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Review

Direct Carboxylation of C(sp^3)-H and C(sp^2)-H Bonds with CO_2 by Transition-Metal-Catalyzed and Base-Mediated Reactions

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Abstract: This review focuses on recent advances in the field of direct carboxylation reactions of C(sp^3)-H and C(sp^2)-H bonds using CO_2 encompassing both transition-metal-catalysis and base-mediated approach. The review is not intended to be comprehensive, but aims to analyze representative examples from the literature, including transition-metal catalyzed carboxylation of benzylic and allylic C(sp^3)-H functionalities using CO_2 which is at a "nascent stage". Examples of light-driven carboxylation reactions of unactivated C(sp^3)-H bonds are also considered. Concerning C(sp^3)-H and C(sp^2)-H deprotonation reactions mediated by bases with subsequent carboxylation of the carbon nucleophile, few examples of catalytic processes are reported in the literature. In spite of this, several examples of base-promoted reactions integrating "base recycling" or "base regeneration (through electrosynthesis)" steps have been reported. Representative examples of synthetically efficient, base-promoted processes are included in the review.

Keywords: carbon dioxide; C-H activation; synthesis of carboxylic acids; transition-metal catalysis; Brønsted-base catalysis; carboxylation reactions

1. Introduction

Viable and efficient conversion of CO_2 into chemicals and fuels is a challenging goal and, at the same time, a subject of scientific debate [1]. The high thermal and kinetic stability of the CO_2 molecule require for a suitable catalyst and energy input when employed in E-CO_2 bond formation (E = O, N, C) or reduction reactions. Current synthetic options for CO_2-fixation into useful chemicals encompasses chemical, electro-chemical, photo-chemical, photo-electrochemical and biological approach that have been overviewed in a number of excellent books and comprehensive reviews [2–17].

An analysis of the scientific literature suggests that a convenient energy-balance in CO_2-conversion processes requires improving energy efficiency through the use of renewable energy sources, advanced reactor technologies (as for example continuous-flow reactors) and efficient catalysts.

It is also widely accepted that present chemical CO_2-utilization does not contribute significantly to reduction of CO_2 emission (chemical industry is estimated to fix about 1.1 Mt of CO_2 per year in a variety of chemicals as urea, salicylic acid, cyclic carbonates and polycarbonates [18]).

Looking from a different perspective, a research topic receiving particular attention over the last decades concerns the possibility to substitute traditional protocols employed in the synthesis of carboxylic acids with more environmental friendly procedures based on the use of CO_2 as a cheap and non-toxic C1 source [19].

Indeed, carboxylic acids and derivatives are commercially valuable synthetic compounds and key intermediates in chemical and pharmaceutical industries [20–23].

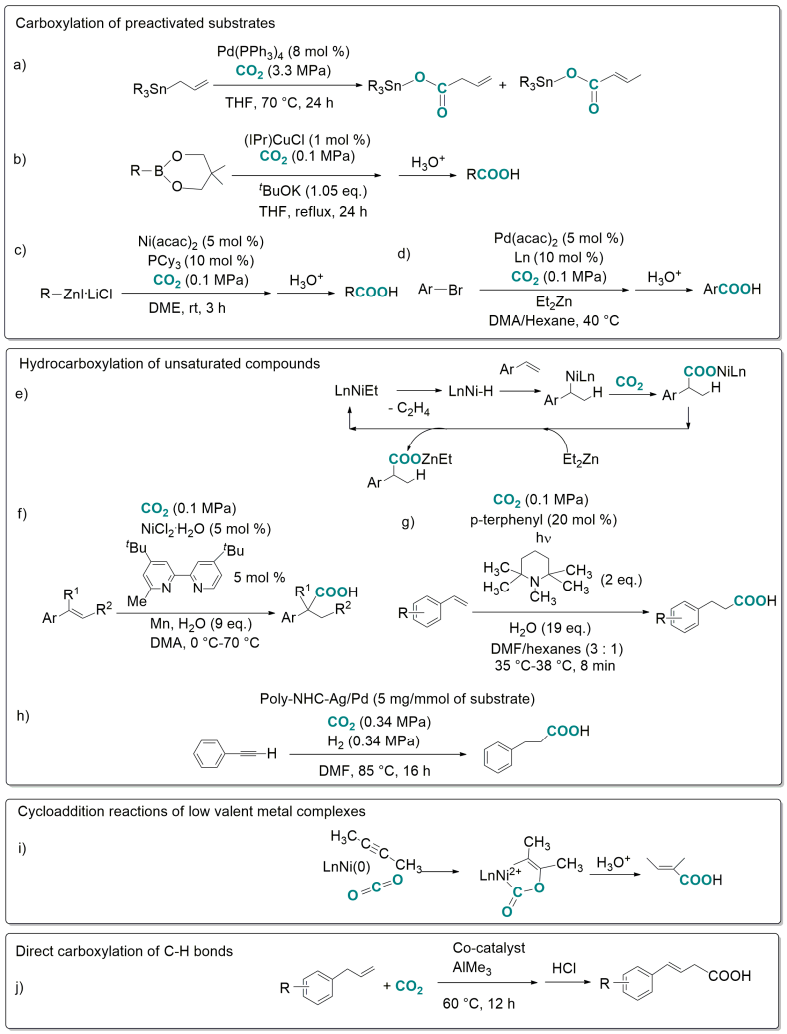
In the context of thermal catalysis, an analysis of synthetic strategies pursued in the synthesis of carboxylic acids (and derivatives) from organic substrates and CO_2 encompasses:

(1) transition-metal-catalysed carboxylation of preactivated substrates including allylstannanes [24–27], organoboronic esters [28–32], organozinc reagents [33,34] and aryl halides [35–37] as exemplified in Scheme 1a–d;

(2) transition-metal-catalysed hydrocarboxylation of unsaturated compounds (olefins, allenes, alkynes) requiring $AlEt_3$ or $ZnEt_2$ co-reactants to generate a metal-hydride species undergoing insertion of the unsaturated substrate and subsequent carboxylation of the organometallic intermediate [38–42] as exemplified in Scheme 1e. It is worth citing very recent examples of hydrocarboxylation reactions involving substrate reduction by a "formal hydride donor": (i) in Scheme 1f, [43] hydride is formally generated from H_2O and Mn; (ii) in Scheme 1g, [44] the substrate is reduced by photo-induced transfer of $2e^-$ and $2H^+$ from a sacrificial amine; (iii) in Scheme 1h, [45] the substrate is carboxylated and subsequently reduced with H_2 in a Poly-NHC/Ag/Pd mediated process;

(3) use of CO_2 in conjunction with alkenes, alkynes, dienes, allenes, diynes, in oxidative cycloaddition reaction of low valent metal complexes to form five-membered metallacycles [46–52] as exemplified in Scheme 1i;

(4) direct carboxylation of C-H bonds with CO_2 avoiding C-H pre-functionalization, hydrocarboxylation or metallacycle formation as exemplified in Scheme 1j [53]).



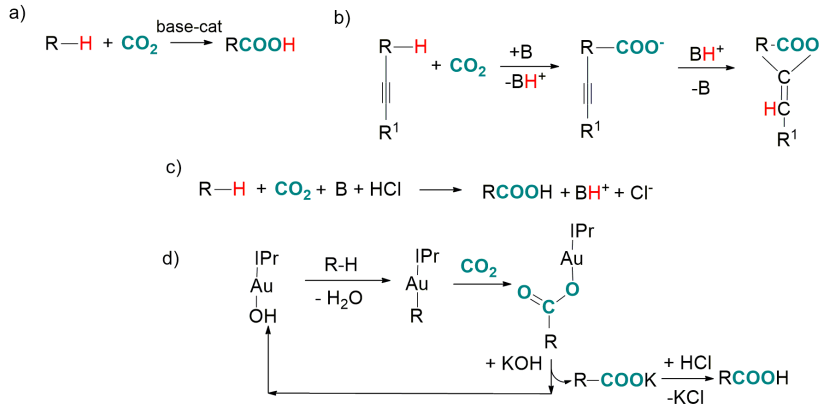
Scheme 1. Examples of transition-metal-catalyzed synthesis of carboxylic acids (and derivatives) from organic substrates and CO_2.

Among abovementioned synthetic strategies, C-H bond functionalisation with CO_2 as defined in point 4 seems to be particularly attractive as it can give straightforward access to value added products. In several reports, the term "direct carboxylation" is used to designate all synthetic strategies exemplified in Scheme 1a–j. Here we will use the term "direct carboxylation" with the meaning of point 4. In this review, we inspect recent advances concerning direct CO_2-based carboxylation reactions of C(sp^3)-H and C(sp^2)-H bonds encompassing both transition-metal-catalyzed and Brønsted-base mediated reactions. Also a few examples of carboxylation of CH_4 in the presence of heterogeneous catalysts as well as light-driven CO_2-based carboxylation of unactivated C(sp^3)-H bonds will be considered.

It is worth noting that the research field of direct functionalisation with CO_2 of aromatic and heteroaromatic compounds has registered many developments in the last decade which have been object of excellent reviews [19,54,55]. Due to space limitations, Friedel-Crafts carboxylation of aromatics [12,55] will be not considered here.

Direct carboxylation of compounds containing activated C(sp^3)-H bond has also received considerable attention. In contrast, the synthetically appealing direct carboxylation of unactivated C(sp^3)-H bonds with CO_2 is a research field in its "nascent stage" (as stated by Sato, Cazin and Nolan [53,56]). We will include in the analysis recent examples of carboxylation of benzylic and allylic C(sp^3)-H functionalities with CO_2 that promise to disclose new future research directions.

Base-mediated carboxylation reactions using CO_2 are initiated by abstraction of a C-H proton with production of a carbon anion able to nucleophilically attack the heterocumulene (Scheme 2). In a few cases the Brønsted base is playing a catalytic role (being deprotonated at the end of the cycle, Scheme 2a,b) while, in most cases, it reacts with the substrate in stoichiometric amount (occasionally a large base excess is required) (Scheme 2c). Stoichiometry applying throughout the course of the reaction for the abovementioned cases is shown in Scheme 2a–c.



Scheme 2. General stoichiometry of base-catalyzed reactions (**a**,**b**); (**c**) General stoichiometry of base-promoted reactions (under the assumption that $pK_{BH^+} > pK_{C\text{-}H}$); (**d**) Carboxylation of heteroarenes catalyzed by IPrAu(OH) catalyst [57].

For stoichiometric reactions falling under Scheme 2c, recent reports have dealt with the problem of Brønsted-base recycling [58,59] or Brønsted-base regeneration through electrodialysis [60] providing, on the overall, very efficient synthetic processes (see Sections 4.1 and 6.3).

Interestingly, several reports [56,57,61] describe the employment of metal complexes bearing OH^- or $^tBuO^-$ ligands acting as proton acceptors during the catalytic cycle (an example is reported in Scheme 2d [57]) (see Section 5.2). These efficient synthetic methods can be "formally" considered as processes in which a base-promoted reaction takes place with the assistance of a metal catalyst.

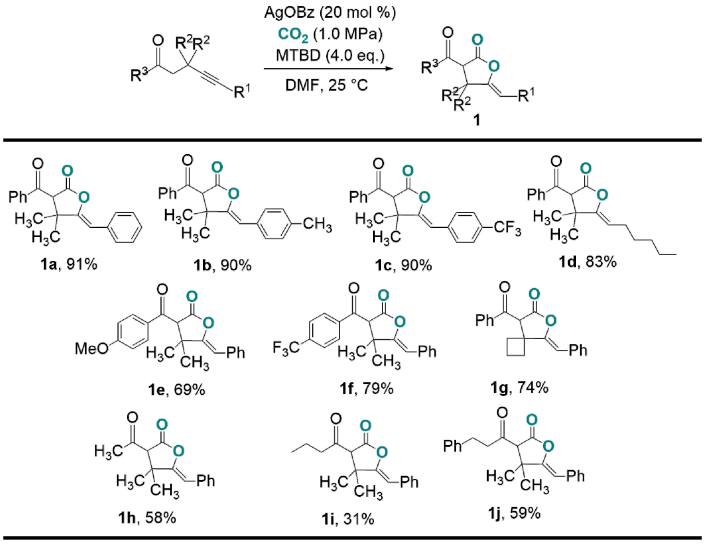
We consider that it is worth including here selected examples reported in the literature concerning Brønsted-base promoted reactions (proceeding according to stoichiometry shown in Scheme 2c) as these processes provide access to efficient synthetic protocols to added value chemicals. Moreover, in

the light of the abovementioned synthetic advances, base-promoted reactions may be integrated with a base-regeneration step or inspire future base-promoted reactions assisted by metal-catalysis.

2. Transition-Metal-Catalyzed Carboxylation of C(sp^3)-H Bonds with CO_2

2.1. Carboxylation of Compounds Possessing Activated C(sp^3)-H Bonds Catalyzed by Ag-Salts in Conjunction with Strong Bases

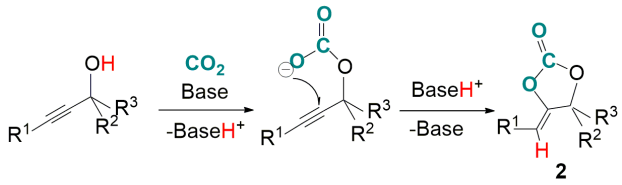
A recent report from the Yamada group [62] describes catalytic incorporation of CO_2 into specific substrates as ketones containing an alkyne unit (Scheme 3).



Scheme 3. Selected examples for carboxylation/cyclization reactions of acetophenone derivatives with alkynyl functionality.

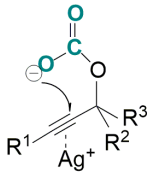
The reaction proceeds through a carboxylation/*dig*-cyclization pathway under mild conditions (P_{CO_2} = 1.0 MPa, 25 °C) affording γ-lactone derivatives (**1**).

This reaction was inspired by the efficient synthesis of cyclic α-methylene carbonates (**2**) from prop-2-ynyl alcohol derivatives and CO_2 shown in Scheme 4 [63–67].



Scheme 4. Carboxylation/cyclization of prop-2-ynyl alcohol derivatives.

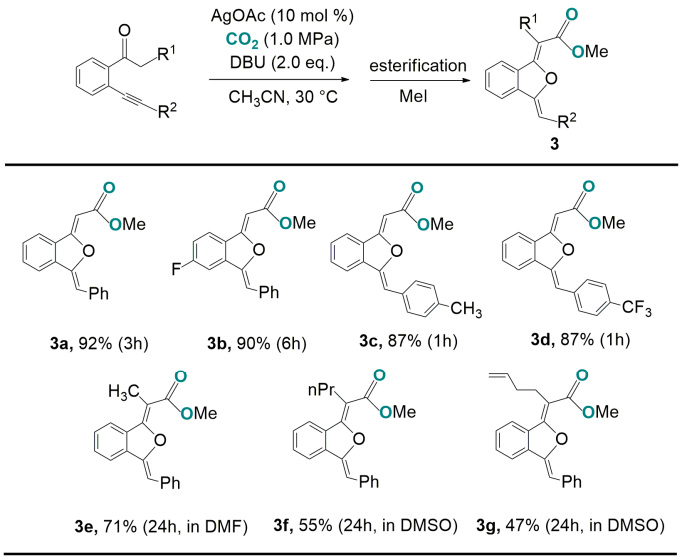
α-methylene cyclic carbonates (**2**) can be obtained in good to excellent yields under transition-metal- or base-catalysis in a synthesis requiring high CO_2 pressure (P_{CO_2} = 0.5–5 MPa) and relatively high temperature (80–120 °C). In previous works dealing with carboxylative cyclization reaction of prop-2-ynyl alcohol derivatives under CO_2, Yamada [68,69] reported the combined use of silver salts and organic bases to enable the employment of milder reaction conditions (P_{CO_2} = 0.1 MPa, 80 °C). Among screened metal salts ($Rh(acac)_3$, $PdCl_2$, $PtCl_2$, CuCl, AgOAc, AuCl, $Hg(OTf)_2$) silver cation showed superior catalytic properties as π-Lewis acid in assisting the *dig*-cyclization process (Scheme 5).



Scheme 5. Ag-catalyst assisting carboxylative *dig*-cyclization of prop-2-ynyl alcohol derivatives.

Yamada applied the silver-based protocol to acetophenone derivatives possessing an alkynyl functionality to afford γ-lactone derivatives (**1**) (Scheme 3). The reaction was typically carried out using AgOBz (20 mol %) and MTBD (7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene) (4 eq.) under P_{CO_2} = 1.0 MPa at 25 °C. By varying the substituent on the 1-phenyl-4-pentyne-1-one skeleton (16 substrates), γ-lactone derivatives **1** were obtained in yield ranging from 36 to 91% with 100% Z selectivity with respect to the double C-C bond. Dihydrofuran derivatives were detected in reaction products at lower amount (5% yield). The scope of the reaction could be extended to aliphatic ketone derivatives (Scheme 3, **1h–j**) [62] possessing two different protons α and α′ to the carbonyl group. Also in this case γ-lactone derivatives were obtained with high selectivity (3 examples, 31–59% yields) without any control of the formation of enolate.

The combined use of silver salts (AgOAc, 10 mol %) and organic base [DBU, (1,8-diazabicyclo(5.4.0)-7-undecene), 2 eq.] catalysis under CO_2 atmosphere was extended by Yamada to *o*-alkynyl acetophenone derivatives (Scheme 6) leading selectively to 1(3*H*)-isobenzofuranylidene acetic acids derivatives (**3**) in moderate to excellent yield (12 examples, 47–99% yields) [70].

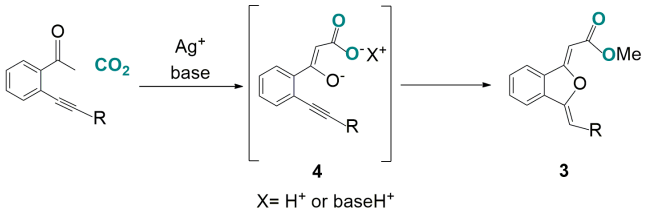


Scheme 6. Selected examples for carboxylation/cyclization reactions of *o*-alkynyl acetophenone derivatives.

In situ esterification of the carboxylic acid functionality with MeI afforded the corresponding methyl esters. Dihydroisobenzofuran products bearing an aromatic substituent (R^2, Scheme 6) at the alkynyl-moiety were isolated in 100% Z selectivity with respect of the two C-C double bonds.

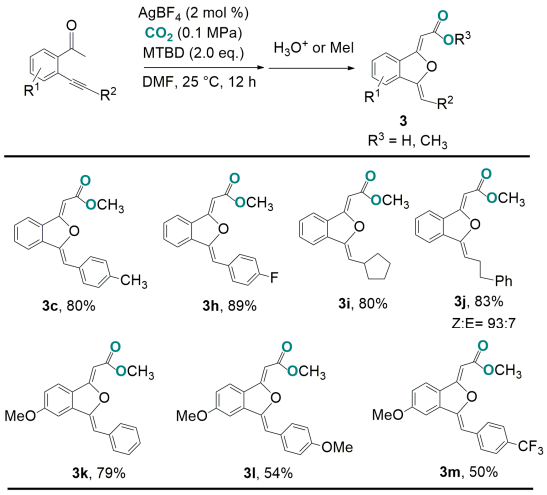
This report appears synthetically interesting as the dihydroisobenzofuran structure is present in several bioactive compounds as Pestacin and Escitalopram. The literature documents the dihydroisobenzofuran skeleton can be obtained by a transition-metal-catalyzed cyclization reaction of *o*-alkynylbenzylalcohol or *o*-alkynylbenzaldehyde derivatives [71–73]. However, this synthetic approach allows only a limited number of substituents of the dihydroisobenzofuran skeleton. In contrast, the Yamada approach shown in Scheme 6 give access to dihydroisobenzofuran derivatives (12 examples) bearing a carboxyl-group substituent. The reaction is proposed to proceed via formation

of an enolate that undergo carboxylation with CO_2 producing intermediate **4** (Scheme 7). The oxygen atom of the enol tautomer **4** reacts through an intramolecular 5-*exo*-*dig* regioselective cyclization pathway affording dihydroisobenzofuran derivatives **3**.



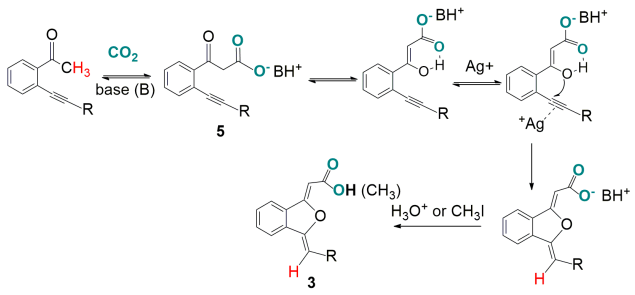
Scheme 7. Proposed reaction mechanism for carboxylation/cyclization reaction of *o*-alkynyl acetophenone derivatives.

A more detailed description of the reaction mechanism was reported Lu (see Scheme 9) [74] who further optimized the reaction conditions for the carboxylation/intramolecular cyclization reaction of *o*-alkynyl acetophenone with CO_2 by using MTBD (2 eq.) and $AgBF_4$ (2 mol %) in DMF under atmospheric CO_2 pressure (Scheme 8).



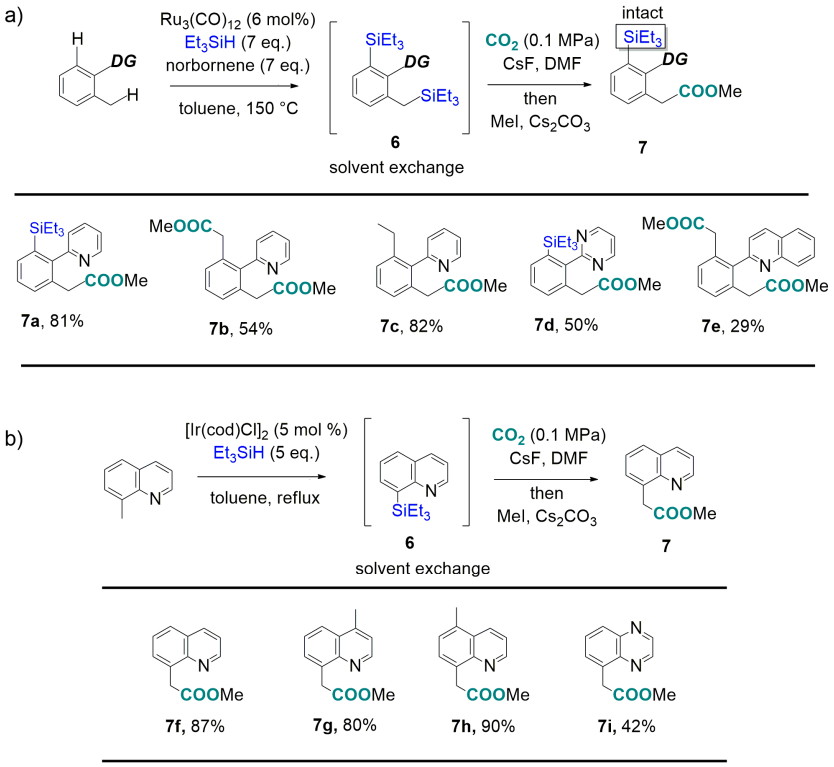
Scheme 8. Selected examples for carboxylation/cyclization reactions of *o*-alkynyl acetophenone derivatives.

By varying the substituents at the aromatic ring (R^1, Scheme 8) and at the alkyne moiety (R^2, Scheme 8), 1(3*H*)-isobenzofuranylidene acetic acids (or ester derivatives **3**) were obtained (15 examples) in 50–95% yields (Scheme 8). On the basis of deuterium-labelling experiments and DFT calculations Lu and co-workers proposed the reaction mechanism shown in Scheme 9.



Scheme 9. Proposed mechanism of carboxylation/cyclization reaction of *o*-alkynyl acetophenone derivatives (hydrogen atom involved in hydrogen shift is shown in red color).

The reaction proceeds through proton abstraction from the methyl group by DBU generating, thus, an enolate that further reacts with CO_2 affording the β-keto carboxylate anion **5**. Subsequently, the negatively charged oxygen atom of the enolate tautomer nucleophilically attacks the Ag-activated alkyne moiety leading to the cyclic product. A deuterium-labelling experiment on 2-(phenylethynyl)phenylethanone has shown that the hydrogen α to the phenyl substituent (R = C_6H_5, Scheme 10) in **3** comes from the methyl group of the reagent, indicating that hydrogen shift is involved in the reaction.



Scheme 10. Selected examples for carboxylation reactions of benzylic C(sp^3)-H bonds of substrates possessing a nitrogen directing group.

To explain the high selectivity towards the 5-*exo* oxygen cyclization product a DFT study using the wB97XD function was implemented. The study revealed the 5-*exo*-oxygen cyclization pathway having the lowest energy barrier for the O atom attack to the alkynyl-moiety during cyclization.

2.2. Carboxylation of Benzylic and Allylic C(sp^3)-H Bonds Catalyzed by Transition-Metal-Complexes

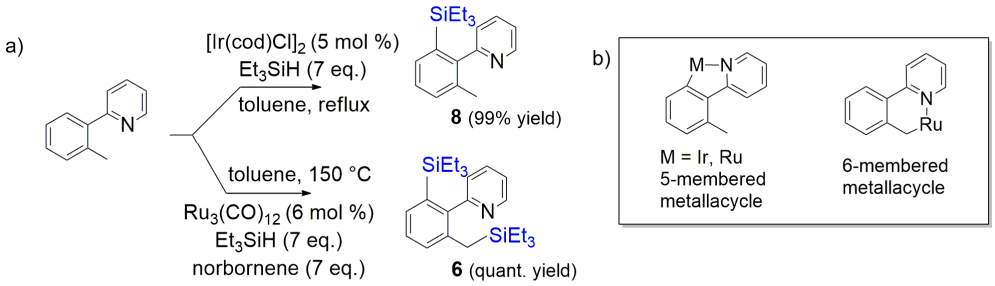
The group of Sato has recently reported direct functionalization with CO_2 of benzylic and allylic C(sp^3)-H bonds catalyzed by transition-metal-complexes.

In 2012, Sato published a sequential protocol for the selective "formal" carboxylation of benzylic C(sp^3)-H bonds applied to substrates possessing a nitrogen directing group (Scheme 10) including substituted 8-methylquinoline, 2-(*o*-tolyl) pyridine, 2-(*o*-tolyl) pyrimidine and 2-(*o*-tolyl) quinoline (11 substrates, 29–90% yields) [75].

At first substrates were silylated with Et_3SiH in toluene by $Ru_3(CO)_{12}$ catalyst according to the Kakiuchi protocol [76] to give benzylsilane derivatives **6** (Schemes 10a and 11a). Interestingly, the $[Ir(cod)Cl]_2$ catalyst was tested for the first time for C(sp^3)-H silylation reactions (Schemes 10b and 11a). Both Ir and Ru catalysts afforded silylated products (**6**,**8**) in almost quantitative yield.

As shown in Scheme 11a, silylation of 2-(*o*-tolyl) pyridine exhibited a different regioselectivity toward C(sp^2)-H and C(sp^3)-H bonds functionalization in the presence of $[Ir(cod)Cl]_2$ and $Ru_3(CO)_{12}$

catalysts. While the Ir catalyst was found to afford selectively the C(sp^2)-silylated product (**8**), the Ru catalyst afforded both C(sp^2)- and C(sp^3)-silylated derivative (**6**). The difference in regioselectivity was explained on the basis of the preference of Ir to participate in 5-membered metallacycles in contrast to Ru that is reported to form both 5- and 6-membered rings (Scheme 11b).



Scheme 11. C(sp^3)-H silylation reactions of 2-(*o*-tolyl) pyridine catalyzed by Ir(I) and Ru(0) catalysts.

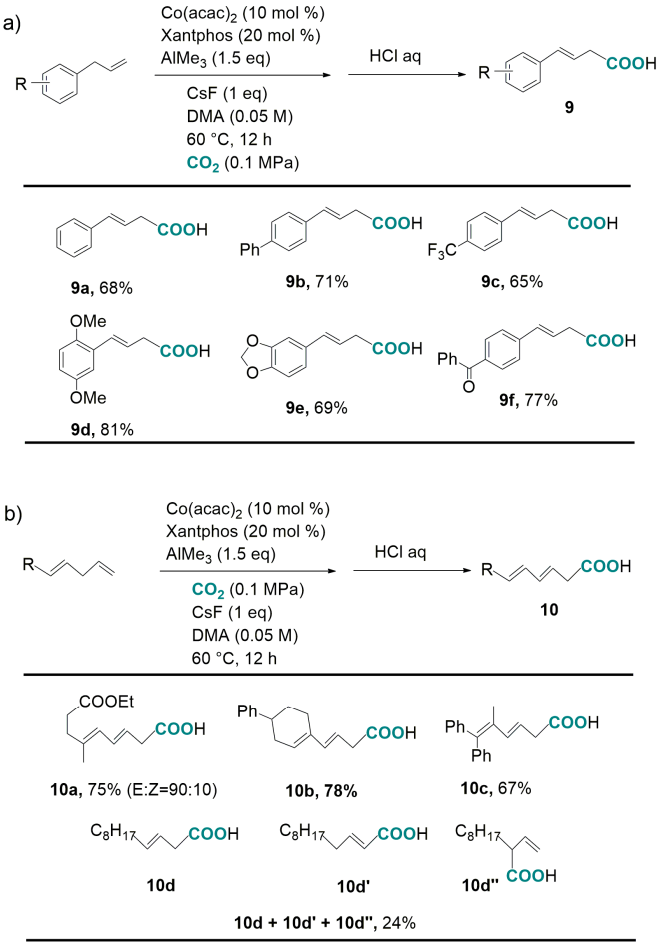
Benzyl-silane derivatives were subsequently carboxylated at the benzylic C(sp^3)-Si bond using CsF and CO_2 after solvent exchange. Unfortunately, the carboxylation reaction was affected by undesired proto-desilylation, therefore carboxylated products (**7**) were obtained in moderate to good yields (29–90%).

A critical examination of the protocol reported by Sato evidentiates the process is a carboxylation of pre-activated silyl-derivatives in analogy with the well documented transition-metal-catalyzed carboxylation of pre-activated substrates shown in Scheme 1a–d. The originality of the process resides in the way the authors concatenate the pre-functionalisation and the carboxylation reactions that require different solvent and reaction conditions. After the silylation procedure, by simple evaporation of toluene and other volatile species (Et_3SiH and norbornene), subsequent addition of DMF and CsF allows to develop the original in situ protocol for the two reactions.

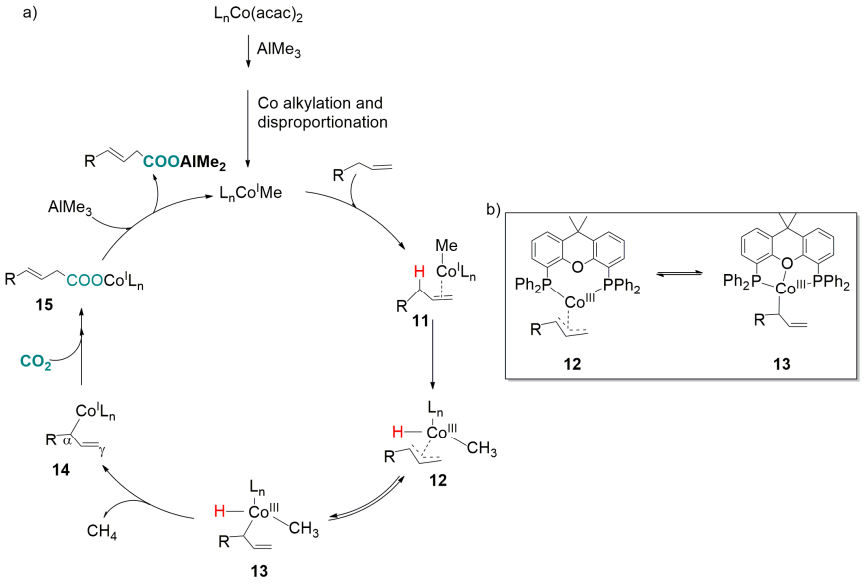
Very recently Mita and Sato have reported the catalytic carboxylation of allylic C(sp^3)-H bond of terminal alkenes with CO_2 in the presence of a Co(acac)$_2$/Xantophos/$AlMe_3$/CsF system [53] (Scheme 12). Allylarenes (15 examples) were carboxylated to linear *trans*-styrylacetic acids (**9**) with moderate to good yields (41–84%) and 100% regioselectivity. Olefin isomers were detected in reaction products at lower amount (Scheme 12a). The scope of the reaction was extended to 1,4-diene derivatives giving access to hexa-3,5-dienoic acid derivatives in moderate to good yields (7 examples, 24–78% yields) (Scheme 12b).

The addition of CsF to the reaction mixture was shown to increase by approximately 40% the yield of the reaction. Sato tentatively attributed the CsF beneficial effect to the interaction of F^- with CO_2 which allows for dissolving more CO_2 into the reaction system.

The mechanism of the reaction has been proposed to involve a $L_nCo(I)Me$ active species (Scheme 13) formed from Co(acac)$_2$ and $AlMe_3$ in the presence of the Xantphos ligand. The $L_nCo(I)Me$ active species is proposed to form through $L_nCo(II)$ alkylation by $AlMe_3$ to $L_nCo(II)Me_2$ and subsequent disproportionation of the latter to $L_nCo(III)Me_3$ and $L_nCo(I)Me$.



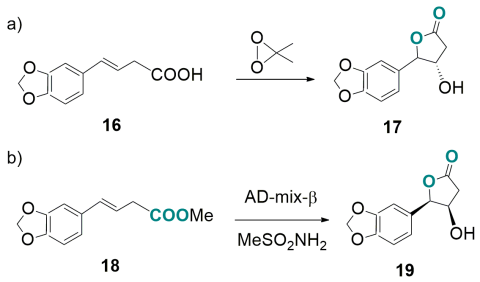
Scheme 12. (**a**) Selected examples for carboxylation reactions of allylic C(sp^3)-H bond of terminal alkenes to *trans*-styrylacetic acids; (**b**) Selected examples for carboxylation reactions of 1,4-diene derivatives to hexa-3,5-dienoic acid derivatives.



Scheme 13. Proposed mechanism for carboxylation of terminal alkenes to *trans*-styrylacetic acids.

The $L_nCo(I)Me$ complex coordinates, thus, the terminal olefin (**11**) with subsequent cleavage of the adjacent allylic C-H bond producing a η^3-allyl-Co specie (**12**). The authors suggest a key role could be played at this stage by the oxygen donor atom of Xantphos ligand as its coordination to Co would assist the tautomerization of η^3-allyl-Co to η^1-allyl-Co complex (Scheme 13b). Reductive elimination of CH_4 from η^1-allyl-Co(H)(CH_3) intermediate (**13**) leads to a low valent allyl-Co complex (**14**) able to undergo electrophilic attack from CO_2 at the γ-position. The last stage involves transmetallation between the carboxylated-Co complex (**15**) and $AlMe_3$ regenerating the $L_nCo(I)Me$ catalyst and producing R-COOAlMe_2. Addition of HCl to the reaction mixture gives the styrylacetic acids.

For selected substrates the authors achieved further transformation of styrylacetic acids into γ-butyrolactones through classical synthetic procedures (Scheme 14).



Scheme 14. Conversion of styrylacetic acids into γ-butyrolactones.

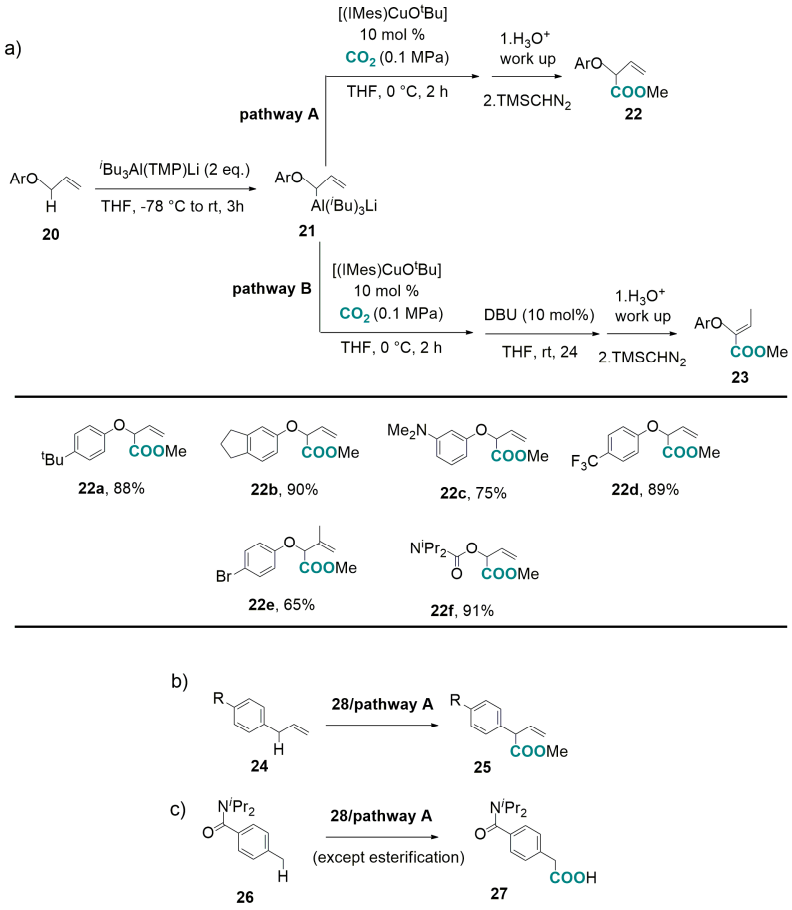
(*E*)-4-(Benzo[*d*][1,3]dioxol-5-yl)but-3-enoic acid (**16**) was converted into *anti*-5-(Benzo[*d*][1,3]dioxol-5-yl)-4-hydroxydihydrofuran-2(3*H*)-one (**17**) by treatment with dimethyldioxirane (68% yield) (Scheme 14a). The ester methyl (*E*)-4-(benzo[*d*][1,3]dioxol-5-yl)but-3-enoate (**18**) was converted into the optically active syn-β-hydroxy-γ-butyrolactone (4*R*,5*R*)-5-(Benzo[*d*][1,3]dioxol-5-yl)-4-iododihydrofuran-2(3*H*)-one (**19**) (80 Yield, 99% *ee*) by Sharpless asymmetric dihydroxylation.

Very recently, the Hou group succeeded in achieving a "formal" Cu(I)-catalyzed carboxylation of C-H bonds of allyl phenyl ethers (**20**) (Scheme 15a) [77] by using an aluminium ate compound such as (^{i}Bu)$_3$Al(TMP)Li (**28**, Scheme 16b) (TMP = 2,2,6,6-tetramethylpiperidide) [78] as base in proton abstraction form the substrate without side reactions.

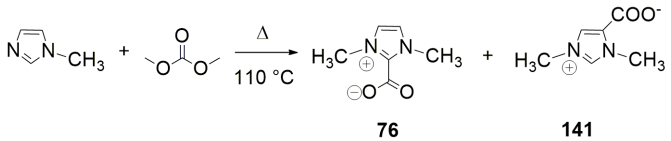
As shown in Scheme 15a, the reaction consists in selective proton abstraction from phenyl allyl ethers (**20**) by (^{i}Bu)$_3$Al(TMP)Li (2 eq.) (**28**) to obtain an η^1-allyl-anion coordinated to Al (**21**) that undergo subsequent transmetallation/carboxylation in the presence of the [(IMes)Cu(O^{t}Bu)] catalyst (**29**) to give methyl 3-butenoate derivatives (**22**) in high yield and high stereoselectivity. Phenyl allyl ethers bearing slightly electron-donating alkyl substituents at the phenyl nucleus as well as electron rich and electron-withdrawing substituents were carboxylated and subsequently esterified to 2-aryloxy-3-butenoate methyl ester derivatives (17 examples, 65–90% yields) with high regio- and stereo-selectivity (Scheme 15a, pathway A). The authors noticed that, during the Cu(I)-catalysed step, by increasing temperature and reaction period significant amount of the (*Z*)-2-aryloxy-2-butenoate isomers (**23**) were formed. The group was able to obtain products **23** with high regio- and stereo-selectivity by addition of DBU in catalytic amounts after the Cu(I)-catalysed reaction step (Scheme 15a, pathway B) (16 examples, 52–91% yields). The scope of the reaction could be extended also to allyl benzenes (**24**) (Scheme 15b) that were converted into 2-aryl-3-butenoate derivatives (**25**) (84–85% yield) via pathway A and into (*E*)-2-aryl-3-butenoate derivatives via pathway B (obtained in high yield). Finally, carboxylation of *p*-methylbenzamide (**26**, Scheme 15c) at the C(sp^3)-H benzylic functionality was obtained via pathway A (Scheme 15c) affording the corresponding carboxylic acid (**27**) in 52% yield and high regioselectivity.

Scheme 16a shows formation of an (η^1-ally)-Al(^{i}Bu)$_3$Li complex **21** by reaction of (^{i}Bu)$_3$Al(TMP)Li (**28**, Scheme 16b) with the substrate through TMP proton abstraction. Subsequently [(IMes)Cu(O^{t}Bu)]

(**29**) (10 mol %) is added to the reaction mixture. Concerning the mechanism of the Cu(I)-catalyzed reaction, the author proposes that **21** undergo transmetallation with [(IMes)Cu(O^{t}Bu)] affording (η^1-ally)-Cu(IMes) complex **30**. Carboxylation of **30** occurs in extremely mild reaction conditions (P_{CO_2} = 0.1 MPa, 0 °C) affording 2-aryloxo-3-butenoate anion coordinated to "Cu(I)(IMes)" fragment (**31**). As final steps, transmetallation between **31** and **21** complexes produces (**32**) and regenerates the (η^1-ally)-Cu(IMes) species (**30**).



Scheme 15. (**a**) Selected examples for carboxylation reactions of phenyl allyl ethers to methyl 3-butenoate derivatives (pathway A) or (*Z*)-2-aryloxy-2-butenoate derivatives (pathway B); (**b**) Carboxylation of allylbenzenes; (**c**) carboxylation of *p*-methylbenzamide.

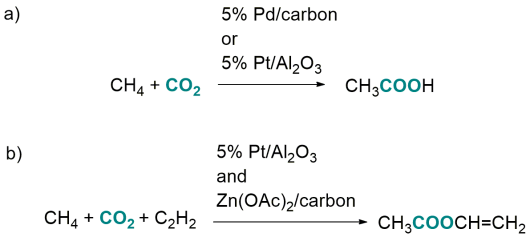


Scheme 16. (**a**) Reaction mechanism for carboxylation of phenyl allyl ethers to methyl 3-butenoate derivatives through proton abstraction by (^{i}Bu)$_3$Al(TMP)Li and Cu(I)-catalysed carboxylation (pathway A, Scheme 15); (**b**) Structure of (^{i}Bu)$_3$Al(TMP)Li.

2.3. Carboxylation of CH_4 with CO_2 by Heterogeneous Catalysis

The reaction of CH_4 with CO_2 to form acetic acid was investigated by the Spivey group under heterogeneous catalysis (5% Pd/carbon and 5% Pt/alumina) at the temperature of 400 °C. (Scheme 17a) [79]. The reaction is highly thermodynamically unfavourable, therefore, to overcome the

unfavorable equilibrium, CO_2 and CH_4 were reacted on the metal oxide to form acetate adsorbed on the catalyst surface. Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRITS) experiments evidenced formation of acetate adsorbed on the catalyst. Subsequently, a Temperature Programmed Reaction (TPR) experiment showed formation of gas phase acetic acid.



Scheme 17. (**a**) Carboxylation of CH_4 to acetic acid by heterogeneous catalysis; (**b**) Synthesis of vinylacetate from CH_4, CO_2 and C_2H_2 by heterogeneous catalysis.

An alternative method to overcome the unfavorable equilibrium of reaction shown in Scheme 17a consisted of reacting an equimolecular gaseous mixture of CH_4, CO_2 and C_2H_2 over 5% Pt/Al_2O_3 and $Zn(OAc)_2$/carbon catalysts at 1 atm over a temperature range of 200 to 400 °C (Scheme 17b) [80]. The reaction of acetic acid with acetylene to form vinyl acetate shifts to the right the unfavourable formation of acetic acid from CH_4 and CO_2.

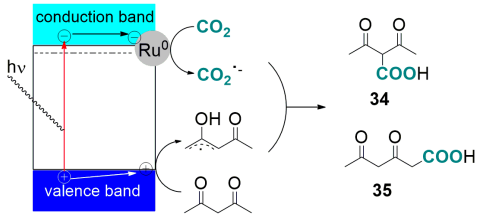
The reaction is proposed to proceed following a two steps pathway: first acetic acid is formed at the Pt-catalyst, then the acid reacts with acetylene affording vinyl acetate at the Zn-catalyst.

3. Light-Driven CO_2-Based Carboxylation Reactions of C(sp^3)-H Bonds

Very recently, two examples of photo-catalysed carboxylation reactions of C(sp^3)-H bonds have been reported by Jamison [81] and Macyck [82]. The Jamison process employs an organic photocatalyst (*p*-terphenyl) while the latter employs a ZnS photocatalyst. In addition, two examples of light-driven reactions exploiting the photochemical properties of ketones reported by Murakami are reviewed [83,84].

3.1. Photo-Catalysed Carboxylation of Acetylacetone with CO_2

Very recently, Macyk has reported the carboxylation of acetylacetone to 2-acetyl-3-oxobutanoic (**34**) and 3,5-dioxohexanoic (**35**) acids by using a photocatalytic system based on the wide band gap (3.6 eV) semiconductor zinc sulphide ($E^\circ = -2.0$ V vs. SHE) with deposited ruthenium nanoparticles (Scheme 18) [82].



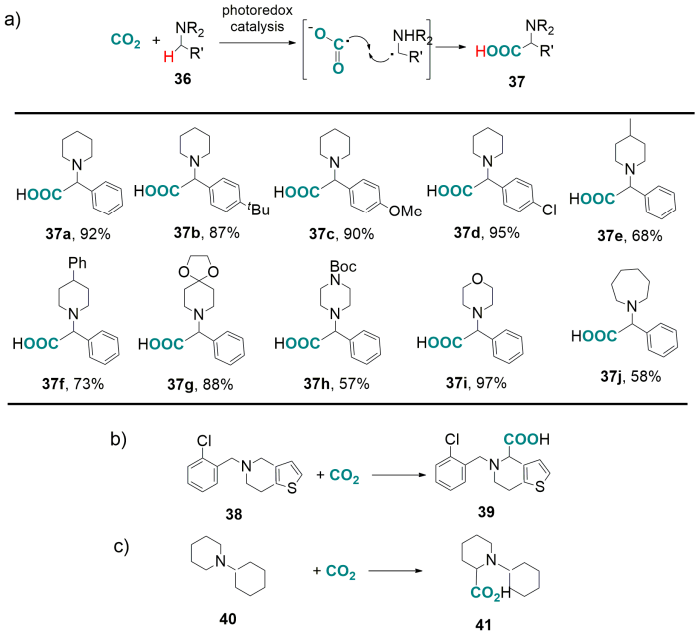
Scheme 18. Photocatalyzed carboxylation of acetylacetone at ZnS with deposited Ru particles.

Temperature-programmed desorption (TPD) experiments showed that Ru-nanoparticles significantly increased CO_2 adsorption at the catalyst surface. Upon irradiation of ZnS nanoparticles suspended in CCl_4 acids **34** and **35** were detected in solution by application of IR and ^{13}C NMR spectroscopies. Although the organic products could not be isolated, **34** and **35** were estimated to form in a 2:1 molar ratio. As shown in Scheme 18 the $CO_2^{\bullet-}$ radical is proposed to form at the Ru-particles surface while interaction of acetylacetone with photogenerated holes produces the organic

radicals. At the last stage the reaction involves a radical-radical coupling to form acids **34** and **35**. EPR spin-trapping experiments confirmed formation of $CO_2^{\bullet -}$ supporting, thus, the proposed mechanism.

3.2. Light-Driven Carboxylation of Benzylic and Allylic C(sp^3)-H Bonds with CO_2

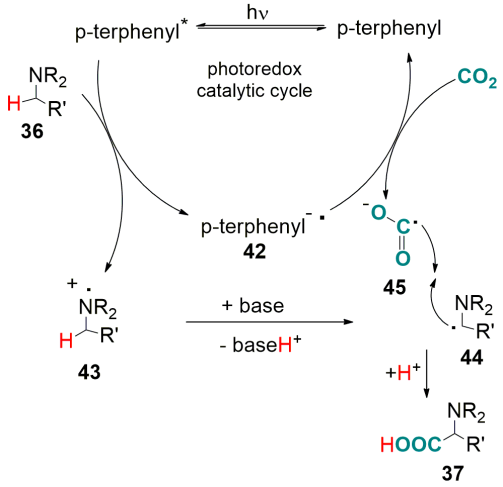
Very recently, Jamison reported the photoredox activation of carbon dioxide to promote carboxylation of *N*-benzyl substituted cyclic amines (**36**) in a continuous flow apparatus (Scheme 19) [81]. In typical reaction conditions, a mixture of substrate (*N*-benzyl substituted cyclic amines, **36**), photoredox catalyst (*para*-terphenyl, 20 mol %), CF_3COOK (3 eq.) and CO_2 was irradiated in DMF under an ultraviolet lamp at the temperature of 30–35 °C during 10 min. CO_2 was introduced in the flow apparatus through a mass flow controller. In optimized conditions irradiation with a λ > 280 nm was used to avoid unproductive reactions promoted by short-wavelenght ultraviolet light.



Scheme 19. (**a**) Selected examples for photocatalyzed carboxylation reactions of *N*-benzyl substituted amines to α-amino acids; Photocatalyzed carboxylation of ticlopidine (**b**) and *N*-cyclohexylpiperidine (**c**).

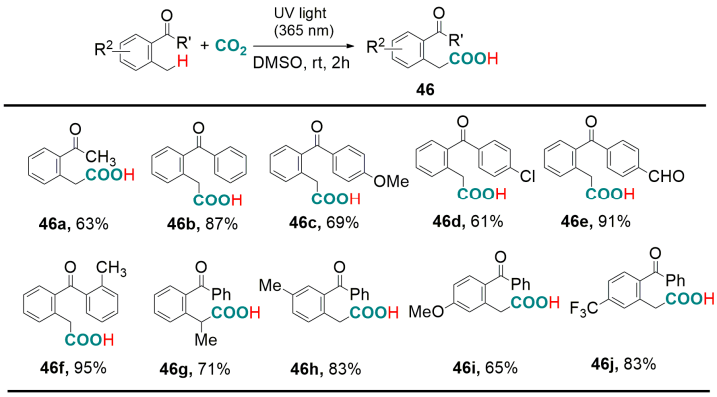
Tertiary *N*-benzylpiperidines bearing electron-neutral or electron-rich aryl-substituents and various *N*-benzyl cyclic amines (16 examples) were carboxylated with high regioselectivity at the benzylic position in good to high yields (46–99% yields) (Scheme 19a). Other *N*-substituted cyclic amines as ticlopidine (**38**) and *N*-cyclohexylpiperidine (**40**) were carboxylated at α-position with respect to N showing that the scope of the reaction may expand to other amines with different regioselectivity (Scheme 19b,c).

Concerning the reaction mechanism, (Scheme 20) Jamison proposes the photochemical reaction is initiated by the photo-excited *p*-terphenyl catalyst ($E^\circ = -2.63$ V vs. SCE in DMF) favoring single-electron transfer with the tertiary amine to provide the strongly reducing *p*-terphenyl radical anion (**42**) and the amine radical cation (**43**). Subsequent deprotonation of the amine radical cation by CF_3COO^- affords the neutral α-amino radical (**44**). The strong reducing *p*-terphenyl radical anion (**42**) is able to reduce carbon dioxide to $CO_2^{\bullet -}$ (**45**) which undergoes radical-radical coupling with the α-amino radical (**44**) leading to α-amino acids (**37**).



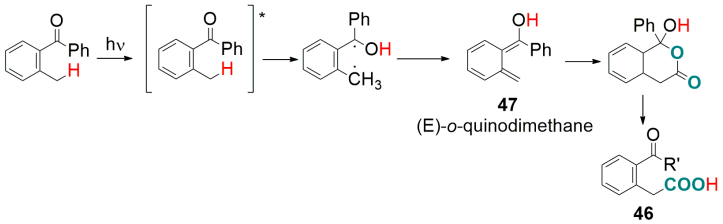
Scheme 20. Proposed mechanism for photocatalyzed carboxylation of *N*-benzyl substituted amines to α-amino acids.

A report by Murakami group describes irradiation by UV or solar light of *o*-alkylphenyl ketones under CO_2 atmosphere (0.1 MPa) to produce *o*-acylphenylacetic acids (**46**) in good to high yields (14 examples, 61–95% yields) (Scheme 21) [83].



Scheme 21. Selected examples for light-driven carboxylation reactions of *o*-alkylphenyl ketones to *o*-acylphenylacetic acids.

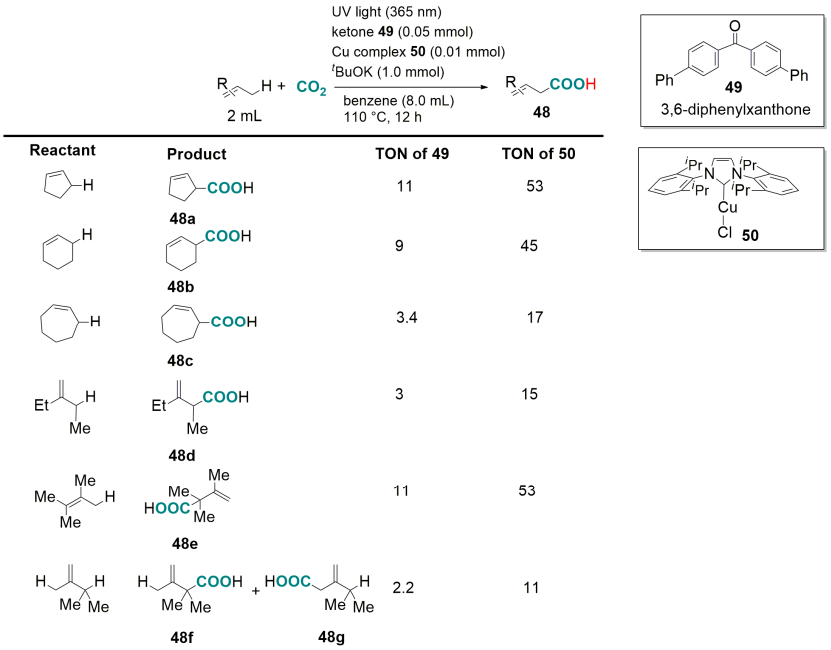
The reaction is proposed to proceed through endergonic isomerisation of *o*-alkylphenyl ketones to *o*-quinodimethanes (**47**) (Norrish Type II photoreaction) and subsequent [4 + 2] cycloaddition reaction of the (*E*)-*o*-quinodimethane with CO_2 (Scheme 22).



Scheme 22. Proposed mechanism of light-driven carboxylation of *o*-alkylphenyl ketones to *o*-acylphenylacetic acids.

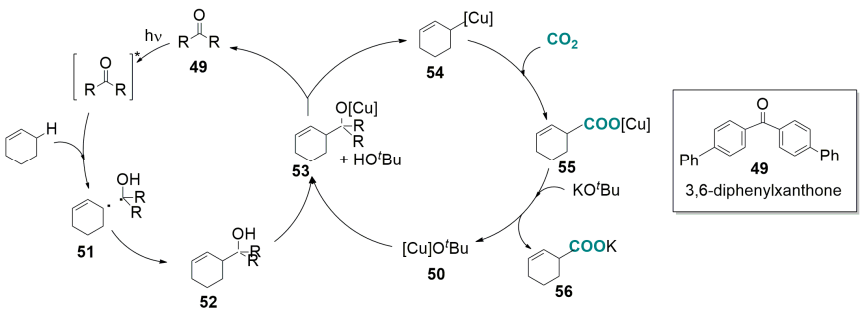
Interestingly, the reaction does not require any sacrificial reagent.

More recently Murakami reported a carboxylation reaction of C(sp^3)-H allylic bonds of simple alkenes (10 examples) to form alkenylacetic acids (**48**) (β,γ-unsaturated carboxylic acids) in the presence of 3,6-diphenylxanthone (**49**), IPrCuCl complex (**50**) and ^{t}BuOK (Scheme 23) [84]. Although the carboxylation of cyclohexene afforded 2-cyclohexene-1-carboxylic acid in approximately 2% yield (based on the alkene reagent) the ketone and the Cu-complex showed to react catalytically with a TON of 9 and 45 respectively (Scheme 23).



Scheme 23. Selected examples for light-driven carboxylation reactions of alkenes to alkenylacetic acids.

The mechanism proposed (Scheme 24) involves light-driven excitation of ketone **49** followed by abstraction of an allylic proton from cyclohexene by the carbonyl oxygen affording a radical pair (**51**). Subsequent radical-radical coupling leads to a tertiary homoallyl alcohol (**52**) (high energy intermediate) which undergo subsequent deprotonation by [Cu]O^{t}Bu (**50**) and complexation by [Cu]. The copper alkoxyde (**53**) undergoes β-carbon elimination leading to an allyl-Cu complex (**54**) regenerating the ketone (**49**). Insertion of CO_2 into the C-Cu bond of **54** leads to a carboxylate-Cu complex (**55**) that undergoes exchange with KO^{t}Bu producing the carboxylate potassium salt (**56**).



Scheme 24. Proposed mechanism of light-driven carboxylation of alkenes to alkenylacetic acids.

4. Brønsted-Base-Mediated Carboxylation of C(sp^3)-H Bonds with CO_2

A significant knowledge has been acquired over the past decades concerning Brønsted-base-promoted carboxylation of acidic C(sp^3)-H bonds proceeding according to stoichiometry reported in Scheme 2c.

As reported in Section 1, acquired kwoledges in this research area might allow future developments through optimization of the base-recycling process or implementation of base/transition-metal co-catalyzed reactions. In light of this view, an analysis of recent advances in this field and relevant developments of this chemistry over the last two decades are reported in the following two sections.

4.1. Recent Advances in Brønsted-Base Mediated Carboxylation of Acidic C(sp^3)-H Bond with CO_2

Thanks to reports by Jessop [58] and Beckman [59], significant advances in the synthesis of β-keto carboxylic acids from ketones and CO_2 and their further conversion into β-ketoesters and β-hydroxycarboxylic acids have been introduced. Very recently an interesting example of base-promoted carboxylative cyclization reaction of 1-propenyl ketones to α-pyrones has been reported by Lu [85].

Interestingly, in the Jessop process DBU can be easily recycled for subsequent reactions while in the Beckmann process DBU is shown to react catalytically. From a synthetic point of view, β-ketoesters are valuable building-block in the preparation of a wide variety of molecular systems as their structural unit is composed of two different electrophilic carbonyls and two nucleophilic carbons that can react selectively under suitable reaction conditions [86].

Moreover, chiral β-hydroxycarboxylic acids are important intermediates widely used as chiral precursors of anti-inflammatory products, [87] β-amino acids, [88] β-lactams, [89] β-lactones, [90] and pheromones [91].

The Jessop group developed an efficient two step procedure for the synthesis of chiral β-hydroxycarboxylic acids from ketones, CO_2 and H_2 [58]. First β-ketocarboxylic acids (**57**) are synthesized in a DBU-promoted reaction, subsequently the acids are stereoselectively reduced with H_2 to chiral β-hydroxycarboxylic acids (**58**) by using the $RuCl_2$[(S)-BINAP] catalyst (Scheme 25). It must be pointed out that, while asymmetric hydrogenation of β-keto carboxylic esters is a well known procedure, there was only one previous example of catalytic hydrogenation of β-keto acids reported by Genêt et al. [92].

Optimal reaction conditions for the carboxylation of acetophenone to benzoylacetic acid (91% yield) were found by working in dry conditions and in the absence of solvents (neat DBU/acetophenone mixture, 2 eq. of DBU, P_{CO_2} = 6.0 MPa, 0 °C). Optimized reaction conditions were applied to other ketones as acetone, cyclohexanone and aryl-substituted acetophenones affording the corresponding β-keto acids in yield ranging from 11 to 78% and high regioselectivity. Several substrates such as isobutyrophenone and (1*R*)-camphor could not be carboxylated by using DBU. Instead NEt_3/MgI_2 and LDA were suitable bases.

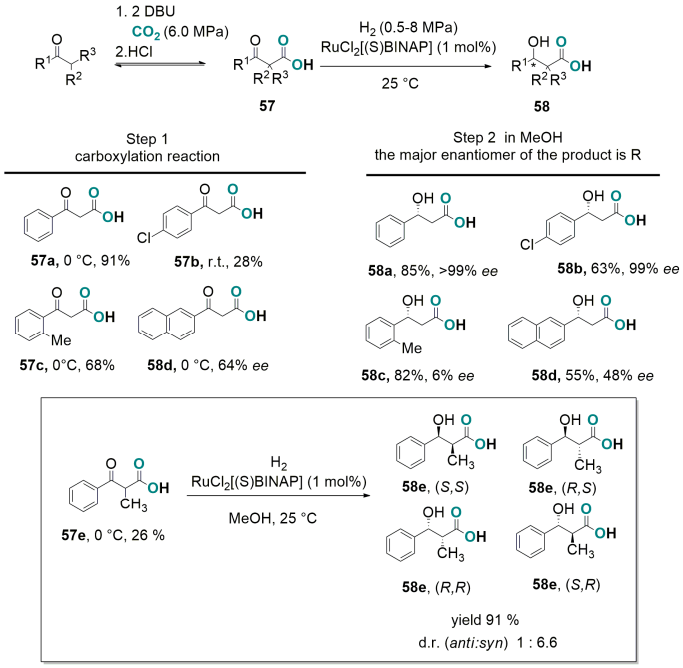
The author underscores that, due to mild conditions adopted and high selectivity of the reaction, unconverted ketones and DBU can be recovered from the reaction mixture and easily recycled. The developed method meets, thus, most of requirement for an industrial application.

In the second reaction step (Scheme 25) β-ketocarboxylic acids are asymmetrically hydrogenated in various polar and nonpolar solvents by using $RuCl_2$[(S)-BINAP] catalyst (1 mol %, P_{H2} ranging from 0.5 to 8.0 MPa, 25 °C).

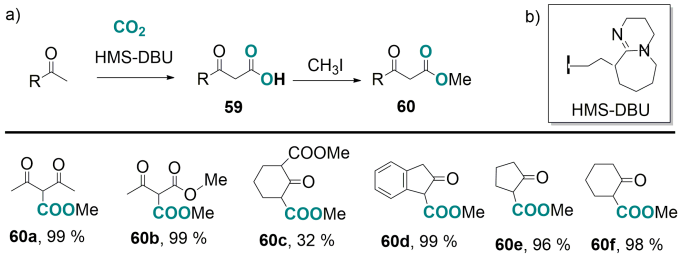
As β-ketoacids easily undergo a decarboxylation reaction, a thorough investigation of solvent effect and other factors affecting the β-hydroxycarboxylic acids yield was required to set conditions favouring slow decarboxylation and fast hydrogenation of ketoacids. Methanol and CH_2Cl_2 were found as optimal solvents allowing to obtain high yield of β-hydroxyphenylacetic acid (85% and 93% yields were respectively obtained in the two solvents) and high *ee* (99% for the *R* enantiomer).

Beckman has developed a "Reversible CO_2-Carrier" (RCC) based on DBU covalently bound to siloxane (methylhydrosiloxane dimethyl siloxane copolymer, HMS) support (Scheme 26b) [59].

Interestingly, HMS-DBU suspended in methanol absorbed CO_2 up to 100% capacity at room temperature under low CO_2-pressure to form HMS-DBU-CO_2. Moreover, HMS-DBU-CO_2 recovered by filtration was shown to release CO_2 at 120 °C in thermogravimetric analysis (TGA) measures. RCC showed, thus, to possess highly desirable properties and to enable high yield conversion of ketones to the corresponding β-ketoacids (**59**) under ambient CO_2 pressure and temperature (Scheme 26a). Reacting in situ β-keto acids with CH_3I allowed easy RCC recovery (by simple filtration) and recycle up to five times without loss of activity.



Scheme 25. Synthesis of chiral β-hydroxycarboxylic acids (selected examples are shown) from ketones, CO_2 and H_2.



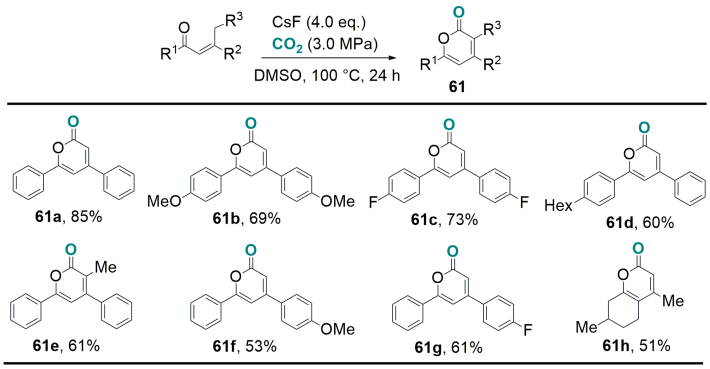
Scheme 26. (**a**) Selected examples for carboxylation reactions of ketones to β-ketoacids and further conversion into β-keto esters; (**b**) Reversible CO_2-Carrier (RCC) based on DBU covalently bound to siloxane support.

Very interestingly, by careful determination of the DBU-active sites in the solid carrier it was possible to show that the covalently-bound-DBU reacts catalytically. In addition, the author notes the ester yields strongly correlates with the enolic content of the reacting ketone. Ketones with higher equilibrium constant for keto ↔ enol equilibrium as 2,4-pentanedione, ethyl acetoacetate, 2-indanone, cyclopentanone and cyclohexanone afforded higher carboxylic ester yield (96–99%) with TON of 200

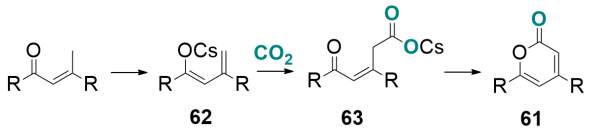
(over 4 h). Reactants as acetophenone and *para*-substituted acetophenones were carboxylated/esterified with low yields (9–29%, 21–61 TON over 4 h).

The research group of Lu reported in 2016 the carboxylative cyclization of substituted 1-propenyl ketones (21 examples) with CO_2 for the synthesis of α-pyrones (**61**) in moderate to good yield (22–83%) (Scheme 27) [85].

The reaction is proposed to proceed through base-promoted enolization of the ketone followed by γ-carboxylation of the enolate (**62**) leading to a β,γ-unsaturated carboxylate intermediate (**63**) (Scheme 28). Proton abstraction from intermediate (**63**) promotes subsequent cyclization leading to α-pyrones (**61**).



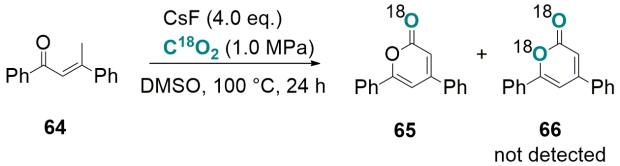
Scheme 27. Selected examples for carboxylative cyclization rections of substituted 1-propenyl ketones to α-pyrones.



Scheme 28. Proposed mechanism for carboxylative cyclization of substituted 1-propenyl ketones to α-pyrones.

Optimized reaction conditions were found using CsF (4 eq.), P_{CO_2} = 1.0 MPa, at 100 °C. Suitable bases for carboxylative cyclization of propenyl ketones were Cs_2CO_3, NaH, and CsF.

A mechanistic investigation using β-methylchalcone (**64**) and $C^{18}O_2$ (Scheme 29) afforded the singly isotopically ^{18}O-labeled 4,6-diphenyl-2*H*-pyran-2-one (**65**) in 45% yield while the doubly labeled isotopologue **66** was not detected.



Scheme 29. Carboxylative cyclization of β-methylchalcone to mono-^{18}O-labeled 4,6-diphenyl-2*H*-pyran-2-one using $C^{18}O_2$.

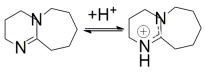
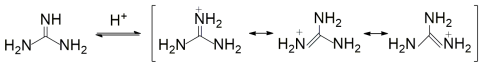
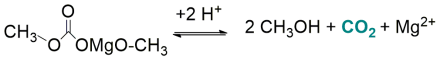
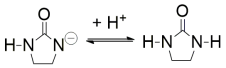
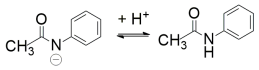
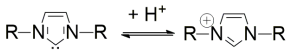
This result indicates that the cyclization proceeds via intramolcular attack of enolate oxygen on the carbonyl group of the carboxylate intermediate **63**.

4.2. Carboxylation of C(sp^3)-H Active Bonds by Using CO_2 Carriers

It is known that Grignard and organolithium reagents readily react with CO_2 affording carboxylates. However, these reactions do not tolerate functionalities as ketone, ester and nitrile. Alternatively, a wide range of organic bases [93–98] have been used to deprotonate an activated C(sp^3)-H bond providing a nucleophilic substrate able to react with CO_2 [99–106].

Table 1 lists organic bases frequently used in Brønsted-base-promoted carboxylation of active hydrogen compounds (pKa value refers to the conjugated acids) using CO_2.

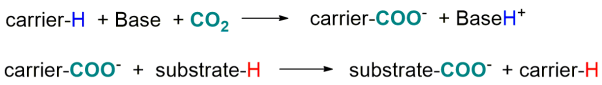
Table 1. Organic bases frequently used in Brønsted-base-promoted carboxylation of active hydrogen compounds with CO_2.

Entry	Acid-Base Equilibrium	pKa Value (of the Conjugated Acid)	Reference
1	$PhO^- \overset{+H^+}{\rightleftharpoons} PhOH$	18.0 in DMSO [93]	[99]
2	$Et_3N \overset{+H^+}{\rightleftharpoons} Et_3NH^+$ (in conjuction with MgI_2)	10.70 in H_2O [94]	[100]
3		11.82 in MeCN [95]	[101]
4		28.5 in DMSO [96]	[102]
5		29.0 in DMSO [93] considering CH_3OH	[103]
6		17.97 in H_2O [97] (calculated value)	[104]
7		21.5 in DMSO [96]	[105]
8		21.1 in DMSO [98] 32.4 in CH_3CN (calculated value)	[106]

An analysis of the scientific literature available on the subject shows that base-promoted carboxylation reactions may proceeds following a "one-step" or a "two-steps" pathway as shown in Scheme 30. In the one-step procedure, the substrate is reacted with the base under CO_2 atmosphere while, in the two-step procedure at first a CO_2-carrier is formed which then transfers CO_2 to the substrate mimicking biotin-dependent enzymatic carboxylation reactions. In both cases, even apparently simple reactions exhibit relatively complex mechanisms.

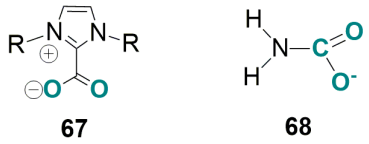
a) one-step pathway

b) two-steps pathway



Scheme 30. "One-step" or "two-steps" pathways for base-promoted carboxylation of activated C(sp^3)-H bonds.

Particular interest has been raised recently for "CO_2-carriers" as carboxylates (**67**) and carbamates (**68**) (Scheme 31) which have been effectively used as "CO_2-bent surrogates" in electrochemical and photochemical production of chemicals from CO_2 [10,107–109].



67 **68**

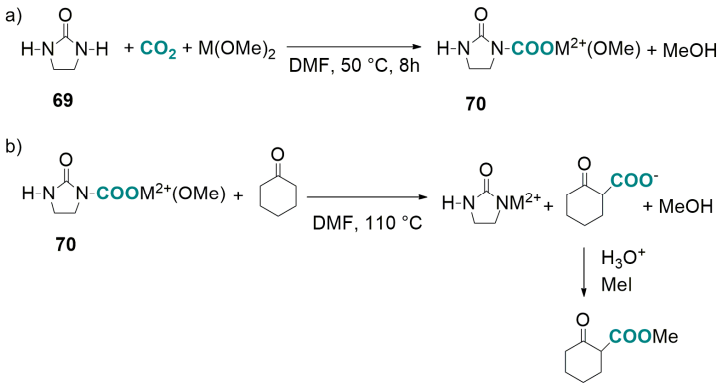
Scheme 31. Carboxylates and carbamates as CO_2-bent surrogates.

We list here on several CO_2-carriers effectively used in carboxylation reactions of activated C(sp^3)-H bond according the "two step pathway" shown in Scheme 30b.

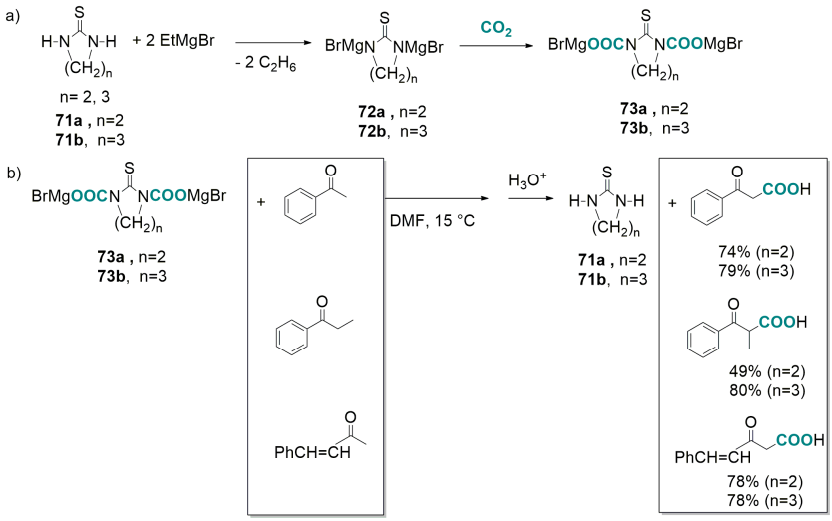
Inspired by biotin-dependent enzymatic carboxylation reactions Saegusa and co-workers synthesized in 1979 a 2-oxoimidazolidine-1-carboxylate complex **70** obtained by reacting 2-oxoimidazolidine (**69**) with $M(OCH_3)_2$ (M = Mg^{2+}, Mn^{2+}) and CO_2 in DMF at 50 °C (Scheme 32a) [104]. Both the Mg^{2+}- and Mn^{2+}-ureido-carboxylate-complexes were able to transfer CO_2 to cyclohexanone at 110 °C in DMF to form 2-oxocyclohexanecarboxylic acid that was converted into ester by reaction with MeI (Scheme 32b). By using the Mg^{2+}-ureide-carboxylate complex **70** in a 10:1 molar ratio with respect to cyclohexanone the 2-oxocyclohexanecarboxylic acid methyl ester was obtained in 43% yield.

In 1983, Matsumura reported the easy carboxylation of cyclic thioureas **71** as ethylenethiourea and 1,3-propylenethiourea with CO_2 in the presence of ethylmagnesium bromide at room temperature (Scheme 33a) [110]. The carboxylato-complexes (**73**) were isolated and used in a transcarboxylation reaction of ketones in DMF at 15 °C (Scheme 33b). After acidification, the corresponding β-keto carboxylic acids were isolated in 49–80% yields.

Interestingly, the thioureide-CO_2 complexes **73** were able to act as CO_2-carriers at temperature significantly lower (15 °C) with respect to analogous 2-oxoimidazolidine-1-carboxylato complexes (Scheme 32b).



Scheme 32. (**a**) Synthesis of 2-oxoimidazolidine-1-carboxylate complexes; (**b**) Carboxylation of cyclohexanone by 2-oxoimidazolidine-1-carboxylate complexes.

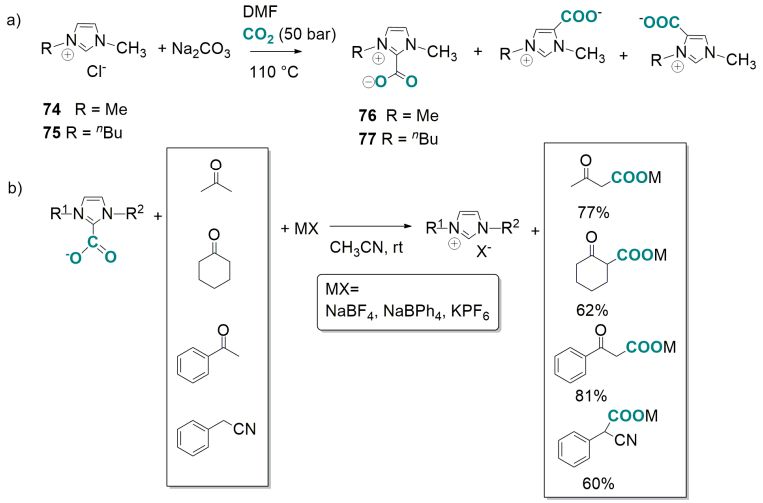


Scheme 33. (**a**) Carboxylation of cyclic thioureas; (**b**) Examples for carboxylation reactions of ketones by thioureide-CO_2 complexes.

Schemes 32 and 33 show the use of molecules containing the carbamate functionality (N-CO_2^-) as CO_2-carriers in the carboxylation of C-H active substrates. More recently 1,3-dialkyl- (**76**–**77**) or 1,3-diaryl-imidazolium-2-carboxylates (**78**) have been used as CO_2-transfer agents for the carboxylation of ketones and nitriles [66,106,111,112].

Reactions in which a "C-COO^-" moiety behave as CO_2-transfer agent towards an organic compound are not common. Previous report is the Henkel reaction converting potassium benzoate into benzene and terephthalic acid, a valuable component for polyesters derivatives [113].

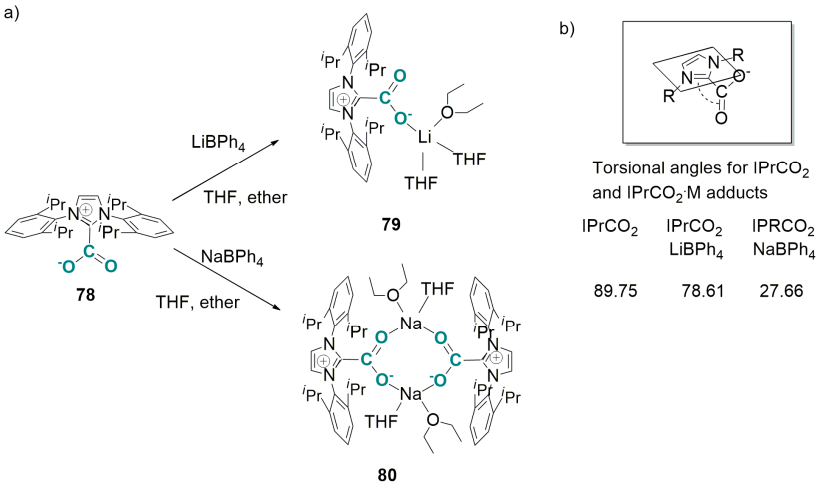
We have reported direct carboxylation of 1,3-dimethyl- (**74**) and 1-butyl,3-methyl-imidazolium chloride (**75**) with Na_2CO_3/CO_2 at high temperature (110 °C) and P_{CO_2} = 5 MPa (Scheme 34a) [111] to afford 1,3-dialkylimidazolium-2-carboxylates (**76**–**77**) in 92% yield and 91% selectivity. Subsequently **76**–**77** have been used as CO_2-carriers able to transfer CO_2 to acetone, acetophenone, cyclohexanone and benzyl cyanide (Scheme 34b) [66,106]. Interestingly, the reaction proceeds at room temperature requiring the presence of a metal salt as $NaBF_4$, $NaBPh_4$ or KPF_6 in stoichiometric amount. Carboxylated products are isolated in the form of metal salts in yield ranging from 60 to 81%.



Scheme 34. (**a**) Carboxylation of 1,3-dialkylimidazolium chlorides with Na_2CO_3/CO_2; (**b**) Carboxylation of C-H acidic compounds by 1,3-diakylimidazol-2-carboxylates in the presence of salts.

More recently Louie has undertaken a detailed mechanistic study on the abovementioned trans-carboxylation reaction by using IPr-CO_2 (**78**), IMes-CO_2 and I^{t}But-CO_2 as CO_2-carriers [112]. Investigating the role played by the alkali metal, Louie succeeded in isolating NHC-CO_2·M (M = Li^+, Na^+) adducts (**79**,**80**) that were characterized by single crystal X-ray diffraction analysis.

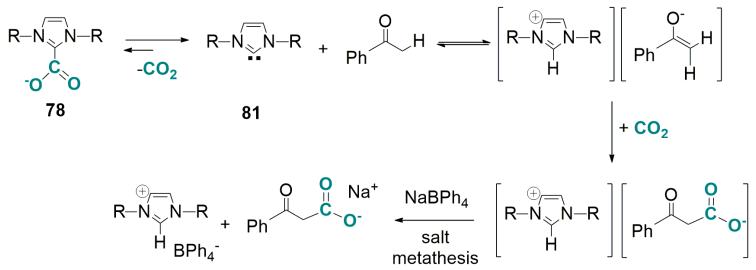
The X-ray structure showed Li^+ and Na^+ cations affording respectively monomeric (**79**) and dimeric (**80**) complexes (Scheme 35a). Most important, it was shown the interaction of the metal ion with the CO_2-moiety decreasing the CO_2-torsion angle with respect to the plane of the ring (Scheme 35b) suggesting, thus, a stabilisation of the carboxylate [114].



Scheme 35. (**a**) Structure of IPrCO_2·M (M = Li^+, Na^+) complexes; (**b**) Torsional angles in IPrCO_2 and IPrCO_2·M complexes.

Information obtained from X-ray structure was contradicted by results of TGA measures on the NHC-CO_2·M adducts. As matter of fact, the metal adducts were shown to lose CO_2 at lower temperature with respect to their parent carboxylate. In addition, kinetic information inherent the carboxylation of acetophenone to benzoylacetic acid showed the reaction was first order in IPrCO_2 but independent of $NaBPh_4$ concentration.

Concerning the reaction mechanism, Louie proposes the trans-carboxylation reaction is initiated by spontaneous decarboxylation of the NHC-CO_2 complex (**78**) with generation of the free NHC carbene (**81**) able to promote hydrogen abstraction from the substrate producing, thus, the corresponding enolate anion (Scheme 36). Subsequent carboxylation of the enolate anion with CO_2 provides benzoylacetate.



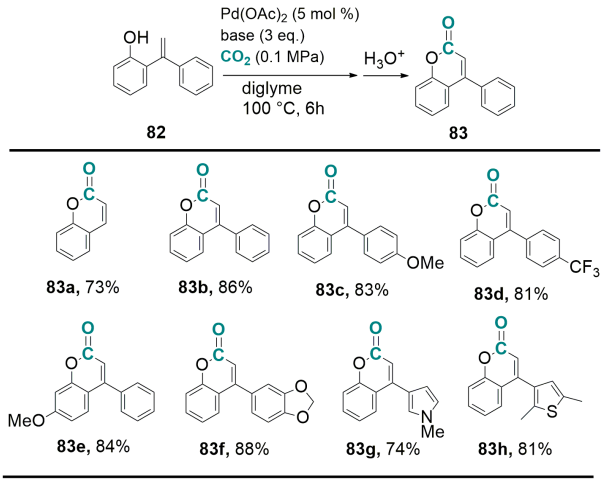
Scheme 36. Proposed mechanism for carboxylation of acetophenone by NHC-CO_2.

On the basis of abovementioned experimental evidence it was concluded that the metal salts increase the solubility of poorly soluble imidazolium-2-carboxylates and is involved in product stabilization through ion pairing.

5. Transition-Metal-Catalyzed Carboxylation of C(sp^2)-H Bonds with CO_2

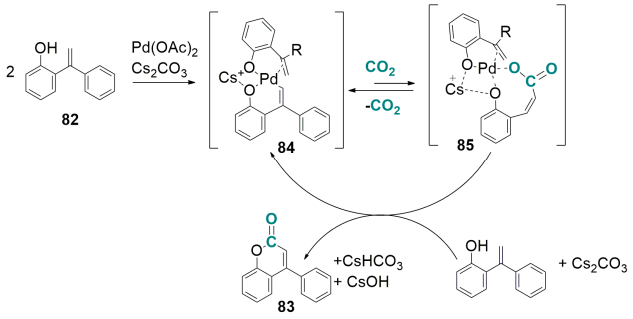
5.1. Carboxylation of Alkenyl-C-H Bonds by Pd-Catalysis

As reported in the introductory section, direct carboxylation of aromatic and/or heteroaromatic substrates with CO_2 has received particular attention in the last decade. Excellent reviews on this topic have appeared recently [19,54,55,115]. Direct carboxylation of alkenyl-C-H bonds is more difficult to achieve, therefore, to the best of our knowledge, only one report from Iwasawa [116] describes direct carboxylation with CO_2 of 2-hydroxystyrenes in the presence of the $Pd(acac)_2/Cs_2CO_3$ catalytic system (Scheme 37). In optimized conditions, α-phenyl-2-hydroxystyrene (**82**) is carboxylated to 4-phenylcoumarin (**83**) (86% yield) in the presence of $Pd(OAc)_2$ (5 mol %) and Cs_2CO_3 under atmospheric CO_2 pressure at 100 °C. A wide range of 2-hydroxystyrene derivatives (16 examples) are carboxylated to the corresponding coumarin derivatives in yield ranging from 73 to 90%.



Scheme 37. Selected examples for carboxylation reactions of 2-hydroxystyrenes to 4-phenylcoumarin derivatives.

As possible reaction mechanism Iwasawa proposes the hydroxyl functionality of **82** undergoing deprotonation and subsequent coordination to the metal (Scheme 38). Then, the alkenyl C-H bond of α-phenyl-2-hydroxystyrene is cleaved (by chelation-assisted alkenyl C-H bond cleavage) producing a six-membered alkenyl palladium intermediate (**84**) bearing an additional 2-hydroxystyrene molecule (as cesium salt) as ligand. The organometallic intermediate **84** undergoes, thus, reversible carboxylation at the alkenyl functionality (affording **85**) and subsequent exchange with an additional substrate molecule (in the presence of Cs_2CO_3) to eliminate the coumarin **83**. At the same time the six-membered alkenyl palladium catalyst **84** is regenerated.

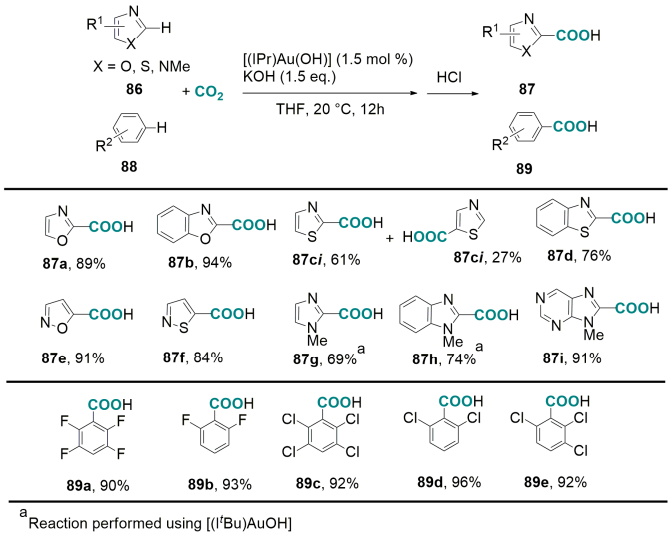


Scheme 38. Proposed mechanism for carboxylation of 2-hydroxystyrenes to 4-phenylcoumarin derivatives.

Iwasawa notes the carboxylation step is reversible and the cyclization reaction (lactonization) helps to shift to the right side the carboxylation-decarboxylation equilibrium.

5.2. Carboxylation of Aromatic and Heteroaromatic Compounds

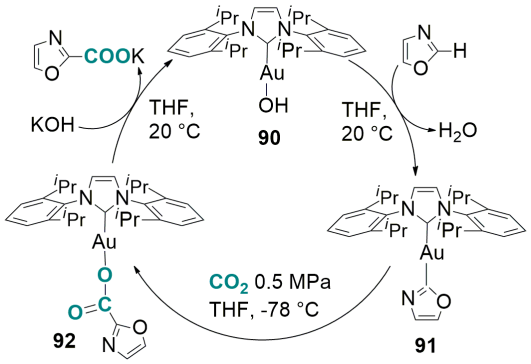
The ability of dicoordinate, linear [Au(NHC)OH] complexes (NHC = 1,3-bis(2,6-diisopropylphenyl) imidazol-2-ylidene or 1,3-di-*tert*-butylimidazol-2-ylidene) to catalyze C-H activation/carboxylation reactions of carbo- and hetero-cycles under mild reaction conditions (P_{CO_2} = 0.15 MPa, ambient temperature) was reported by Nolan and coworkers in 2010 (Scheme 39) [57]. A wide range of substrates (including oxazoles, isoxazoles, thiazoles, isothiazoles, imidazoles, pyridazine and some aromatic heterocycles containing three or four heteroatoms) were carboxylated, in the presence of a stoichiometric amount of KOH, in yield ranging from 76 to 92% at the most acidic C-H bond. Furthermore, the synthetic method could be applied to polyfluoro- and polychloro-substituted benzene derivatives (Scheme 39).



Scheme 39. Selected examples for carboxylation reactions of carbo- and hetero-cycles by [(IPr)AuOH] complex catalysis.

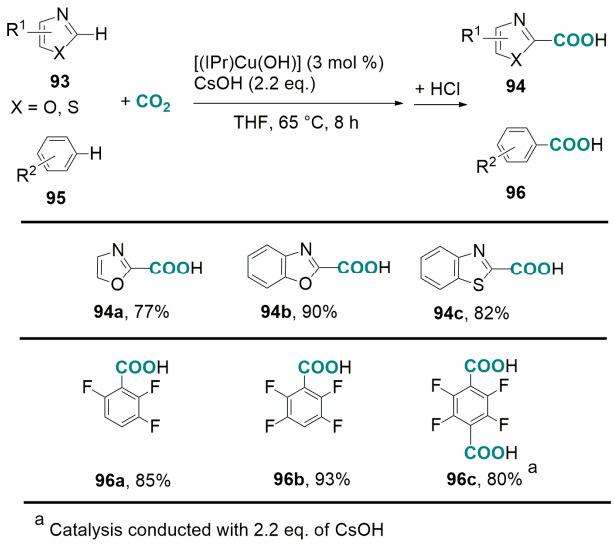
There is also an almost contemporary report by Larrosa concerning C-H bond activation of electron deficient (hetero)aromatics by $L_nAu(I)$-complex to provide the corresponding aryl-Au(I) species [117].

The reaction described in Scheme 39 is considered to proceed via C-H deprotonation assisted by the Au-complex (Scheme 40). The basicity of the [Au(NHC)OH] complexes was measured by acid-base potentiometric titrations giving a pKa_{DMSO} = 30.3(4) value for [(IPr)AuOH] and a pKa_{DMSO} = 32.4(2) value for the [(I^tBu)AuOH] complexes. As a consequence, assuming simple Brøensted acid/base theory could be used to predict the feasibility of C-H bond functionalisation, substrates possessing C-H bond with a pKa below 32.1 could be carboxylated [118]. Nolan noted that mechanistic features of the Au(I)-catalyzed carboxylation reaction (shown in Scheme 40) are similar to the generally accepted mechanism of the copper(I)-catalyzed carboxylation of organoboronic esters [30,119]. Indeed, the [(IPr)AuOH] complex (**90**) is proposed to abstract the most acidic C-H proton from oxazole affording a [(IPr)Au(oxazolyl)] complex (**91**) able to insert CO_2 into Au-C bond. The author was able to isolate [2-oxazolyl-Au(NHC)] (**91**) and [2-oxazolyl-COOAu(NHC)] (**92**) intermediates by reacting [(IPr)AuOH] with oxazole in stoichiometric amounts (according to reaction conditions shown in Scheme 40) to obtain **91** and **92** in 93% and 86% yield respectively. Experimental evidence supports, thus, the proposed mechanism. The last stage of the cycle involves metathesis of the carboxylate complex **92** with KOH releasing oxazolyl-COOK and regenerating the [(IPr)AuOH] complex **90**.



Scheme 40. Proposed mechanism for carboxylation of heterocycles by [(IPr)AuOH] complex catalysis.

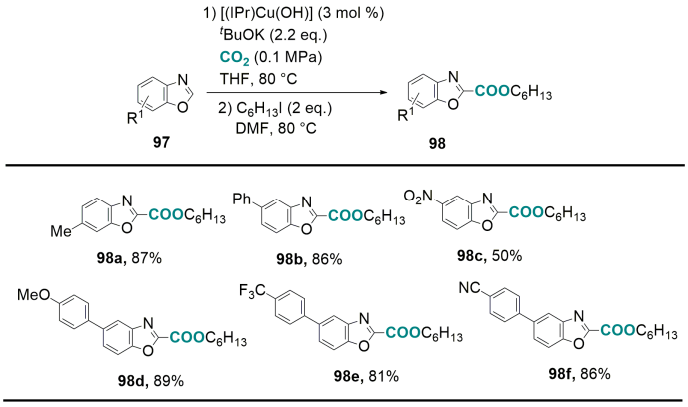
Further development of the abovementioned study led to the carboxylation of oxazole, benzoxazole, benzothiazole, and polyfluorobenzenes with CO_2 by employing the cheaper [(IPr)CuOH] catalyst [56] in the presence of CsOH (2.2 eq.) under low CO_2 pressure (0.15 MPa) at the temperature of 65 °C (Scheme 41).



Scheme 41. Selected examples for carboxylation reactions of carbo- and hetero-cycles by [(IPr)CuOH] complex catalysis.

Acid-base potentiometric titration of [(IPr)CuOH] complex gave a pKa_{DMSO} = 27.7(2) value. The reaction is proposed to occur through a mechanism similar to that described in Scheme 40 for the Au(I)-catalyst. The lower pKa value for [(IPr)CuOH] complex with respect to [(IPr)AuOH] complex allows to predict a more limited substrate scope. Substrates **93** and **95** were carboxylated with high selectivity at the most acidic C-H position in high yields (77–93%).

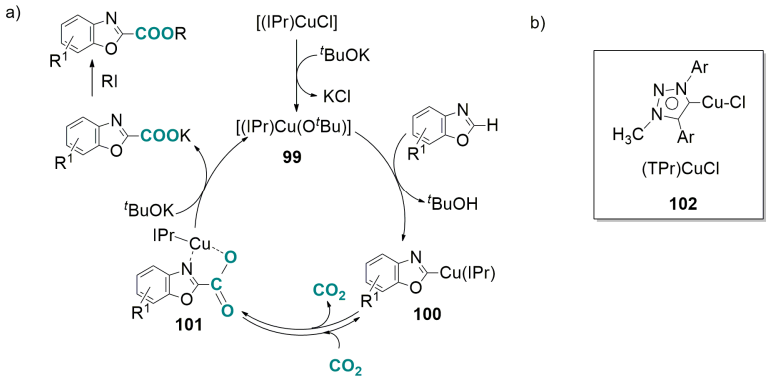
Cu(I)-NHC-based catalysts were also used by the Hou [54] group. The Cu(I)-chloride pre-catalyst [(IPr)CuCl] (5 mol %) in the presence of KO^{t}Bu (1.1 eq.) under atmospheric CO_2 pressure at 80 °C was employed in carboxylation of various benzoxazole derivatives bearing both electron-donating and electron-withdrawing substituents at the aryl moiety. Carboxy-derivatives were esterified in situ with alkyl iodides providing the corresponding ester derivatives (11 examples, 50–89% esters yields) (Scheme 42).



Scheme 42. Selected examples for carboxylation reactions of benzoxazole derivatives by [(IPr)CuOH] complex catalysis.

1-methyl-benzimidazole and 5-phenyl-1,3,4-oxadiazole were also carboxylated selectively at C2 position in 14% and 36% yield respectively.

Concerning the reaction mechanism, the [(IPr)Cu(O^{t}Bu)] (**99**) active species is proposed to form by metathesis with ^{t}BuOK of the [(IPr)CuCl] pre-catalyst. Isolation and fully characterization of [2-benzoxazolyl-Cu(IPr)] (**100**) and [2-benzoxazolyl-COO-Cu(IPr)] (**101**) complexes by the Hou group allowed to propose a catalytic cycle analogous to that proposed by Nolan for the Au-catalyzed reaction (Scheme 43a). Therefore, also Cu(I)-catalyzed carboxylation reactions are considered to proceed via C-H deprotonation.



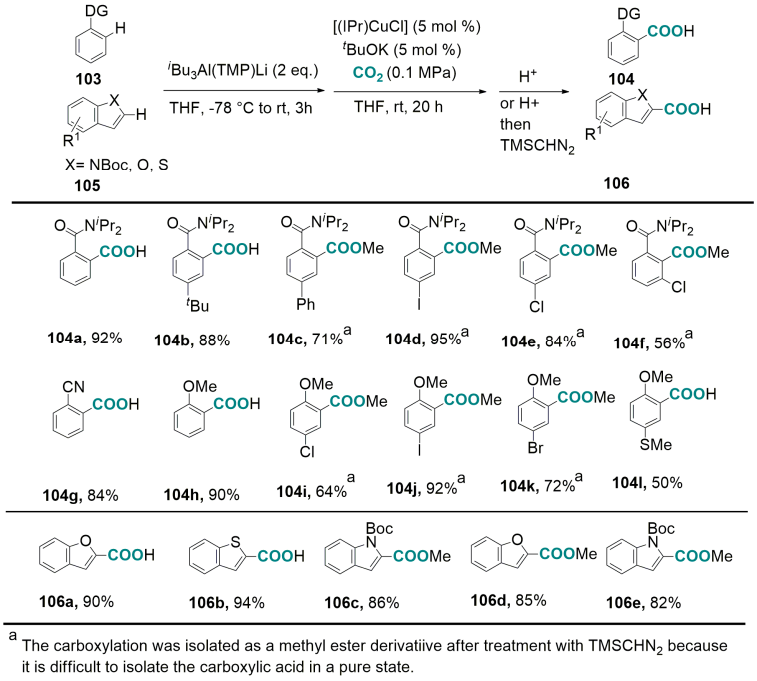
Scheme 43. (**a**) Carboxylation of benzoxazole derivatives by [(IPr)CuOH] complex; (**b**) [(TPr)CuCl] complex.

Interestingly, X-ray crystallographic analysis of [2-benzoxazolyl-COO-Cu(IPr)] complex (**101**) showed the benzoxazolylcarboxylate ligand is bound in a chelating fashion to the Cu-atom (as shown in Scheme 43a).

Carboxylation of benzoxazoles derivatives (8 examples, 41–88% yields) and benzothiazole derivatives (7 examples, 33–79% yield) was reported by Hou employing the 1,4-di(2,6-diisopropylphenyl)-3-methyl-1,2,3-triazol-5-ylidene ligand (TPr) coordinated to Cu(I) (**102**) (Scheme 43b) [120] under the same reaction conditions adopted for the [(IPr)Cu(OH)] analogue.

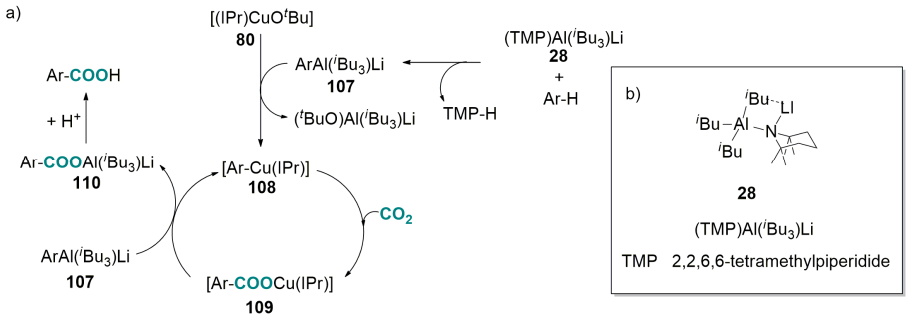
The aluminium ate compound (^{i}Bu)$_3$Al(TMP)Li (**28**) employed by Hou in the Cu(I)-catalyzed carboxylation of allyl aryl ethers (see Section 2.2) was employed also in carboxylation of arylic-C-H bonds (Scheme 44) [121]. Benzene derivatives as *N*,*N*-diisopropylbenzamide, benzonitrile and anisole (bearing both electron-withdrawing and electron-donating substituents) were carboxylated in high yield (16 examples, 50–95% yields) and high selectivity. In addition, heteroarenes such as benzofuran,

benzothiophene, and indole derivatives (7 examples) were effectively carboxylated at the C(2)-position (72–94% yields).



Scheme 44. Selected examples for carboxylation reactions of aromatic compounds bearing a directing group and heteroarenes by ($^{i}Bu)_3Al(TMP)Li$ base in conjunction with [(IPr)CuO^{t}Bu] complex catalysis.

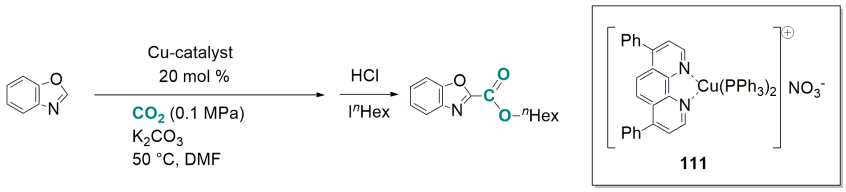
The aluminate base (**28**, Scheme 45b) (TMP = 2,2,6,6-tetramethylpiperidide) [78] was used in proton abstraction from the substrate to give a Ar-Al($^{i}Bu)_3Li$ complex (**107**) (Scheme 45a). Subsequent transmetallation in the presence of [(IPr)CuO^{t}Bu] (5 mol %) and KO^{t}Bu (5 mol %) under atmospheric CO_2 pressure afforded carboxylic acids in extremely mild reaction conditions (room temperature).



Scheme 45. (**a**) Proposed mechanism for carboxylation of benzene derivatives and heteroarenes by ($^{i}Bu)_3Al(TMP)Li$ base in conjunction with [(IPr)CuCl] complex catalysis; (**b**) Structure of ($^{i}Bu)_3Al(TMP)Li$.

Having isolated and fully characterizated several key intermediates as copper aryl- and isobutyl-complexes and their carboxylated products, Hou proposed a reaction mechanism implying transmetallation of the (Ar)Al($^{i}Bu)_3Li$ complex **107** with (IPr)Cu(O^{t}Bu) to obtain the (Ar)Cu(NHC) species **108** (Scheme 45a). The (Ar)Cu(NHC) complex **108** undergoes, thus, CO_2-insertion into Cu-C bond affording the (ArCOO)Cu(NHC) carboxylate complex **109**. As final step, transmetallation between (ArCOO)Cu(NHC) and (Ar)Al($^{i}Bu)_3Li$ complex produces (ArCOO)Al($^{i}Bu)_3Li$ (**110**) and regenerates the (NHC)CuAr species **108**.

The research group of Gooßen developed a, (4,7-diphenyl-1,10-phenanthroline)bis(trisphenylphosphine) copper(I) nitrate (**111**) catalyst for the carboxylation of benzoxazole under atmospheric CO_2 pressure (Scheme 46) [122].

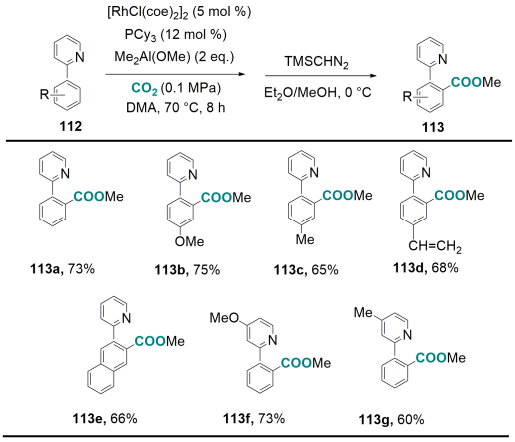


Scheme 46. Carboxylation of benzoxazole by Cu(I)-complex catalysis.

It is worth citing, catalyst (**111**) and (4,7-diphenyl-1,10-phenanthroline)bis-[tris(4-fluorophenyl)-phosphine] copper(I) nitrate catalysts effectively promotes the insertion of CO_2 into the C-H bond of terminal alkynes under very mild conditions.

Above reported examples of Au- and Cu-catalyzed direct C(sp^2)-H carboxylation are proposed to proceedes via a C-H deprotonation type mechanism. Iwasawa and coworkers have recently reported the Rh(I)-catalyzed direct C-H carboxylation of 2-phenylpyridines and 1-phenylpyrazoles derivatives under ambient CO_2 pressure proceeding via a reaction mechanism involving chelation-assisted C-H bond activation (C-H oxidative addition) [123]. Iwasawa noted the new approach can be extended to substrates featuring C-H bond with pKa_{DMSO} above 30.

Iwasawa envisioned to generate a $L_nRh(I)$-(Me)-catalyst (**114**, Scheme 48) by reacting $[RhCl(coe)_2]_2$ in the presence of PCy_3 and a methylmetallic reagent. Among methylmetallic reagents $AlMe_2(OMe)$ was shown as the most efficient in promoting carboxylation of target substrates. 2-Phenylpyridine derivatives (**112**) were shown as excellent substrates undergoing *mono*-carboxylation regioselectively at the *ortho*-position of the aryl-substituent (Scheme 47). The synthetic method included esterification in situ with $TMSCHN_2$ of the Ar-carboxylated products, therefore methyl-ester derivatives **113** were isolated in good to high yields (11 examples, 51–88% yield). Interestingly, 2-phenylpyridine derivatives bearing both electron-donating and electron withdrawing substituents in *para*-position of the benzene ring were suitable substrates.

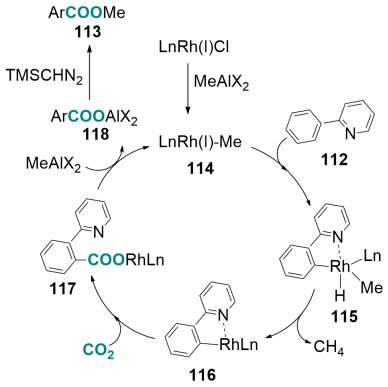


Scheme 47. Selected examples for carboxylation reactions of 2-phenylpyridines by Rh(I)-catalyst.

When using 1-phenylpyrazole as substrate both *mono*- and *di*-carboxylated products at *ortho*-positions were obtained in 80% combined yield.

The reaction mechanism proposed by Iwasawa involves coordination of the substrate to the LnR(I)-Me active specie (**114**) with subsequent chelation assisted C-H bond activation (oxidative

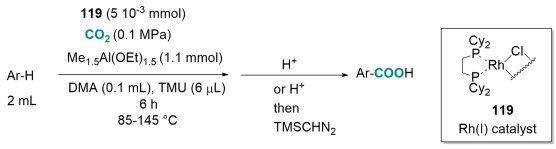
addition) at the C(2)-benzene position to obtain complex **115**. Reductive elimination of CH_4 from the six-coordinated intermediate complex leads to a ArRh(I) cyclometallated specie (**116**) undergoing CO_2 insertion into C-Rh bond to give the *mono*-carboxylated product ArCOORh(I)L_n (**117**). Subsequent transmetallation of ArCOORh(I)L_n with methylalluminium reagent produces $ArCOOAlX_2$ (**118**) and regenerates the LnRh(I)Me complex **114** (Scheme 48).

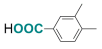
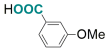
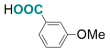
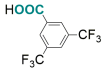


Scheme 48. Proposed mechanism for carboxylation of 2-phenylpyridine by Rh(I)-catalyst.

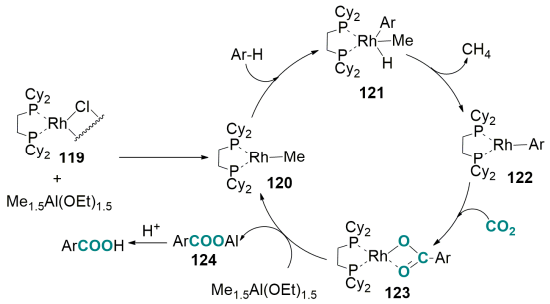
More recently, Iwasawa and co-workers succeeded in CO_2-promoted carboxylation of simple arenes in the absence of directing groups [124].

A Rh(I)-complex coordinated by 1,2-bis(dialkylphosphino)ethane ligands (preferentially 1,2-bis(dicyclohexylphosphino)ethane) (**119**, Scheme 49) was shown to be an efficient carboxylation catalyst of simple arenes (Scheme 49) (under P_{CO_2} = 0.1 MPa, closed reactor) in the presence of $AlMe_{1.5}(OEt)_{1.5}$, 1,1,3,3-tetramethylurea (TMU) and DMA solvent. However, quite high temperature was required, ranging from 85 to 145 °C. TMU was believed to stabilize coordinatively unsaturated Rh(I)-species (Scheme 50). In optimized conditions, various arenes were carboxylated to afford the corresponding carboxylic acids in moderated TON. Electron-donating substituents such as methyl- or methoxy-group attached to the benzene-nucleus afforded *mono*-carboxylated products with TON ranging from 15 to 46.



Reactant	T (°C)	Main product	TON	Regioselectivity α : β: γ
	85		37	
	120		18	17 : 57 : 26
	145		46	12 : 88
	145		15	23 : 54 : 23
	145		15	23 : 54 : 23
	145		49	0 : 0 : 100
	145		22	55 : 45 : 0

Scheme 49. Selected examples for carboxylation reactions of simple arenes by Rh(I)-catalyst.

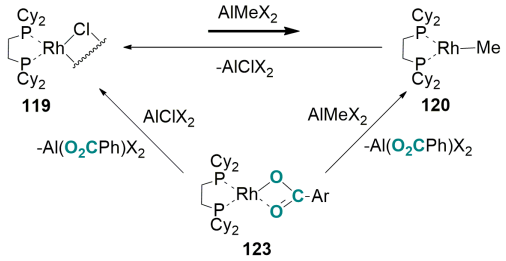


Scheme 50. Proposed mechanism for carboxylation of simple arenes by Rh(I)-catalyst.

The carboxylation of several heteroaromatic compounds as benzofuran and *N*-methylindole proceeded selectively at the 2-position with TON of 12 and 21 respectively.

A detailed mechanistic investigation was conducted by the Iwasawa group by application of an accurate kinetic study [125]. The reaction was shown to proceeds via a mechanism very similar to the carboxylation of 2-phenylpyridine derivatives (Scheme 48). Key steps were the formation of a $L_nRh(I)$-Me species (**120**) interacting with the Ar-H substrate which undergoes C-H oxidative addition to produce a six-coordinated $L_nRh(III)(Ar)(H)(Me)$ complex (**121**). Further reductive elimination produces CH_4 and $L_nRh(I)$-Ar complex (**122**) that undergoes CO_2 insertion into the C-Rh bond (Scheme 50).

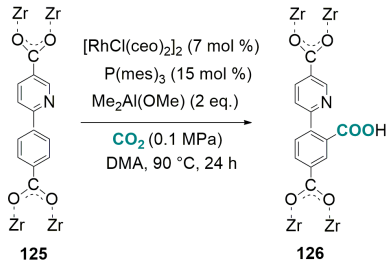
Moreover, the mechanistic study [125] evidenced that transmetallation of the $ArCOORhL_n$ complex (**123**) with methylaluminium may involve a quite complex reaction pathway (Scheme 51). Dedicated experiments have shown that transmetallation of $ArCOORh(I)L_n$ (**123**) and chloroaluminate species or $AlMeX_2$ may convert the catalyst back to $[RhCl(dcype)]_2$ (**119**) and to [RhMe(dcype)] (**120**) respectively. In turn, $[RhCl(dcype)]_2$ may reacts with $AlMeX_2$ affording the $L_nRh(I)$-Me species (**120**). The two Rh(I)-complexes ($[RhCl(dcype)]_2$ (**119**) and $L_nRh(I)$-Me (**120**) are, thus, in equilibrium. Interestingly, the equilibrium seems to limit the concentration of the active specie $L_nRh(I)$-Me and to suppress its decomposition.



Scheme 51. Proposed mechanism for transmetallation of the $ArCOORhL_n$ complex with methylaluminium.

More recently, the chlorobis(cyclooctadiene)rhodium(I) dimer ($[Rh(ceo)_2Cl]_2$) catalyst in the presence of methylaluminium was used to *mono*-carboxylate 2-phenylpyridine-5-4′-dicarboxylic acid (dcppy) (**125**) selectively at the *ortho*-position of the aryl-substituent to give the **126** derivative (Scheme 52) [126].

The reaction was used in post-modification of UiO-67(dcppy) MOF affording UiO-67(dcppy)-COOH. The resultant carboxylated MOF was used as a solid-state Brønsted acid catalyst in ring-opening reactions of epoxides with methanol.



Scheme 52. Carboxylation of 2-phenylpyridine-5-4′-dicarboxylic acid as linker of UiO-67(dcppy) MOF.

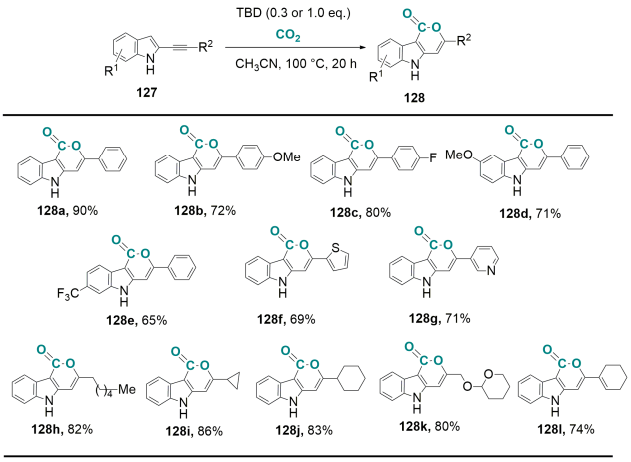
6. Brønsted Base-Mediated Carboxylation Reactions of C(sp^2)-H Bonds with CO_2

As reported in Section 1, particular attention has been devoted over the last decade to base-promoted carboxylation of C(sp^2)-H bonds due to the relevance of aryl-carboxylates as bioactive substances [23]. Studied reactions often proceed according to stoichiometry reported in Scheme 2c. However, Kanan [60] has recently reported the carboxylation of 2-carboxy pyrrole to furan-2,5-dicarboxylic acid(a highly desirable biobased feedstock [127]) with Cs_2CO_3/CO_2 adding to the process a base-regeneration step (by electrodialysis). The CO_2-foot print of the overall synthetic method depends, thus, on intelligent use of renewable energy sources.

In the following Sections an example of base-catalyzed carboxylation of 2-alkynyl indoles with CO_2 is reported followed by an overview of base-promoted carboxylation reactions of C(sp^2)-H bonds. The synthetic process reported by Kanan will be analyzed in Section 6.3.

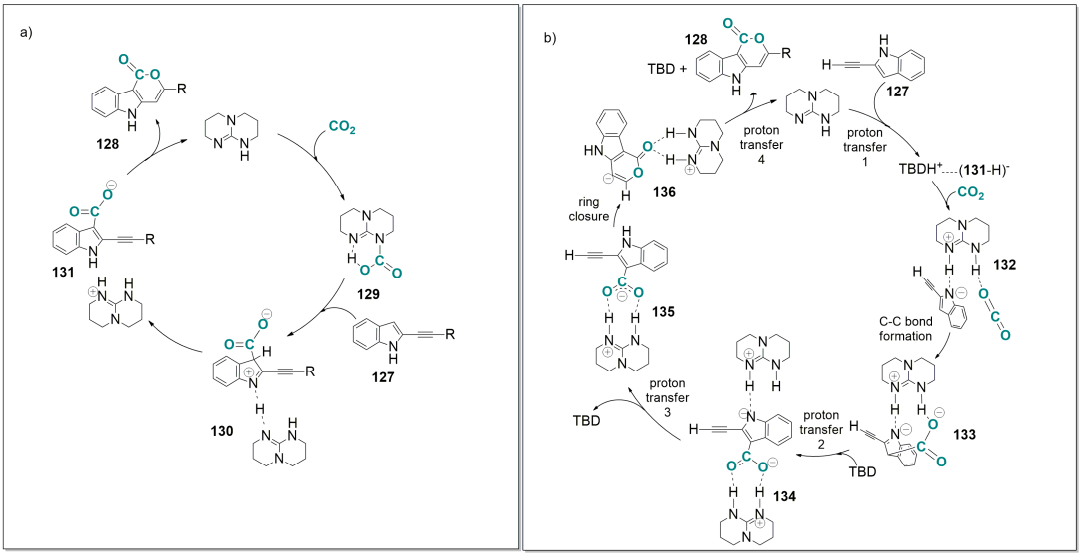
6.1. Base-Catalyzed Carboxylation of 2-Alkynyl Indoles with CO_2

A TBD base was used by Skyrdrup to catalyze a carboxylation/cyclization reaction applied to 2-alkynyl indoles (**127**) with aromatic or aliphatic substituents at the alkyne unit (Scheme 53) to produce selectively the new heterocyclic structures **128** [128]. Aromatic 2-alkynyl indoles (R^2 = aryl, Scheme 53) (0.20 mmol) were reacted in the presence of 0.3 eq. of TBD at the temperature of 100 °C after injection of a definite amount of CO_2 (0.61 mmol) into a 10 mL reaction vial. Substrates underwent the carboxylation/cyclization reaction in high yield (10 examples, 71–90% yields). Using aliphatic 2-alkynyl indoles (R^2 = alkyl, Scheme 53) the reaction proceeded under the same reaction conditions but the substrates proved less reactive requiring 1 eq. of TBD for optimal conversion (9 examples, 53–86% yields).



Scheme 53. Selected examples for carboxylation/cyclization reactions of aromatic 2-alkynyl indoles.

A plausible reaction mechanism was proposed by Skrydstrup (Scheme 54) encompassing the formation of the well characterized TBD-CO_2 zwitterionic adduct (**129**). Interaction of the 2-alkynyl indole with the TBD-CO_2 adduct promotes deprotonation of the NH-functionality and subsequent electrophilic attack by CO_2 at the 3 position of the indole ring (**130**). Re-aromatization of the indole ring by 3,1-hydrogen shift produces the carboxylate (**131**) which is prone to attack the alkynyl-moiety via a 6-*endo-dig*-cyclization mechanism. Recently, the reaction mechanism proposed by Skrydstrup has been reanalyzed by Wong and co-workers via a DFT study [129] using the energetic span model developed by Shaik and Kozuch [130] to calculate turnover frequencies (TOFs). The DFT analysis suggests that the more favored activation pathway encompasses a bifunctional mechanism in which TBD is able to deprotonate **127** at the nitrogen atom (proton transfer 1, Scheme 54b) engaging, at the same time, hydrogen bond with CO_2 (**132**). Next, C-C bond formation affords the **133** species which requires a second TBD molecule for C-H proton abstraction (proton transfer 2) to give **134**. Strong hydrogen bonding between guanidinium $TBDH^+$ and the anionic CO_2 moiety stabilizes intermediate **134**. Additional transfers of hydrogen ion between $TBDH^+$ and nitrogen of indole-CO_2 regerates TBD and gives **135** which can undergo a ring closure reaction to provide **136**. Proton transfer 4 from $TBDH^+$ to **136** gives finally TBD and product **128**. Calculated TOF for the bifunctional activation pathways was 1.2×10^{-13} h^{-1}, which was the higher value as compared to alternative pathways.

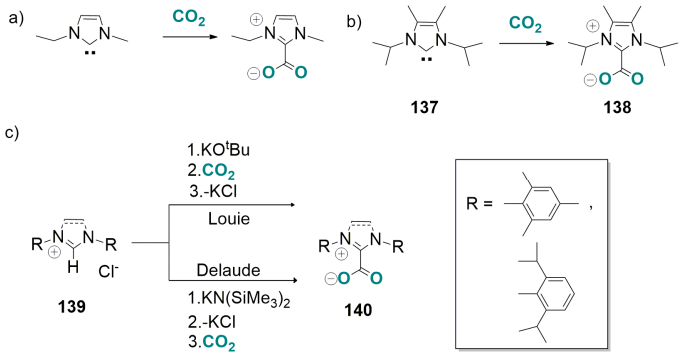


Scheme 54. (**a**) Reaction mechanism proposed by Skrydstrup for carboxylation/cyclization of 2-alkynyl indoles with CO_2; (**b**) Bifunctional activation mechanism proposed on the basis of DFT analysis by Wong and coworkers.

6.2. Base-Promoted Carboxylation of Aromatic and Heteroaromatic Compounds with CO_2

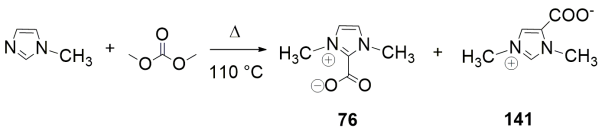
One impressive example of improved energy efficiency in CO_2 reduction to CO comes from an electrochemical reduction process (96% selectivity) reported by Masel and co-workers by application of a cell overpotential of only 0.17 V on a 1-ethyl-3-methylimidazolium tetrafluoroborate (EMIM BF_4)-coated silver catalyst. Masel proposed CO_2 to react with EMIM to form a EMIM $CO_2[BF_4]$ complex [131]. Analogous results were reported by Brennecke and co-workers [132] by using Pb electrodes and (EMIM)(Tf_2N) electrolyte. By spectroscopic characterization of the precipitate formed during electrolysis, Brennecke reported the formation of the NHC-CO_2 adduct shown in Scheme 55a. NHC-CO_2 adducts seems, thus, to play a significant role in electrochemical CO_2 reduction to CO at low overpotential. NHC-CO_2 adducts are well characterized species which chemistry has been developed after isolation of stable *N*-heterocyclic carbenes (NHC) (**137**) started by Arduengo in 1991 [133]. In Section 4.2, we have mentioned the carboxylation of 1,3-dialkyimidazolium chlorides

with CO_2/Na_2CO_3 and the use of 1,3-dialkyimidazolium-2-carboxylates as CO_2-carriers in the carboxylation of C(sp^3)-H acidic compounds. NHC-CO_2 compounds can be also synthesized by carboxylation of imidazol-2-yilidene precursors as reported by Kuhn in 1999 (Scheme 55b) [134] or by carboxylation of imidazol-2-ylidenes generated in situ by deprotonation of imidazolium salts (**139**) with potassium *tert*-butoxide or $KN(SiMe_3)_2$ as reported by Louie [135] and Delaude [136] (Scheme 55c).



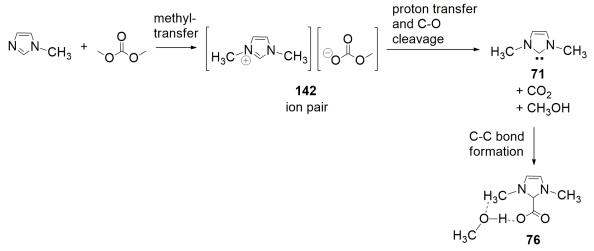
Scheme 55. (**a**,**b**) Carboxylation of 1,3-dialkylimidazol-2-ylidenes. (**c**) Carboxylation of 1,3-dialkylimidazolium salts.

Although the reaction is not involving CO_2, it is worth citing that, unexpected synthesis of 1,3-dimethylimidazolium-2-carboxylate was reported by Rogers et al. in 2003 [137] by reaction of 1-methylimidazole with dimethylcarbonate. Carrying the reaction at temperature lower than 95 °C affords selective formation of the imidazolium-2-carboxylate regioisomer (**76**) in 76% yield. At higher temperature (110 °C) the imidazolium-4-carboxylate regioisomer (**141**) forms in approximately 15% yield (Scheme 56).



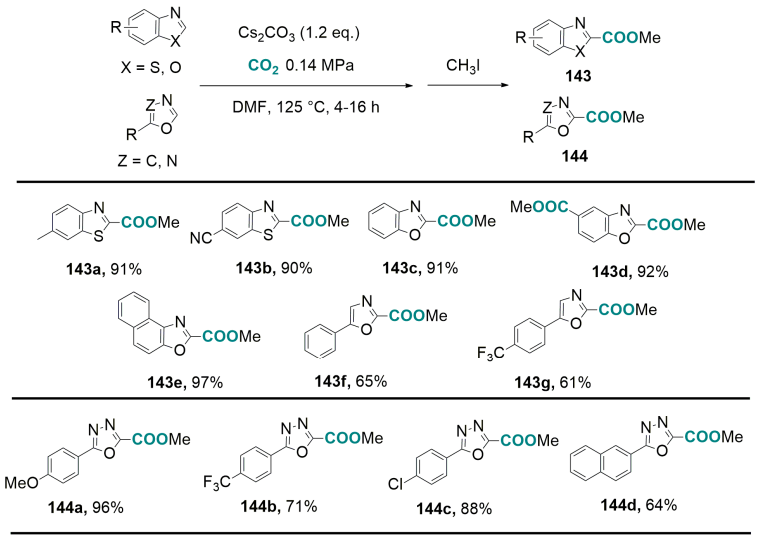
Scheme 56. Synthesis of imidazolium-2-carboxylate and imidazolium-4-carboxylate from 1-methylimidazole and dimethylcarbonate.

The mechanism of this unexpected reaction was modelled via DFT by Crabtree in 2007 (Scheme 57) [138]. According to DFT analysis, *N*-methylation of 1-methyimidazole by dimethylcarbonate affords an imidazolium/$CH_3OC(O)O^-$ ion pair (**142**). Proton abstraction from the imidazolium cation by $CH_3OC(O)O^-$ generates the 1,3-dimethylimidazol-2-ylidene (**71**) that promptly reacts with CO_2. NHC-CO_2 adduct forms, thus, via a reaction pathway similar to the carboxylation reported by Louie and Delaude (Scheme 55c). Methanol formed during the reaction may be engaged into H-bonding stabilization of the carboxylate product (**76**).



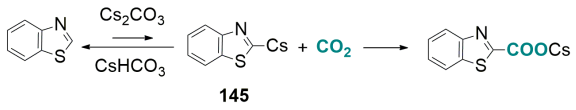
Scheme 57. Proposed mechanism for synthesis of 1,3-dimethylimidazolium-2-carboxylate (**76**) from 1-methylimidazole and dimethylcarbonate.

Concerning the base-promoted carboxylation of heteroarenes, in 2010 Hu and coworkers reported the carboxylation of benzothioazole and benzoxazole derivatives under CO_2 (0.14 MPa) using Cs_2CO_3 (1.2 eq.) at the temperature of 125 °C in DMF solution (Scheme 58) [139]. In order to avoid decomposition of unstable carboxylic acids the products were converted in situ into stable esters with MeI or trimethylsilyldiazomethane ($TMSCHN_2$). Benzothiazole and benzoxazole derivatives bearing both electron-withdrawing and moderately electron-donating substituents at the phenyl ring (8 examples) gave the corresponding 2-carboxy methyl esters (**143**) in 68–97% yields. Excellent regioselectivity for carboxylation at the C(2)-position was registered. 5-Phenyloxyoxazole and 2-aryl-1,3,4-oxadiazole derivatives were also carboxylated (**144**) in good to high yield (8 examples, 55–96% yields).



Scheme 58. Selected examples for carboxylation reactions of benzothioazole, benzoxazole and 2-aryl-1,3,4-oxadiazole derivatives.

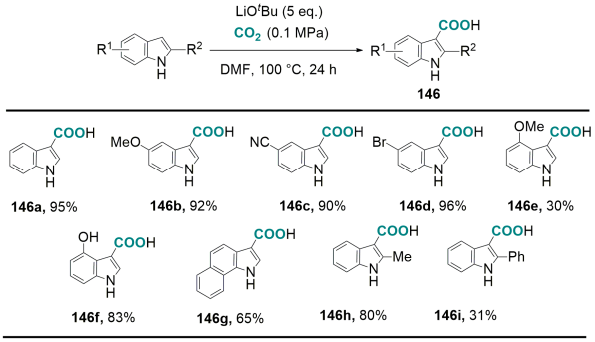
Hu proposes the carboxylation to proceed via a mechanism different from the Kolbe-Schmitt reaction encompassing deprotonation of benzothiazole at the C(2) position with subsequent carboxylation of the 2-benzothiazolyl anion (**145**) (Scheme 59).



Scheme 59. Proposed mechanism for carboxylation of benzothioazole with CO_2.

However, spectroscopic analysis of the reaction mixture did not provide evidence of 2-benzothiazolyl anion (**145**) formation. Therefore, it was concluded C-H cleavage to proceed via an uphill reaction step.

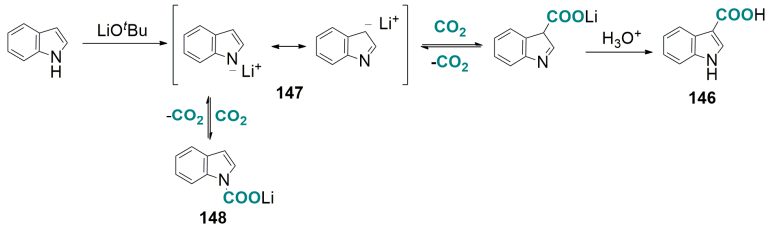
LiO^tBu was reported as active base in direct carboxylation of unprotected indole derivatives. (Scheme 60) [140]. Under optimized conditions (ambient CO_2 pressure, 100 °C) the use of a large excess of LiO^tBu was found (5 eq.) to suppress products decarboxylation. Indole derivatives with both electron-rich and -poor substituents at the C(5)-, C(4)- and C(7)-positions afforded selectively indole-3-carboxylic acid derivatives (**146**) with low to excellent yield (11 examples, 19–96% yields). 2-methyl-substituted indole afforded the carboxylic acid derivative in good yield (80%) while 2-phenyl-substituted indole was carboxylated in only 31% yield.



Scheme 60. Selected examples for carboxylation reactions of indole derivatives with CO_2.

Later, Kobayashi published the extension of the carboxylation reaction to pyrrole derivatives [141].

Concerning the reaction mechanism, Kobayashi proposes substrate deprotonation to occur at the N-H proton affording indolyl anion (**147**) able to undergo subsequent carboxylation with CO_2 to form the 1-indolyl carbamate salt (**148**) (Scheme 61). As stated before the free N-H functionality was a required feature as N-CH_3 substituted indoles were inert towards carboxylation under reported conditions. The possibility for having a resonance structure with the negative charge delocalized at C3 position explains formation of the observed indole-3-carboxylic acid derivatives (**146**).



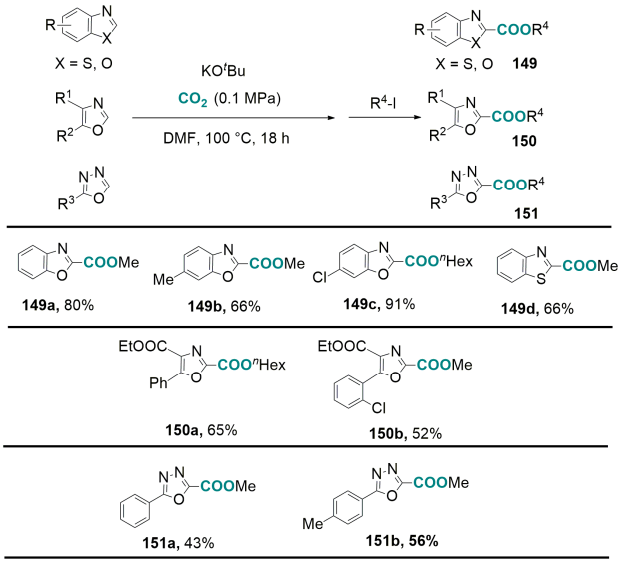
Scheme 61. Proposed mechanism for carboxylation of unprotected indole.

More recently, Ackermann reported efficient carboxylation of heteroarenes by using a strong base as KO^{t}Bu (1.2 eq.) in DMF at 100 °C under atmospheric CO_2 pressure (Scheme 62) [142]. Benzoxazole, benzothiazole, oxazole and 1,3,4-oxadiazole derivatives were carboxylated selectively at the C(2) position (12 examples, 43–80% yields).

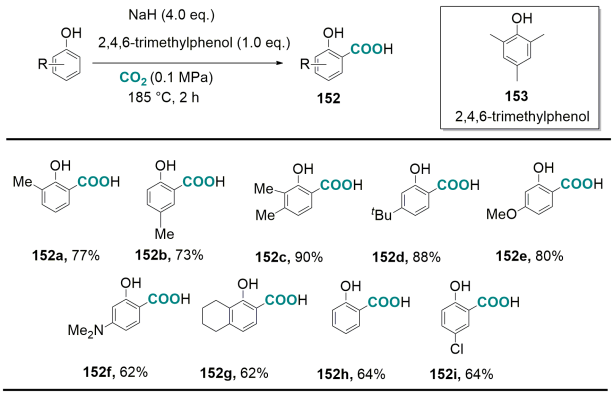
In analogy with the reaction mechanism proposed by Hu (Scheme 59), the reaction may proceed via initial reversible C-H deprotonation, followed by subsequent CO_2 carboxylation.

In 2016, Larrosa reported an advanced protocol for a Kolbe-Schmitt-type carboxylation reaction based on reacting PhOH (and phenol derivatives) with NaH under an atmospheric CO_2 pressure at the temperature of 185 °C [143] in the absence of organic solvent. The procedure avoided the isolation of the PhONa precursor and the undesired formation of H_2O.

Interestingly, the addition of 2,4,6-trimethylphenol (TMP, **153**) as a recyclable additive had a beneficial effect on the reaction by increasing both the initial reaction rate and final yield (Scheme 63). Phenol derivatives possessing both electron-donating and halogen substituents were carboxylated with excellent regioselectivity affording *ortho*-carboxylated products (18 examples, 55–91% yields). Substrates as 3-methylphenol, 3-chlorophenol and 3-bromophenol afforded both C2- and C6-carboxylated regioisomers. However selectivity was significantly higher for the C6-carboxylated product.

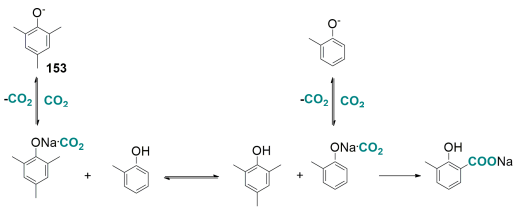


Scheme 62. Selected examples for carboxylation reactions of heteroarenes.



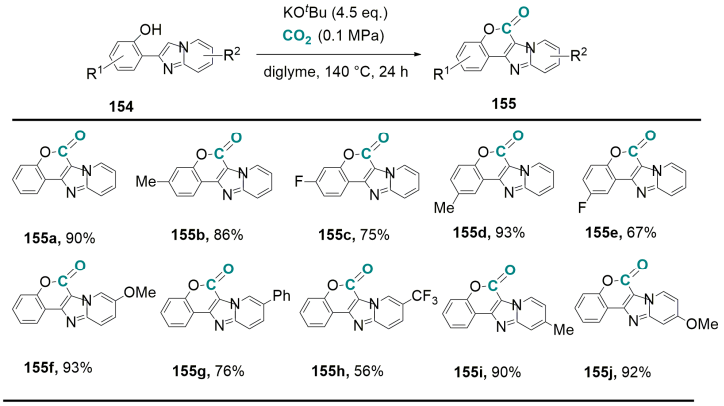
Scheme 63. Selected examples for carboxylation reactions of phenol derivatives in the presence of NaH and CO_2.

The author proposes that sodium 2,4,6-trimethylphenoxide (**153**), formed in situ from 2,4,6-trimethylphenol and NaH, plays a role as CO_2-carrier. A large body of evidence suggests that only "fixed CO_2" (absorbed or adsorbed) by the solid reagent is involved in the carboxylation reaction, therefore 2,4,6-trimethylphenoxide may increase the amount of CO_2 able to react being inert towards *ortho*-carboxylation itself (Scheme 64).

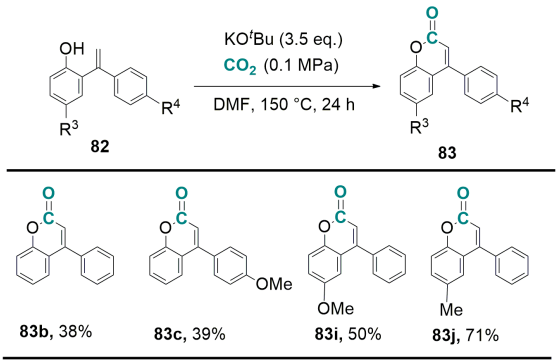


Scheme 64. Role of 2,4,6-trimethylphenoxide in carboxylation of *o*-cresol in the presence of NaH and CO_2.

Very recently Zhi reported a transition-metal-free carboxylation of C(sp^2)-H bond with CO_2 followed by a lactonization reaction applied to 2-(imidazo[1,2-*a*]pyridine-2-yl)phenol (**154**, Scheme 65) and 2-(1-arylvinyl)phenol derivatives (**82**, Scheme 66) [144].



Scheme 65. Selected examples for carboxylation reactions of 2-(imidazo[1,2-*a*]pyridine-2-yl)phenol derivatives followed by lactonization.

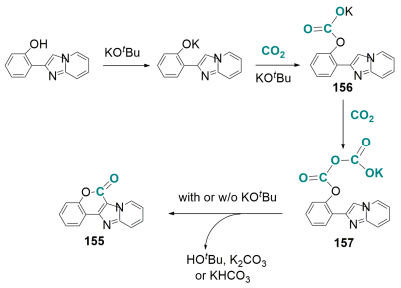


Scheme 66. Carboxylation reactions of 2-(1-aryvinyl)phenol derivatives followed by lactonization.

For reaction shown in Scheme 65 substrates bearing electron-donating and electro-withdrawing group substituents both at the phenoxy-(R^1) and pyridine-(R^2)-moieties were functionalized in good to excellent yield (17 examples, 56–96% yields).

Concerning 2-alkenylphenol derivatives (**82**), mono-substituted substrates with electron-donor groups (R^3) afforded the corresponding lactone (**83**) in moderate to good yield (4 examples, 38–71% yields).

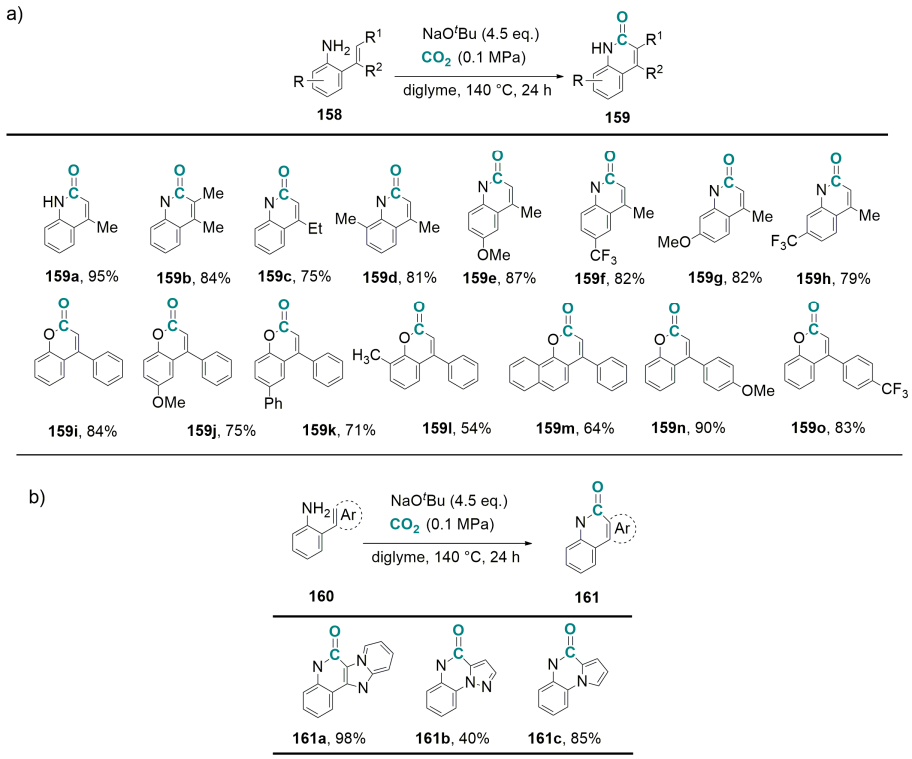
A careful mechanistic investigation brought to propose that, under basic conditions, a carbonate (**156**) or a dicarbonate (**157**) potassium salt may form, that subsequently undergo cyclization to the lactone derivative (**155**) (Scheme 67).



Scheme 67. Proposed mechanism for carboxylation followed by lactonization of 2-(imidazo[1,2-*a*]pyridine-2-yl)phenol derivatives.

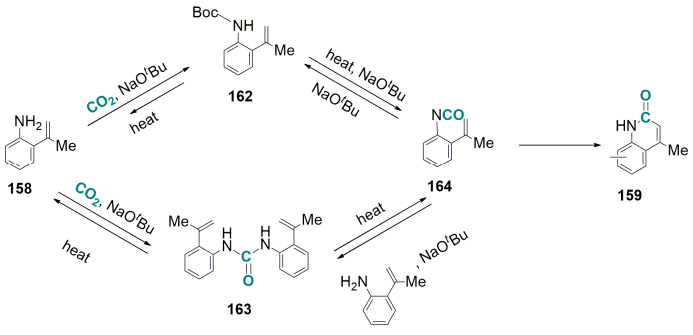
Yu and coworkers succeded in obtaining the first example of lactamization of 2-alkenylanilines (**158**) with CO_2 to form 2-quinolinone derivatives (**159**) in high yields (26 examples, 42–95% yields)

under atmospheric pressure (Scheme 68a) [145]. The 2-quinolinone motif is widely exploited in synthetic medicinal chemistry and photoelectric materials [146–148] and was previously accessed by the groups of Alper [149], Zhu [150] and Chuang [151] via lactamization of alkenyl and aryl C-H bonds with CO. Yu implemented, thus, a lactonization reaction using CO_2 founding that 2-alkenylanilines with R^2 = CH_3 (Scheme 68a) are more reactive than substrates with R^2 = H, Et. In contrast, both electron-donating and electron withdrawing substituents on the aniline nucleus do not affect significantly the substrate reactivity. Moreover, Yu has shown that also anilines with *ortho*-heteroarene substituents (Scheme 68b) as imidazo[1,2-*a*]pyridine (**161a**), pyrazole (**161b**) and pyrrole (**161c**) are suitable substrates for the reaction.



Scheme 68. (**a**) Selected examples for lactamization reactions of 2-alkenylanilines with CO_2; (**b**) Selected examples for lactamization reactions of *ortho*-heteroarene substituted anilines with CO_2.

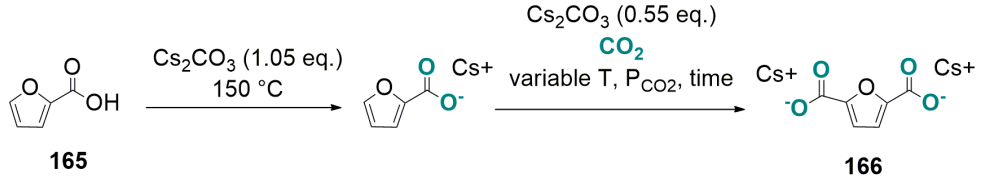
As aniline derivative **162** and urea **163** were isolated as reaction intermediates, Yu proposes the reaction mechanism shown in Scheme 69, encompassing formation of isocyanate **164** that undergo irreversible cyclization leading to **159**.



Scheme 69. Proposed reaction mechanism for lactamization of 2-alkenylaniline with CO_2.

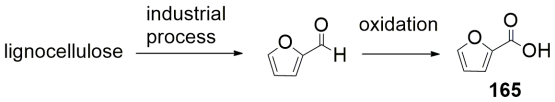
6.3. Base-Promoted Carboxylation of Furan-2-Carboxylic Acid to Furan-2,5-Dicarboxylate

A capstone work reported by Kanan describes the use of molten Cs_2CO_3 in the carboxylation of furan-2-carboxylic (**165**) acid to furan-2,5-dicarboxylate ($FDCA^{2-}$) (**166**) under CO_2 (pressure range from 0.1 to 0.8 MPa) at temperature ranging from 195 to 260 °C (Scheme 70) [60]. As shown in Scheme 70, at first furan-2-carboxylic acid (**165**) is converted into furan-2-carboxylate salt with Cs_2CO_3 (1.05 eq.) at the temperature of 150 °C. Then furan-2-carboxylate is converted into furan-2,5-dicarboxylate (**166**) with additional Cs_2CO_3 (0.55 eq.). Reacting 1 mmol of furan-2-carboxylate at 200 °C under P_{CO_2} = 0.8 MPa during 5 h afforded furan-2,5-dicarboxylate in 89% yield and 100% regioselectivity (detected decomposition products represented only 5%). Scale up of the reaction by using 10 or 100 mmol of the starting compound required a fine adjustement of the reaction parameters to give the dicarboxylate in 81% and 71% yield respectively.



Scheme 70. Carboxylation of furan-2-carboxylic to furan-2,5-dicarboxylate.

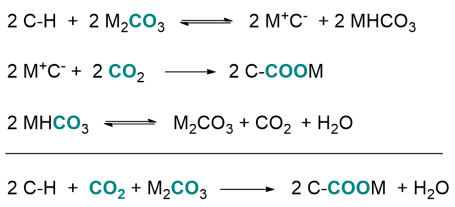
Since 2-furoic acid can be readily made from lignocelluloses (Scheme 71), the reaction give access to furan-2,5-dicarboxylic acid (**166**) which has been shown an excellent substitute for terephthalic acid.



Scheme 71. Production of furan-2-carboxylic from lignocelluloses.

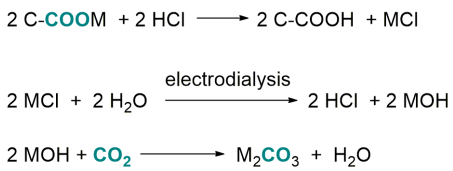
Assuming the pKa for the C-H at the 5 position of furan-2-carboxylic acid being similar to the pKa of unsubstituted furan a pKa value of ≈35 can be considered.

Considering the reaction shown in Scheme 70, the stoichiometry of the overall process can be written as shown in Scheme 72. By acidification of the obtained furan-2-carboxylate salt with HCl, furan-2,5-dicarboxylic acid and CsCl were obtained. By using bipolar membrane electrodialysis CsCl was converted into HCl and CsOH. At this stage, HCl could be recycled in the acidification step and CsOH could be reacted with 2-furanoic acid to regenerate furan-2-carboxylate. At the same time reaction of 2 CsOH with CO_2 gave Cs_2CO_3 and H_2O.



Scheme 72. Stoichiometry for the carboxylation reaction of furan-2-carboxylic with fused M_2CO_3.

The stoichiometry of the "protonation with HCl and CO_3^{2-} regeneration steps" can be written as shown in Scheme 73.

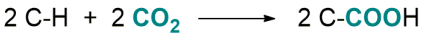


Scheme 73. Stoichiometry of the "protonation and CO_3^{2-} regeneration steps".

Considering the overall process encompassing:

(i) carboxylation of furan-2-carboxylic to furan-2,5-carboxylate;
(ii) protonation of furan-2,5-carboxylate with HCl (to give furan-2,5-carboxylic acid);
(iii) regeneration of HCl and Cs_2CO_3 from CsCl and CO_2.

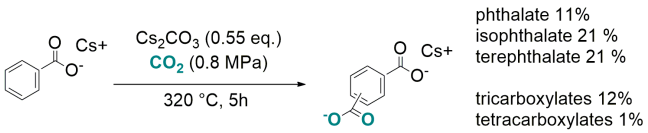
The stoichiometry of the reaction can be written as shown in Scheme 74.



Scheme 74. Stoichiometry of the overall reaction encompassing carboxylation of furan-2-carboxylic, protonation and CO_3^{2-} regeneration steps.

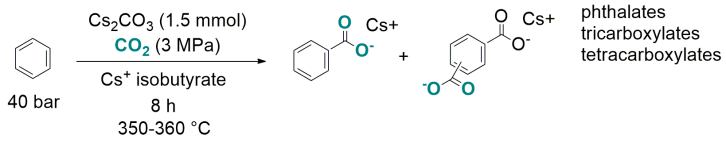
Moreover, a method for esterification of $FDCA^{2-}$ to dimethyl furan-2,5-carboxylate (DMFD) by heating 1 mmol of caesium $FDCA^{2-}$ to 200 °C in 100 mL anhydrous methanol under P_{CO_2} = 0.45 MPa for 30 min was also developed. The dimethyl furan-2,5-carboxylate was obtained in 50% yield.

The scope of the carboxylation reaction was extended to benzoate salt and benzene. The carboxylation of benzoate salt afforded phthalates (53% combined yields) besides tri- and tetra-carboxylates (13% combined yields) (Scheme 75).



Scheme 75. Carboxylation of benzoate salt.

As expected, benzene carboxylation required more drastic reaction conditions. 1.5 mmol of Cs_2CO_3 and 1 mmol of caesium isobutyrate (used as additive to obtain a molten mixture) were heated to 350–360 °C, under P_{CO_2} = 3.1 MPa and $P_{benzene}$ = 4.2 MPa (Scheme 76). At the temperature of 350 °C benzoate, phthalates and benzene tricarboxylates were obtained in 12% combined yield, while at 360 °C the yield increased to 19% (yield was based on Cs_2CO_3).

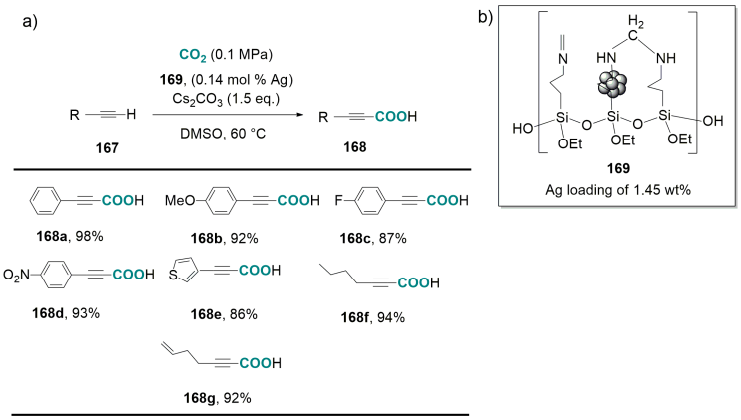


Scheme 76. Carboxylation of benzene.

Very interestingly Kanan notes that accessing carboxylates derivatives of substrates possessing unactivated C-H bonds open to the possibility to synthesize alcohols and hydrocarbons derivatives by combining carboxylation and hydrogenation reactions with use of renewable H_2.

7. C-H Carboxylation with CO_2 via Heterogeneous Catalysis

The role of homogeneous catalysis in carboxylation reactions of C(sp^3)-H and C(sp^2)-H bonds with CO_2 has been touched upon in previous Sections. With a view to developing at industrial scale C-H carboxylation reactions the use of active heterogeneous catalysts is highly desirable to allow easy catalyst recovery from the reaction mixture and subsequent recycle. However supported metal catalysts are often affected by unsatisfactory activity [152]. Recent advances in the field have been reported by Huang and coworkers by using a Shiff base-modified silver catalyst (**169**, Scheme 77b) employed in conjuction with Cs_2CO_3 to carboxylate terminal alkynes (**167**) to alkynyl carboxylic acids (**168**, Scheme 77a) [152] in high yields (86–98%) at ambient pressure.



Scheme 77. Carboxylation of terminal alkynes to alkynyl carboxylic acids by a Shiff base-modified silver catalyst.

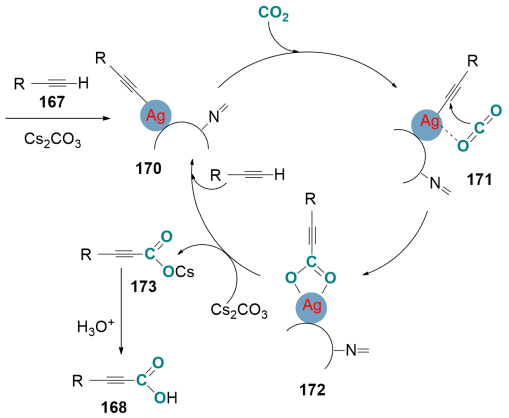
The robust and green catalyst **169** was obtained by deposition of silver nanoparticles (NPs) on the solid support by direct reduction of $AgNO_3$ with a metastable aminal under ultrasonic conditions. The catalyst was fully characterized by powder X-ray diffraction (PXRD), X-ray photoelectron spectroscopy (XPS), and inductively coupled plasma (ICP) analysis showing excellent recyclability under reaction conditions in five runs with a total TON of 3430.

The reaction mechanism proposed by Huang (Scheme 78) involves coordination of the alkyne to Ag-NPs which is thought to increase C(sp)-H acidity allowing deprotonation by Cs_2CO_3 and formation of a silver acetylide intermediate (**170**). CO_2 insertion into C-Ag bond leads to the silver carboxylate (**172**) that in the presence of a large amount of Cs_2CO_3 and alkyne undergo transmetallation producing cesium carboxylate (**173**) and regenerating **170**. Propiolic acid derivatives (**168**) are finally produced by acidification with concentrated HCl.

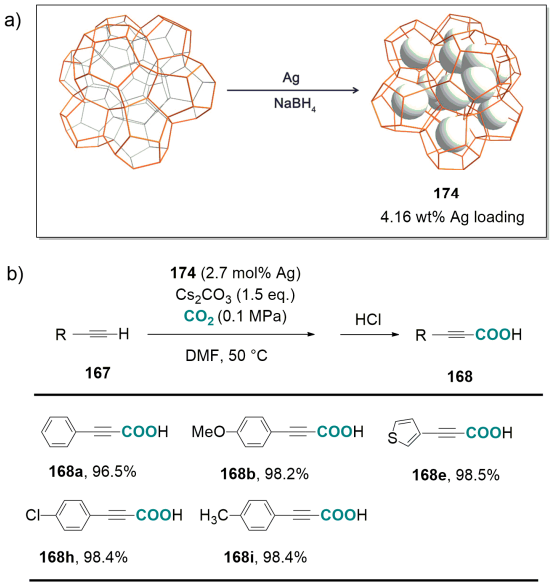
Furthermore, very recently porous MOF have been used as efficient heterogeneous catalysts in carboxylation of terminal alkynes with CO_2. Considering that MOF have emerged as promising porous materials with a wide range of applications encompassing CO_2 capture, separation, storage and regeneration as well as CO_2 photo- and electro-catalytic reduction, future directions in MOF chemistry point at their use in CO_2-epoxides co-polymerization (to make commodity polymers) and in CO_2-olefins co-polymerization [153].

Cheng and coworkers [154] have reported the synthesis of an efficient nanoscale heterogeneous catalyst obtained by introducing Ag NPs into the pores of MIL-101(Cr) (**174**) via a simple impregnation-reduction method to obtain Ag@MIL-101 (4.16 wt % Ag) (Scheme 79a). In optimized conditions, terminal alkynes are carboxylated at C(sp)-H bond by reacting 1 mmol of the substrate with 70 mg of Ag@MIL-101 (2.7 mol % Ag), in the presence of Cs_2CO_3 (1.5 mmol) under 0.1 MPa of CO_2 (at 50 °C in DMF) (Scheme 79b). Subsequent acidification with HCl affords propiolic acids

derivatives. Interestingly, Cheng reports that, after catalysis, Ag@MIL-101 can be easily separated by centrifugation and reused at least five times without decrease of the catalytic activity.



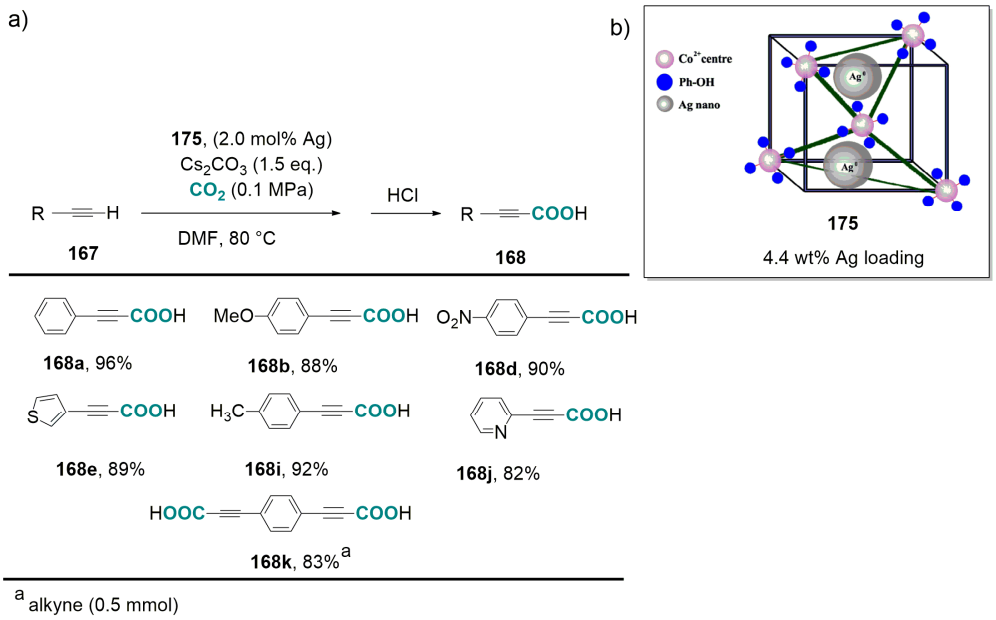
Scheme 78. Proposed mechanism for carboxylation of alkynes to propiolic acids with CO_2.



Scheme 79. (**a**) Impregation of MIL-101(Cr) with Ag NPs. Reprinted with permission from [154]. 2015 Copyright, John Wiley and Sons, Ltd., Chichester, UK; (**b**) Carboxylation of terminal alkynes to propiolic acid derivatives with Ag@MIL-101 catalyst.

The success of MOF as catalysts is thought to be linked to their ability to act as a microreactor with the terminal alkynes entering the channels and coordinating to Ag NPs. The mechanism proposed by Cheng and coworkers for carboxylation of alkynes is analogous to pathway shown in Scheme 78.

Bhaumick has also reported the synthesis of Ag NPs/Co-MOF (**175**) containing Ag in 4.40 wt % (Scheme 80b) [155]. The catalyst has been fully characterized by powder X-ray diffraction, thermogravimetric analysis, energy dispersive X-ray spectrometry and high-resolution transmission electron microscopy. By reacting 1 mmol of terminal alkynes with 50 mg of Ag NPs/Co-MOF (2 mol % Ag) in the presence of Cs_2CO_3 (1.5 mmol) under 0.1 MPa of CO_2 at 80 °C in DMF the corresponding propiolic acid derivatives were obtained in 84–98% yield (7 examples) (Scheme 80a). Analogously to Ag@MIL-101, Ag NPs/Co-MOF can be easily recovered by filtration from reaction solution and reused in up to six reaction cycles with slight loss of activity. ICP-MS analysis of the reused catalyst confirmed that Ag NPs are strongly bound to the framework and insignificant amount of Ag is lost in the filtrate.

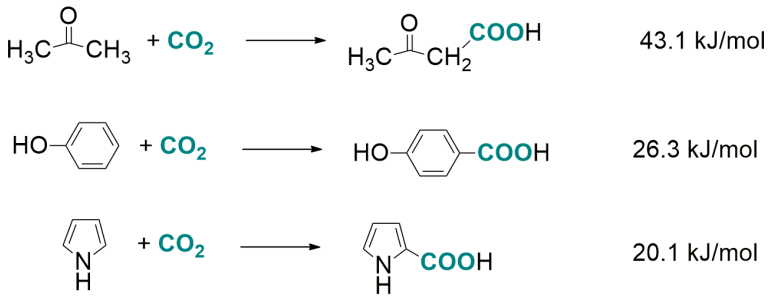


Scheme 80. (**a**) Carboxylation of terminal alkynes to propiolic acid derivatives with Ag/Co-MOF catalyst. (**b**) Ag NPs/Co-MOF catalyst. Reprinted with permission from [155]. 2016 Copyright, Elsevier, The Netherlands.

The reaction mechanism proposed by Bhaumick for carboxylation of alkynes is analogous to previously reported pathways (Scheme 78).

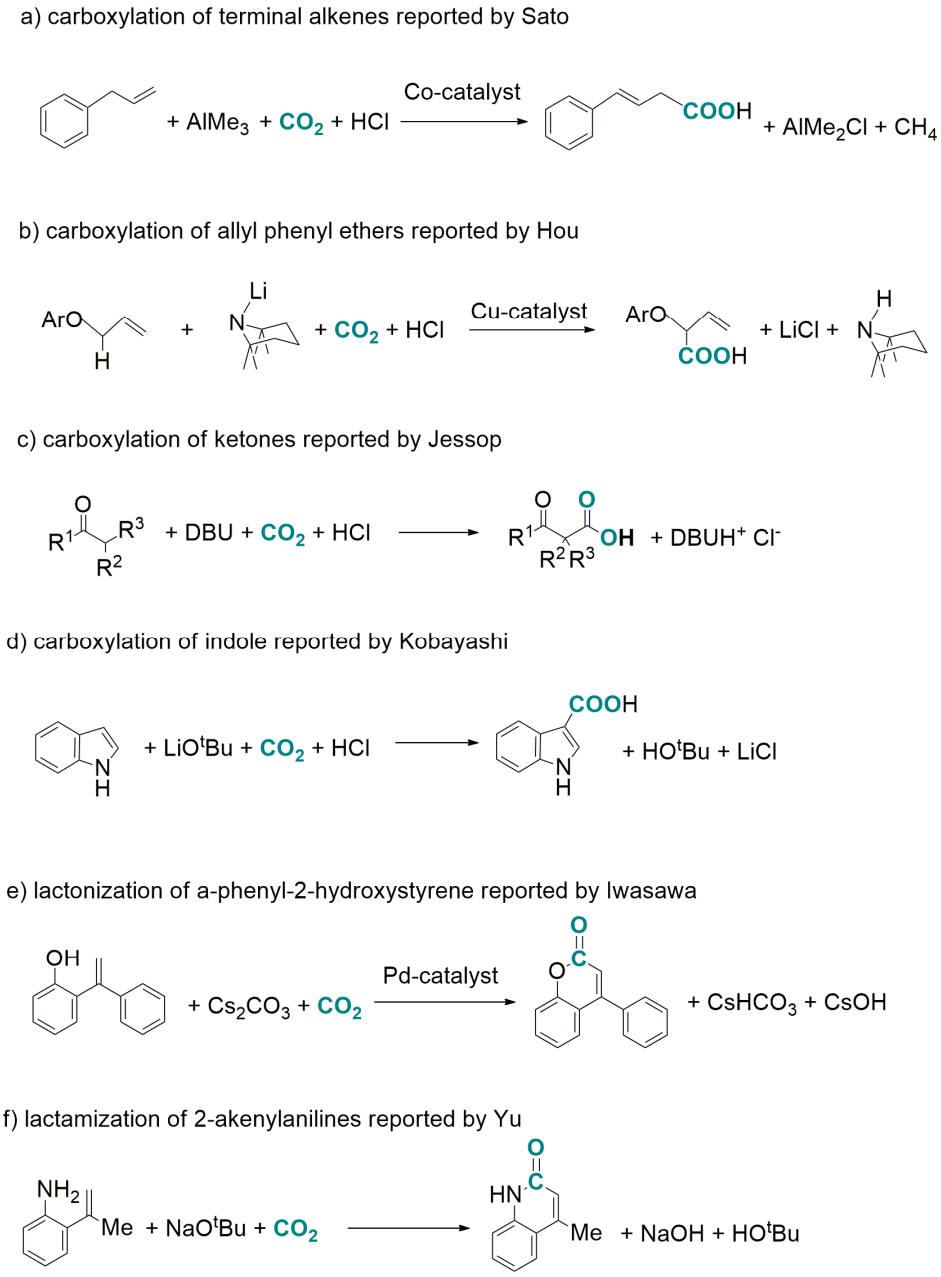
8. Thermodynamics of C-H Carboxylation Reactions with CO_2

Due to high thermodynamic stability of the CO_2 molecule ($\Delta G°_f$ = −394.6 kJ/mol) C-H carboxylation reactions are endoergonic processes. $\Delta G°_{react}$ values for several biologically relevant C-H carboxylation reactions have been calculated by Faber and co-worker using the IEFPCM (H_2O)-G3MP2B3 method [156]. Selected values of $\Delta G°_{react}$ relevant to the topic of this review are reported in Scheme 81.



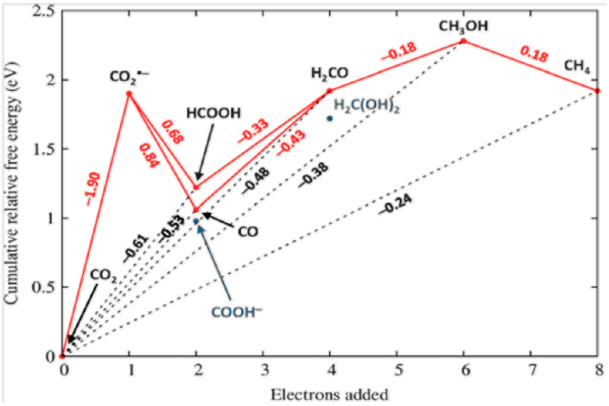
Scheme 81. Selected $\Delta G°_{react}$ (calculated values) for C-H carboxylation reactions with CO_2.

For thermal carboxylation reactions considered in above Sections thermodynamic constraints are overcome: (i) by using high energy co-reactants in stoichiometric amount (or even in excess) with respect to the organic substrate (overall stoichiometry of selected reactions is shown in Scheme 82a–d); (ii) by promoting C-H carboxylation reactions followed by a lactonization or lactamization step (overall stoichiometry of selected reactions is shown in Scheme 82e–f).



Scheme 82. Overall stoichiometry of several C-H carboxylation reactions with CO_2.

With reference to light-driven carboxylation reactions discussed in Sections 3.1 and 3.2, the proposed one electron reduction of CO_2 to $CO_2^{\bullet-}$ is affected by an extremely negative $E^{\circ\prime}$ redox potential of −1.90 V versus NHE (under standard conditions in aqueous solution at pH = 7, 25 °C, 0.1 MPa of gases and 1M solutes) as can be seen in Figure 1 (red points, Equation (1)) [157]. This redox potential is even more negative (−2.21 V vs. SCE) in dry dimethylformamide [158]. Multi-electron and multi-proton reduction of CO_2 in acqueous solutions (Equations (2)–(6), Figure 1) are affected by a lower thermodynamic barrier.



$CO_2 + e^- \rightarrow CO_2^{\bullet-}$ E°' = -1.90 V (Eq.1)

$CO_2 + 2H^+ + 2e^- \rightarrow CO + H_2O$ E°' = -0.53 V (Eq.2)

$CO_2 + 2H^+ + 2e^- \rightarrow HCOOH$ E°' = -0.61 V (Eq.3)

$CO_2 + 4H^+ + 4e^- \rightarrow HCOH + H_2O$ E°' = -0.48 V (Eq.4)

$CO_2 + 6H^+ + 6e^- \rightarrow CH_3OH + H_2O$ E°' = -0.38 V (Eq.5)

$CO_2 + 8H^+ + 8e^- \rightarrow CH_4 + H_2O$ E°' = -0.24 V (Eq.6)

Figure 1. Latimer-Frost diagram for the multi-electron, multi-proton reduction of CO_2 in homogeneous aqueous solution (redox potential are reported vs. NHE, under standard conditions at pH = 7, 25 °C, 0.1 MPa of gases and 1 M solutes). Reprinted with permission from [157]. 2012 Copyright, Royal Society of Chemistry, UK.

Jamison [81] noted that *para*-terphenyl ($E^\circ = -2.63$ V vs. SCE in DMF) could overcome this high energy barrier as previous work by Yanagida [159] report use of this photoredox catalyst for the reduction of CO_2 to formic acid under UV irradiation. Macyk also declares use of ZnS as a wide band gap semiconductor [82] with a E° in the range of -1.8 to -2.0 V vs. NHE previously used in photocatalytic water splitting and CO_2 reduction [160,161].

In summary, C-H carboxylation reactions using CO_2 are endoergonic processes requiring an energy input that can be supplied in the form of: (i) high energy co-reactants; (ii) electrons or irradiation; (iii) energy employed in electrodialysis to regenerate bases. As stated by Aresta [1] intelligent use of renewable energy sources (solar, wind and other renewable) and the analysis of the complete CO_2-balance will allow selecting environmentally sustainable processes that reduce (or avoid) the use of fossil fuels.

9. Conclusions

The above reported literature analysis shows that catalytic and stoichiometric reactions giving straightforward access to carboxylation of C-H bonds with CO_2 are a high appealing research field addressed by the research community. Transition-metal catalyzed carboxylation reaction of unactivated C(sp^3)-H bond reported by Mita, Sato and Hou as well as photo-catalyzed carboxylation reported by Jamison provide new and promising routes in catalysis. Base-mediated carboxylation reactions reported by Jessop, Beckmann and Kanan represent also a significant advance in the field of metal-free conversion processes encompassing base-recycling or base regeneration.

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

Abbreviation

AgOBz	silver benzoate
BINAP	2,2′-bis(difenilfosfino)-1,1′-binaftile
coe	cyclooctene
DBU	1,8-diazabicyclo(5.4.0)-7-undecene
Dcppy	2-phenylpyridine-5-4′-dicarboxylic acid
DFT	density functional theory
DMA	dimethylacetamide
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DRITS	diffuse reflectance infrared Fourier transform spectroscopy
EMIM BF_4	1-Ethyl-3-methylimidazolium tetrafluoroborate
EMIM Tf_2N	1-Ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide
HMS	methylhydrosiloxane dimethyl siloxane copolymer
HMPT	hexamethylphosphoric acid triamide
I^tBuCO_2	1,3-bis(*tert*-butyl)imidazolium-2-carboxylate
ICP	Inductively coupled plasma
$IMesCO_2$	1,3-bis(2,4,6-trimethylphenyl)imidazolium-2-carboxylate
$IPrCO_2$	1,3-bis(2,6-diisopropylphenyl)imidazolium-2-carboxylate
LDA	Lithium diisopropylamide
MMC	Magnesium methylcarbonate
MOF	Metal-organic framework
MTBD	7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene
NHC	*N*-Heterocyclic carbene
NPs	Nanoparticles
PXRD	Powder X-ray diffraction
RCC	reversible CO_2-carrier
TBD	1,5,7-Triazabicyclo[4.4.0]dec-5-ene
TGA	thermogravimetric analysis
TMP	2,4,6-trimethylphenol
TMU	1,1,3,3-tetramethylurea
$TMSCHN_2$	trimethylsilyldiazomethane
TON	Turn Over Number
TOF	Turn Over Frequency
TPD	Temperature-programmed desorption
TPR	Temperature programmed reaction
XPS	X-ray photoelectron spectroscopy

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