heterogeneous copper catalyst, and is driven by the formation of strong C–F bonds.[97] The main observed impurity is CF_4, obtained from the disproportionation of the product. The carbonylation of Br_2 has been much less studied than its fluorinated and chlorinated counterparts because of less favourable thermodynamics.[98] Nonetheless, $C(O)Br_2$ is liquid at room temperature, and more easily manipulated. The first claim for its preparation was made in 1863 by Schiel, by exposing a mixture of CO and Br_2 vapours to sunlight, similar to the previously described synthesis of phosgene.[99] Vogt further improved it, demonstrating that the high-pressure reaction between CO and Br_2 in the presence of flint glass in sealed tube at >600 °C allows for the formation of $C(O)Br_2$.[100] Finally, $C(O)I_2$ has never been isolated due to its intrinsic reactivity.[94] It has sometimes been proposed as a reaction intermediate, but was never directly synthesized from CO and I_2.[94]

3.3 Carbonylation of dihydrogen

Formaldehyde is an important molecule in the chemical industry where it is used in the manufacture of cosmetics, polymers, glues or organic synthesis.[101] The current industrial synthesis of formaldehyde relies on the partial oxidation of methanol with oxygen (Formox process). The production of CH_2O *via* this industrial process has several limitations related to the prior synthesis of methanol, the use of harsh conditions for the oxidation of methanol and a limited atom-efficiency (>50 %).[102] The carbonylation of H_2 would be the best and most direct pathway, and highly desirable if performed from biomass-derived syngases, because it would avoid the energy loss inherent in the Formox process, and presents an atom-efficiency of 100 %. It has not been considered at industrial scale because of unfavourable thermodynamics: in the gas phase, at room temperature, the exergonicity of the reaction is only 35 kJ.mol^{-1}, and increases with the temperature. Recently however, the group of Tanksale demonstrated that the use of Ru–Ni/Al_2O_3 in water at 80 °C under 100 bar of a 1:1 CO/H_2 mixture yielded 4.55 mmol.L^{-1}.g_{cat}^{-1} after 72 h at 353 K, with 100 % selectivity (Scheme 26). The equilibrium shift towards formaldehyde is due to its hydration and further conversion into methylene glycol.[103]

Tanksale *et al.*, 2015



Scheme 26: Carbonylation of dihydrogen for the formation of formaldehyde.

3.4 Carbonylation of C–C and C–H bonds

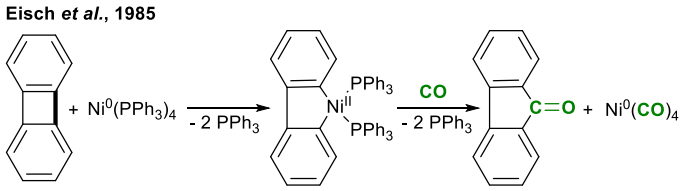
The synthesis of ketones and aldehydes through the insertion of CO in C–C and C–H bonds would be of the utmost importance, as it would allow for atom economic syntheses and avoid current oxidation routes.[104] It could also complement hydroformylation approaches and enable the production of benzaldehyde from benzene. However, the activation of C–C and C–H bonds represents a significant challenge alone, and the oxidative addition of a metallic fragment in a C–C or a C–H bond requires unsaturated, electron-rich complexes, for which CO coordination is usually favoured.

Carbonylation of strained cycles, including cyclopropanes and activated cyclobutanes

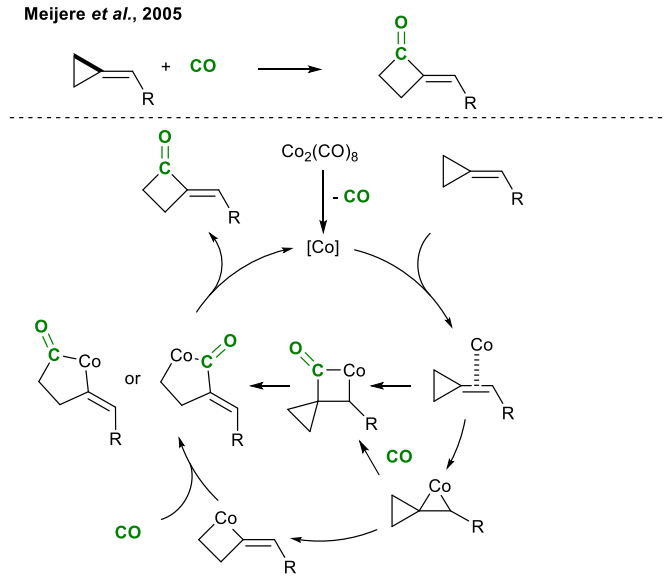
The carbonylation of strained cycloalkanes has been mostly performed in stoichiometric conditions. In 1985, the team of

Eisch described the stoichiometric oxidative addition of a Ni^0 complex into the C–C bond of biphenylene to form the corresponding metallacycle.[105] After bubbling CO on the cyclic intermediate, a yield of 89 % of 9-fluorenone was obtained. The reduced Ni^0 complex is however trapped by CO, preventing the closure of a catalytic cycle (Scheme 27). The same strategy has been used by other groups on cyclopropane derivatives with Fe[106] and Cr[107] complexes.

The first catalytic example of a C–C bond carbonylation of cyclopropane was described in 1980 with 0.3 mol% of $[Rh(CO)_2Cl]_2$ under 50 bar of CO and 160 °C, yielding 3.6% of cyclobutanone.[108] More recently, the catalytic use of $[Co_2(CO)_8]$ has allowed *via* a [3 + 1] co-cyclization of methylenecyclopropane derivatives with CO under milder condition (1 atm of CO, 50 °C).[109] The coordination of the methylene fragment to the cobalt centre allowed for an easier activation of the endocyclic C–C bond, leading to the formation of a cobaltocyclopropane moiety that undergoes carbonylation and further reductive elimination to release the cyclobutanone (Scheme 28).



Scheme 27 : Carbonylation of the biphenylene by a nickel complex

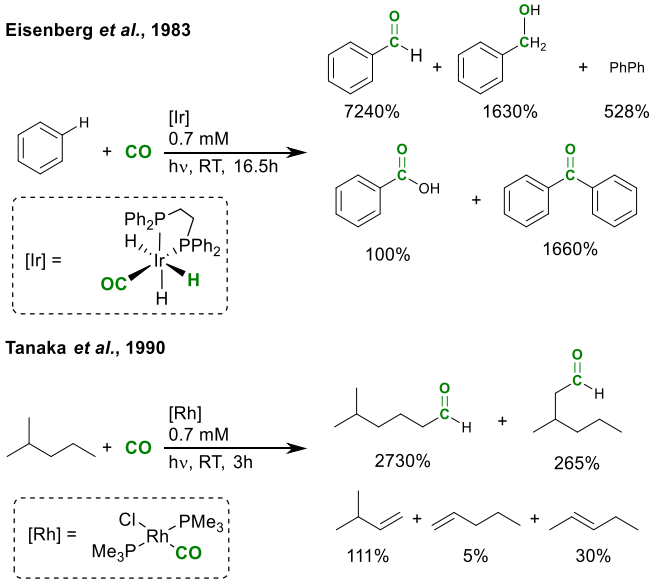


Scheme 28: Mechanism for the carbonylation of methylenecyclopropane

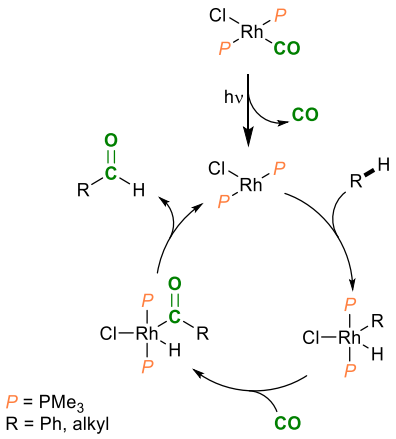
Carbonylation of aromatic and aliphatic C–H bonds

In 1983, Eisenberg *et al.* described the use of an iridium carbonyl hydride complex, $[IrH_3(CO)(dppe)]$, which, under light irradiation and under 1 atm of CO or syngas, converted benzene (used as a solvent) to benzaldehyde.[110] (Scheme 29) The strategy was extended to other catalysts based on Rh and Ru under irradiation, leading to similar results.[111] Despite a promising selectivity, yields were low. This low efficiency is linked to many factors including unfavourable thermodynamics ($\Delta G° = +1.7$ kcal.mol^{-1}), and the formation of a number of side-products.[112]

Tanaka demonstrated that a Vaska-type Rh^I complex $[RhCl(CO)(PMe_3)_2]$ catalyzes the carbonylation of cyclic and linear alkanes, while having a high selectivity for terminal C-H bonds.[112] The proposed mechanism involves the formation of a 14-electron complex, $[RhCl(PMe_3)_2]$ formed upon photoactivation of the starting complex (Scheme 30). This unsaturated species activates the C–H bond of benzene (or of the alkane), to form an hydrido aryl (or hydrido alkyl) complex. Under CO, carbonylation of the Rh–C bond can occur, and further reductive elimination leads to the corresponding aldehyde and regeneration of the active species.[113] In this case, the photolysis of CO from the starting complex allows the generation of a sufficiently reactive complex that can react with C–H bonds, closely related to species already described by Bergman or Jones.[114]



Scheme 29: Rhodium catalyzed photocarbonylation of C–H bonds. Percentages calculated compared to the catalyst.



Scheme 30: Mechanism for the photocatalytic carbonylation of C–H bonds

A second approach developed by the group of Olah and Prakash utilizes superacids. $HF{\cdot}BF_3$ is indeed able to protonate CO and generate the linear carboxonium ion HCO^+. The latter is a superelectrophilic formylating agent that can react with the C–H bond of isobutane and form pivalaldehyde. An acid-catalyzed rearrangement leads further to methyl isobutyl ketone.[115] An analogous approach was used for the carbonylation of toluene to *p*-tolualdehyde in pure triflic acid by the group of White.[116] Yet, extension of this strategy to more complex molecules is not trivial due to the sensitivity of functional groups towards super-acids.

4 Conclusions and perspectives

Over the course of this perspective, we showed that the direct carbonylation of σ bonds can be highly atom economic for the synthesis of high-value carbonyl-containing chemicals. Although a myriad of carbonylation reactions have been developed using transition metal catalysts, the carbonylation of σ bonds remains a significant challenge due to the inert nature of σ bonds. Successful examples of such transformations rely on either the use of Lewis acid co-catalysts or the utilization of alkyliodide promotors. These strategies allow the carbonylation of a number of simple molecules such as methanol, DME or anisoles, but more complex substrates remain a challenge. The activation and subsequent carbonylation of very inert bonds such as C–H or C–C bonds is poorly described so far, in part due to the inherent endergonicity of the reaction.

Further research in the field should focus on two main points. On one hand, developing additive-free and selective routes would allow the carbonylation of complex substrates, leading to an extension of the scope of such reactions. On the other hand, an effort on the carbonylation of unactivated σ bonds will allow for the spreading of these greener routes to the formation of high-value chemicals in a simpler and more efficient way compared to the current oxidation pathways. To perform this deed, different fields of chemistry such as photochemistry, radical chemistry or electrochemistry will have to be involved, to overcome the difficulties that have been outlined in the carbonylation of σ bonds. The main challenges will deal with the design of catalysts able to carbonylate poorly reactive σ bonds, while leaving a number of functional groups untouched. A particular focus should be made on functional groups coming from bio-based substrates, such as aldehydes, alcohols or carboxylic acids.

These substrates can be used as useful carbon sources for the production of high-value chemicals, but the question will remain of the sourcing of CO. In the perspective of substituting fossil resources in the chemical industry, it appears as an appealing alternative carbon source, possibly coming from CO_2 (electro)reduction or biogas gasification (See Introduction for details). A challenge in bringing these reactions incorporating green CO in bio-based chemicals to an industrial scale will also lie in mastering the coupling of such processes, e.g. the production and utilisation of CO, with new catalysts able to cope with the presence of contaminants in the gas stream.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

For financial support of this work, we acknowledge the CEA, CNRS, and the European Union (Carbon4PUR project, Grant agreement n°768919; ERC project ReNewHydrides, Grant agreement n°818260).

Notes and references

1 dena (German Energy Agency), *Feedstocks for the chemical industry*, 2019.
2 (a) Food and Agriculture Organization, *Journal*, 2019; (b) A. Bazzanella and D. Krämer, *Technologies for sustainability and climate protection – chemical processes and use of co_2*, DECHEMA, 2019.
3 J.-B. Peng, H.-Q. Geng and X.-F. Wu, *Chem*, 2019, **5**, 526-552.
4 J. Hagen, *Industrial catalysis: A practical approach*, John Wiley & Sons, 2015.
5 Carbon monoxide, J. Bierhals, in *Ullmann's encyclopedia of industrial chemistry*, 2001.
6 (a) 6 - biomass gasification, Y. Neubauer, in *Biomass combustion science, technology and engineering*, ed. L. Rosendahl, Woodhead Publishing, 2013, pp. 106-129; (b) A. Molino, S. Chianese and D. Musmarra, *J. Energy Chem.*, 2016, **25**, 10-25.
7 (a) G. Lopez, M. Artetxe, M. Amutio, J. Alvarez, J. Bilbao and M. Olazar, *Ren. Sust. Energy Rev.*, 2018, **82**, 576-596; (b) C. Block, A. Ephraim, E. Weiss-Hortala, D. P. Minh, A. Nzihou and C. Vandecasteele, *Waste and Biomass Valorization*, 2019, **10**, 483-509.
8 (a) G. J. S. Dawes, E. L. Scott, J. Le Nôtre, J. P. M. Sanders and J. H. Bitter, *Green Chem.*, 2015, **17**, 3231-3250; (b) X. Zhang, F. Jordan and M. Szostak, *Organic Chemistry Frontiers*, 2018, **5**, 2515-2521; (c) A. Börner and R. Franke, *Hydroformylation: Fundamentals, processes, and applications in organic synthesis*, John Wiley & Sons, 2016.
9 J. Artz, T. E. Müller, K. Thenert, J. Kleinekorte, R. Meys, A. Sternberg, A. Bardow and W. Leitner, *Chem. Rev.*, 2018, **118**, 434-504.
10 Typical contaminants in biogas include H_2S, H_2 and volatile siloxanes. (a) L. Appels, J. Lauwers, J. Degrève, L. Helsen, B. Lievens, K. Willems, J. Van Impe and R. Dewil, *Ren. Sust. Energy Rev.*, 2011, **15**, 4295-4301; (b) *Global bioenergy statistics 2020*, World Bioenergy Association, 2020.
11 (a) F.-Y. Gao, R.-C. Bao, M.-R. Gao and S.-H. Yu, *Journal of Materials Chemistry A*, 2020, **8**, 15458-15478; (b) C. Costentin, M. Robert and J.-M. Savéant, *Chem. Soc. Rev.*, 2013, **42**, 2423-2436; (c) H.-R. M. Jhong, S. Ma and P. J. A. Kenis, *Current Opinion in Chemical Engineering*, 2013, **2**, 191-199.
12 (a) Phosgene, L. Cotarca, C. Lange, K. Meurer and J. Pauluhn, in *Ullmann's encyclopedia of industrial chemistry*, 2019, pp. 1-30; (b) Acetic acid, C. Le Berre, P. Serp, P. Kalck and G. P. Torrence, in *Ullmann's encyclopedia of industrial chemistry*, 2014, pp. 1-34; (c) Methanol, J. Ott, V. Gronemann, F. Pontzen, E. Fiedler, G. Grossmann, D. B. Kersebohm, G. Weiss and C. Witte, in *Ullmann's encyclopedia of industrial chemistry*, 2012; (d) Butanals, D. K. Raff, in *Ullmann's encyclopedia of industrial chemistry*, 2013.
13 R. Kungas, *J. Electrochem. Soc.*, 2020, **167**, 044508.
14 (a) C. F. J. Barnard, *Organometallics*, 2008, **27**, 5402-5422; (b) X.-F. Wu, H. Neumann and M. Beller, *Chem. Soc. Rev.*,

2011, **40**, 4986-5009; (c) X.-F. Wu, H. Neumann and M. Beller, *ChemSusChem*, 2013, **6**, 229-241; (d) S. T. Gadge and B. M. Bhanage, *RSC Advances*, 2014, **4**, 10367-10389; (e) Carbonylation, M. Beller, B. A. Steinhoff, J. R. Zoeller, D. J. Cole-Hamilton, E. Drent, X.-F. Wu, H. Neumann, S. Ito and K. Nozaki, in *Applied homogeneous catalysis with organometallic compounds*, 2017, ch. 3, pp. 91-190; (f) J.-B. Peng, F.-P. Wu and X.-F. Wu, *Chem. Rev.*, 2019, **119**, 2090-2127; (g) Y. Li, Y. Hu and X.-F. Wu, *Chem. Soc. Rev.*, 2018, **47**, 172-194.

15 (a) N. S. Shamsul, S. K. Kamarudin, N. A. Rahman and N. T. Kofli, *Ren. Sust. Energy Rev.*, 2014, **33**, 578-588; (b) G. A. Olah, A. Goeppert and G. K. S. Prakash, *Beyond oil and gas: The methanol economy*, Wiley, 2018.

16 (a) J. S. Lee, J. C. Kim and Y. G. Kim, *Appl. Catal.*, 1990, **57**, 1-30; (b) Chapter 1 - catalytic methanol carbonylation, A. Haynes, in *Advances in catalysis*, eds. B. C. Gates and H. Knözinger, Academic Press, 2010, vol. 53, pp. 1-45.

17 (BASF AG), GB252848A, 1926.

18 S. P. Tonner, D. L. Trimm, M. S. Wainwright and N. W. Cant, *J. Mol. Catal.*, 1983, **18**, 215-222.

19 D. J. Darensbourg, R. L. Gray and C. Ovalles, *J. Mol. Catal.*, 1987, **41**, 329-347.

20 (a) Carbonylation and homologation of methanol, methyl ethers and esters in the presence of ruthenium catalysts, G. Braca, G. Sbrana, G. Valentini, G. Andrich and G. Gregorio, in *Fundamental research in homogeneous catalysis*, Springer, 1979, pp. 221-238; (b) S. J. Choi, J. S. Lee and Y. G. Kim, *J. Mol. Catal.*, 1993, **85**, L109-L116.

21 S. Jali, H. B. Friedrich and G. R. Julius, *J. Mol. Catal. A: Chem.*, 2011, **348**, 63-69.

22 It is interesting to note that the presence of water or iodide additives do not influence the yield of the reaction.

23 (a) J. Chatt and P. Chini, *J. Chem. Soc. A*, 1970, 1538-1542; (b) P. Chini and G. Longoni, *J. Chem. Soc. A*, 1970, 1542-1546.

24 R. A. Head and M. I. Tabb, *J. Mol. Catal.*, 1984, **26**, 149-158.

25 W. M. Haynes, *Crc handbook of chemistry and physics*, CRC press, 2014.

26 W. Reppe and H. Friederich, US2789137A, 1953.

27 W. Reppe, H. Friederich and W. Morsch, US2729651A, 1953.

28 F. E. Paulik and J. F. Roth, *Chem. Commun. (London)*, 1968, 1578a-1578a.

29 D. Brodzki, B. Denise and G. Pannetier, *J. Mol. Catal.*, 1977, **2**, 149-161.

30 G. J. Sunley and D. J. Watson, *Catal. Today*, 2000, **58**, 293-307.

31 Mechanistic pathways in the catalytic carbonylation of methanol by rhodium and iridium complexes, D. Forster, in *Adv. Organomet. Chem.*, eds. F. G. A. Stone and R. West, Academic Press, 1979, vol. 17, pp. 255-267.

32 P. W. Van Leeuwen, *Homogeneous catalysis: Understanding the art*, Springer Science & Business Media, 2006.

33 (a) H. Zabed, J. N. Sahu, A. Suely, A. N. Boyce and G. Faruq, *Ren. Sust. Energy Rev.*, 2017, **71**, 475-501; (b) Y.-S. Jang, B. Kim, J. H. Shin, Y. J. Choi, S. Choi, C. W. Song, J. Lee, H. G. Park and S. Y. Lee, *Biotechnol. Bioeng.*, 2012, **109**, 2437-2459.

34 T. W. Dekleva and D. Forster, *J. Am. Chem. Soc.*, 1985, **107**, 3565-3567.

35 (a) Biodegradable polyesters, C. Sasikala and C. V. Ramana, in *Adv. Appl. Microbiol.*, eds. S. L. Neidleman and A. I. Laskin, Academic Press, 1996, vol. 42, pp. 97-218; (b) 5.15 - biodegradable polyesters, S. Agarwal, in *Polymer science: A comprehensive reference*, eds. K. Matyjaszewski and M. Möller, Elsevier, Amsterdam, 2012, pp. 333-361.

36 (a) E. W. Dunn, J. R. Lamb, A. M. LaPointe and G. W. Coates, *ACS Catal.*, 2016, **6**, 8219-8223; (b) R. Zhu, J.-L. Jiang, X.-L. Li, J. Deng and Y. Fu, *ACS Catal.*, 2017, **7**, 7520-7528; (c) S. Sookraj, WO2019006366A1, 2017.

37 J. T. Lee, P. J. Thomas and H. Alper, *J. Org. Chem.*, 2001, **66**, 5424-5426.

38 J. W. Kramer, E. B. Lobkovsky and G. W. Coates, *Org. Lett.*, 2006, **8**, 3709-3712.

39 M. D. Wang, S. Calet and H. Alper, *J. Org. Chem.*, 1989, **54**, 20-21.

40 Y. D. Getzler, V. Kundnani, E. B. Lobkovsky and G. W. Coates, *J. Am. Chem. Soc.*, 2004, **126**, 6842-6843.

41 (a) I. Wender and P. Pino, *Organic syntheses via metal carbonyls*, Interscience Publishers, 1977; (b) G. Jenner, H. Kheradmand and A. Kiennemann, *J. Organomet. Chem.*, 1984, **277**, 427-435.

42 (a) S. Paul, Y. Zhu, C. Romain, R. Brooks, P. K. Saini and C. K. Williams, *Chem. Commun.*, 2015, **51**, 6459-6479; (b) J. M. Longo, M. J. Sanford and G. W. Coates, *Chem. Rev.*, 2016, **116**, 15167-15197.

43 J. M. Rowley, E. B. Lobkovsky and G. W. Coates, *J. Am. Chem. Soc.*, 2007, **129**, 4948-4960.

44 J. Jiang, S. Rajendiran and S. Yoon, *Asian Journal of Organic Chemistry*, 2019, **8**, 151-154.

45 A. Hofman, S. Słomkowski and S. Penczek, *Makromol. Chem.*, 1984, **185**, 91-101.

46 Y.-S. Lin and A. Yamamoto, *Tetrahedron Lett.*, 1997, **38**, 3747-3750.

47 Y.-S. Lin and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 723-734.

48 G. Papadogianakis, L. Maat and R. A. Sheldon, *J. Chem. Soc., Chem. Commun.*, 1994, 2659-2660.

49 E. J. Jang, K. H. Lee, J. S. Lee and Y. G. Kim, *J. Mol. Catal. A: Chem.*, 1999, **138**, 25-36.

50 A. Seayad, S. Jayasree and R. V. Chaudhari, *J. Mol. Catal. A: Chem.*, 2001, **172**, 151-164.

51 (a) K. D. Rainsford, *Ibuprofen: Discovery, development and therapeutics*, John Wiley & Sons, 2015; (b) M. Poliakoff and P. Licence, *Nature*, 2007, **450**, 810-812.

52 C. S. Chin, H. J. Jung and S.-g. Hong, *Bull. Korean Chem. Soc.*, 1992, **13**, 391-395.

53 J. Tsuji, J. Kiji, S. Imamura and M. Morikawa, *J. Am. Chem. Soc.*, 1964, **86**, 4350-4353.

54 D. Medema, R. van Helden and C. F. Kohll, *Inorg. Chim. Acta*, 1969, **3**, 255-265.

55 M. Sakamoto, I. Shimizu and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, 1996, **69**, 1065-1078.

56 J. Tsuji, K. Sato and H. Okumoto, *J. Org. Chem.*, 1984, **49**, 1341-1344.

57 J. Zakzeski, P. C. A. Bruijnincx, A. L. Jongerius and B. M. Weckhuysen, *Chem. Rev.*, 2010, **110**, 3552-3599.

58 Esters, organic, W. Riemenschneider and H. M. Bolt, in *Ullmann's encyclopedia of industrial chemistry*, 2005.

59 N. Lassauque, PhD Thesis, Université de Toulouse, 2006.

60 (a) G. Braca, G. Sbrana, G. Valentini, G. Andrich and G. Gregorio, *J. Am. Chem. Soc.*, 1978, **100**, 6238-6240; (b) G. Braca, L. Paladini, G. Sbrana, G. Valentini, G. Andrich and G. Gregorio, *Ind. Eng. Chem. Prod. Res. Dev.*, 1981, **20**, 115-122.

61 E. Zhan, Z. Xiong and W. Shen, *J. Energy Chem.*, 2019, **36**, 51-63.

62 Acetic anhydride and mixed fatty acid anhydrides, H. Held, A. Rengstl and D. Mayer, in *Ullmann's encyclopedia of industrial chemistry*, 2000.

63 (a) N. Rizkalla, DE2610036, 1976; (b) J. R. Zoeller, V. H. Agreda, S. L. Cook, N. L. Lafferty, S. W. Polichnowski and D. M. Pond, *Catal. Today*, 1992, **13**, 73-91.

64 (a) T. H. Larkins, S. W. Polichnowski, G. C. Tustin and D. A. Young, US4374070A, 1980; (b) S. W. Polichnowski, *J. Chem. Educ.*, 1986, **63**, 206.

65 Q. Mei, Y. Yang, H. Liu, S. Li, H. Liu and B. Han, *Science Advances*, 2018, **4**, eaaq0266.

66 (a) Q. Mei, H. Liu, X. Shen, Q. Meng, H. Liu, J. Xiang and B. Han, *Angew. Chem. Int. Ed.*, 2017, **56**, 14868-14872; (b) X. Shen, Q. Meng, M. Dong, J. Xiang, S. Li, H. Liu and B. Han, *ChemSusChem*, 2019, **12**, 5149-5156.
67 T. Saegusa, S. Kobayashi, K. Hirota and Y. Ito, *Tetrahedron Lett.*, 1966, **7**, 6125-6129.
68 D. Durand and C. Lassau, *Tetrahedron Lett.*, 1969, 2329-&.
69 B. D. Dombek and R. J. Angelici, *J. Catal.*, 1977, **48**, 433-435.
70 W. E. Martin and M. F. Farona, *J. Organomet. Chem.*, 1981, **206**, 393-397.
71 Y. Yoshida, S. Asano and S. Inoue, *Chem. Lett.*, 1984, 1073-1076.
72 (a) Y. Tsuji, T. Ohsumi, T. Kondo and Y. Watanabe, *J. Organomet. Chem.*, 1986, **309**, 333-344; (b) G. Sussfink, M. Langenbahn and T. Jenke, *J. Organomet. Chem.*, 1989, **368**, 103-109.
73 J. Ramioulle and W. Couteau, GB1568833, 1976.
74 X. Li, K. Liu, X. Xu, L. Ma, H. Wang, D. Jiang, Q. Zhang and C. Lu, *Chem. Commun.*, 2011, **47**, 7860-7862.
75 W. Li and X.-F. Wu, *Chem. Eur. J.*, 2015, **21**, 14943-14948.
76 F. Merger, R. Kummer and H.-M. Hutmacher, EP0153476, 1984.
77 (a) S. I. Murahashi, Y. Imada and K. Nishimura, *J. Chem. Soc., Chem. Commun.*, 1988, 1578-1579; (b) S. I. Murahashi, Y. Imada and K. Nishimura, *Tetrahedron*, 1994, **50**, 453-464.
78 H. Yu, G. Y. Zhang, Z. J. Liu and H. M. Huang, *Rsc Advances*, 2014, **4**, 64235-64237.
79 H. Yu, B. Gao, B. Hu and H. Huang, *Org. Lett.*, 2017, **19**, 3520-3523.
80 (a) M. D. Wang, PhD Thesis, University of Ottawa (Canada), 1993; (b) Octacarbonyldicobalt, in *Encyclopedia of reagents for organic synthesis*, 2014, pp. 1-26; (c) N. Piens and M. D'Hooghe, *Eur. J. Org. Chem.*, 2017, **2017**, 5943-5960.
81 Z. Yin, J.-X. Xu and X.-F. Wu, *ACS Catal.*, 2020, **10**, 6510-6531.
82 K. Nozaki, US3412151A, 1966.
83 H. E. Bellis, CA1304408C, 1985.
84 E. J. Moore, J. M. Sullivan and J. R. Norton, *J. Am. Chem. Soc.*, 1986, **108**, 2257-2263.
85 (a) Y. Lei, R. Zhang, L. Wu, Q. Wu, H. Mei and G. Li, *Appl. Organomet. Chem.*, 2014, **28**, 310-314; (b) Y. Lei, R. Zhang, Q. Wu, H. Mei, B. Xiao and G. Li, *J. Mol. Catal. A: Chem.*, 2014, **381**, 120-125.
86 H. Mei, W. Han, J. Hu, S. Xiao, Y. Lei, R. Zhang, W. Mo and G. Li, *Appl. Organomet. Chem.*, 2013, **27**, 177-183.
87 (a) Y. Lei, R. Zhang and G. Li, *International Journal of Chemical, Environmental and Biological Sciences* 2013, **1**, 762-764; (b) Y. Z. Lei, R. Zhang, W. J. Han, H. Mei, Y. L. Gu, B. Xiao and G. X. Li, *Catal. Commun.*, 2013, **38**, 45-49.
88 T. Nasr Allah, S. Savourey, J.-C. Berthet, E. Nicolas and T. Cantat, *Angew. Chem. Int. Ed.*, 2019, **58**, 10884-10887.
89 S. W. Ragsdale and E. Pierce, *Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics*, 2008, **1784**, 1873-1898.
90 W. T. Dent, G. H. Whitfield and R. Long, *J. Chem. Soc.*, 1964, 1588-&.
91 E. Monflier, PhD Thesis, Université de Lille, 1992.
92 Syntheses involving carbon monoxide, in *Industrial organic chemistry*, 2003, pp. 127-144.
93 (a) H. Hopff and M. Dunkel, US1891930A, 1929; (b) (IG Farbenindustrie AG), FR671241A, 1929.
94 Carbonyl diiodide, in *Topics in inorganic and general chemistry*, eds. T. A. Ryan, C. Ryan, E. A. Seddon and K. R. Seddon, Pergamon, 1996, vol. 24, pp. 679-683.
95 J. Davy and H. Davy, *Philos. Trans. R Soc. London*, 1812, **102**, 144-151.
96 Synthesis and formation of phosgene, in *Topics in inorganic and general chemistry*, eds. T. A. Ryan, C. Ryan, E. A. Seddon and K. R. Seddon, Pergamon, 1996, vol. 24, pp. 223-266.
97 Carbonyl difluoride, in *Topics in inorganic and general chemistry*, eds. T. A. Ryan, C. Ryan, E. A. Seddon and K. R. Seddon, Pergamon, 1996, vol. 24, pp. 545-664.
98 Carbonyl dibromide, in *Topics in inorganic and general chemistry*, eds. T. A. Ryan, C. Ryan, E. A. Seddon and K. R. Seddon, Pergamon, 1996, vol. 24, pp. 665-677.
99 J. Schiel, *Liebig's Annal. Chem. Pharm., Suppl.*, 1863, **2**, 311.
100 H. Vogt and L. Riesel, *Z. Chem.*, 1989, **29**, 342-343.
101 Formaldehyde, A. W. Franz, H. Kronemayer, D. Pfeiffer, R. D. Pilz, G. Reuss, W. Disteldorf, A. O. Gamer and A. Hilt, in *Ullmann's encyclopedia of industrial chemistry*, 2016, pp. 1-34.
102 L. E. Heim, H. Konnerth and M. H. G. Prechtl, *Green Chem.*, 2017, **19**, 2347-2355.
103 (a) A. M. Bahmanpour, A. Hoadley and A. Tanksale, *Green Chem.*, 2015, **17**, 3500-3507; (b) A. M. Bahmanpour, A. Hoadley, S. H. Mushrif and A. Tanksale, *Acs Sustainable Chemistry & Engineering*, 2016, **4**, 3970-3977.
104 Ketones, H. Siegel and M. Eggersdorfer, in *Ullmann's encyclopedia of industrial chemistry*, 2000.
105 J. J. Eisch, A. M. Piotrowski, K. I. Han, C. Kruger and Y. H. Tsay, *Organometallics*, 1985, **4**, 224-231.
106 R. Yamaguchi, S. Tokita, Y. Takeda and M. Kawanisi, *J. Chem. Soc., Chem. Commun.*, 1985, 1285-1286.
107 (a) P. Muller, G. Bernardinelli and Y. Jacquier, *Helv. Chim. Acta*, 1988, **71**, 1328-1330; (b) P. Muller, G. Bernardinelli, Y. Jacquier and A. Ricca, *Helv. Chim. Acta*, 1989, **72**, 1618-1626.
108 M. Hidai, M. Orisaku and Y. Uchida, *Chem. Lett.*, 1980, 753-754.
109 T. Kurahashi and A. de Meijere, *Angew. Chem. Int. Ed. Engl.*, 2005, **44**, 7881-7884.
110 B. J. Fisher and R. Eisenberg, *Organometallics*, 1983, **2**, 764-767.
111 (a) A. J. Kunin and R. Eisenberg, *Organometallics*, 1988, **7**, 2124-2129; (b) E. M. Gordon and R. Eisenberg, *J. Mol. Catal.*, 1988, **45**, 57-71.
112 T. Sakakura, T. Sodeyama, K. Sasaki, K. Wada and M. Tanaka, *J. Am. Chem. Soc.*, 1990, **112**, 7221-7229.
113 C. T. Spillett and P. C. Ford, *J. Am. Chem. Soc.*, 1989, **111**, 1932-1933.
114 (a) J. M. Buchanan, J. M. Stryker and R. G. Bergman, *J. Am. Chem. Soc.*, 1986, **108**, 1537-1550; (b) W. D. Jones and F. J. Feher, *J. Am. Chem. Soc.*, 1982, **104**, 4240-4242.
115 G. A. Olah, G. K. S. Prakash, T. Mathew and E. R. Marinez, *Angew. Chem. Int. Ed.*, 2000, **39**, 2547-2548.
116 D. S. Sood, S. C. Sherman, A. V. Iretskii, J. C. Kenvin, D. A. Schiraldi and M. G. White, *J. Catal.*, 2001, **199**, 149-153.

Picture	Biography
	*Tawfiq Nasr Allah received his MSc in chemistry from the Paris Descartes university in 2015. He joined the group of Thibault Cantat for his PhD, where he focused on the development of catalysts and processes for the creation of C–C and C–N bond through the utilization of CO and CO_2 as a carbon source.*

	*Louise Ponsard graduated from the chemical engineer school Chimie ParisTech in 2017. She then joined the team of Thibault Cantat for a PhD, focusing on the development of novel catalytic systems for the carbonylation of strained cyclic C–O bonds using gaseous carbon monoxide within the Carbon4PUR project. (www.carbon4pur.eu)*
	*Emmanuel Nicolas graduated in 2010 from Ecole Polytechnique. After his PhD in the group of Dr Nicolas Mézailles, he moved to the Netherlands in the group of Ass Prof Dr Chris Slootweg where he worked on the use of Frustrated Lewis Pairs as mimics for transition metals. He then moved back to France to join the group of Thibault Cantat where he was recruited as a permanent researcher in 2017, working on the conversion and valorisation of small molecules such as CO, CO_2, N_2O, or formic acid, for the production of valuable chemicals.*
	*Thibault Cantat studied chemistry at the École Normale Superieure in Paris, and obtained his Ph.D. in Chemistry in 2007, at the Ecole Polytechnique, France. After a postdoctoral stay at Los Alamos National Laboratory, he joined CEA in 2010 where he leads a research group focused on the activation and recycling of CO_2, biomass and waste plastics using renewable hydride donors. His research interests therefore span organometallic chemistry of the transition metals and the f–elements to homogenous catalysis and computational chemistry.*