二氧化碳作为羧化试剂用于羧酸及其衍生物的合成

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摘要: 二氧化碳是储量丰富、廉价易得且可再生的 C_1 资源, 将其催化转化成高附加值精细化学品的研究已经引起了人们的广泛关注。目前, 虽然二氧化碳用作初始原料的反应已经工业化的很少, 但过去几十年中仍有二十多个具有实际应用前景的二氧化碳参与的新反应被发现, 其中以二氧化碳作为羧化试剂合成各种羧酸及其衍生物的反应为突出代表。本文综述了过渡金属催化合成羧酸及其衍生物的二氧化碳与多种碳亲核试剂、碳氢键以及碳碳多重键化合物的反应, 并总结了无过渡金属参与或有有机小分子催化条件下将二氧化碳转化成羧酸及其衍生物的反应。

关键词: 二氧化碳; 羧酸及其衍生物; 羧化反应; 氢羧化反应; 均相催化

中图分类号: O643

文献标识码: A

收稿日期: 2012-02-20. 接受日期: 2012-03-23.

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基金来源: 国家自然科学基金 (21172026, U1162101); 国家重点基础研究发展计划 (973 计划, 2009CB825300).

本文的英文电子版(国际版)由Elsevier出版社在ScienceDirect上出版(<http://www.sciencedirect.com/science/journal/18722067>).

Synthesis of Carboxylic Acids and Derivatives Using CO_2 as Carboxylative Reagent

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Abstract: The catalytic transformation of carbon dioxide into high value-added fine chemicals has attracted attention because this will make CO_2 into an abundant, inexpensive, and renewable C_1 feedstock. More than 20 reactions involving CO_2 as a starting material have been developed in recent decades but their successful industrialization is limited. One type of reactions that is technologically viable is to use CO_2 as a carboxylative reagent in the production of a wide range of carboxylic acids and derivatives. This review focused on transition metal-catalyzed reactions for the synthesis of various carboxylic acid and derivatives from CO_2 , by the carboxylation of carbon nucleophiles and C-H bonds and reactions of CO_2 with unsaturated organic compounds (especially those with a carbon-carbon multiple bond). This review also included transition metal-free or organocatalytic reactions for the transformation of CO_2 into carboxylic acid and derivatives.

Key words: carbon dioxide; carboxylic acids and derivative; carboxylation; hydrocarboxylation; homogeneous catalysis

Received 20 February 2012. Accepted 23 March 2012.

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This work was supported by the National Natural Science Foundation of China (21172026, U1162101) and the National Basic Research Program of China (973 Program, 2009CB825300).

English edition available online at Elsevier ScienceDirect (<http://www.sciencedirect.com/science/journal/18722067>).

The increase of CO_2 in the atmosphere and its impact on the environment is an important issue for the world. This issue has prompted effort to reduce CO_2 emissions and to develop efficient catalytic processes for transforming this main greenhouse gas into valuable compounds, which will make CO_2 an abundant, nontoxic, and inexpensive C_1 feed-

stock [1–10].

Carboxylic acids and derivatives are common structural units that are frequently found in a vast array of natural products, and they are highly versatile starting materials for the preparation of biologically active compounds and other fine chemicals. The transition metal-catalyzed carboxylation

of various nucleophiles or unsaturated hydrocarbons that use CO_2 as a carboxylative agent is an attractive route to produce carboxylic acids and derivatives. In most of these reactions, a transition metal catalyst plays an important role to help them proceed smoothly in an efficient and selective manner under mild conditions. Also, transition metal-free or organocatalytic reactions that use relatively high energy substrates have emerged as another attractive way to transform CO_2 into carboxylic acids and its derivatives, and has become an important complementary strategy to the transition metal-catalyzed process.

In this review, we focus on transition metal-catalyzed reactions for the synthesis of carboxylic acids and derivatives that use CO_2 as a carboxylative reagent. These include the carboxylation of carbon and other nucleophiles, carboxylation of a C–H bond, and reactions of CO_2 with unsaturated organic compounds (especially those with a carbon–carbon multiple bond). Transition metal-free or organocatalytic reaction for the transformation of CO_2 into carboxylic acid and derivatives are also considered.

1 Carboxylation of carbon nucleophiles

From a structural point of view, CO_2 can be considered an electrophile. An attack at its weak electrophilic carbon center by a nucleophile affords carboxylic acids and their derivatives. Among various nucleophiles, carbon nucleophiles have gained attention for their diversity, versatility, and availability, and also the possibility of forming a new C–C bond. Due to the thermodynamic and kinetic stability of CO_2 , only high energy carbon nucleophiles such as organolithium and Grignard reagents can easily react with CO_2 in the absence of a catalyst. However, the high reactivity of these reagents makes the reaction hard to handle and their functional group compatibility is very poor. Recently, transition metal-catalyzed carboxylation of less reactive carbon and other nucleophiles with CO_2 that have high efficiency, broad substrate scope, and good applicability were successfully developed, which allowed a more convenient access to various functionalized carboxylic acids and derivatives [5].

1.1 Carboxylation of organotin reagents

In 1997, Shi and Nicholas [11] reported the reaction of allylstannanes with CO_2 , which at a high pressure of 33×10^5 Pa and catalyzed by 8 mol% $\text{Pd}(\text{PPh}_3)_4$ or $\text{Pd}(\text{PBu}_3)_4$, afforded stannyl carboxylates quantitatively (Scheme 1). Actually, CO_2 cannot insert into the C–Sn bond of allylstannanes without a $\text{Pd}(0)$ catalyst. In the presence of a catalytic amount of a $\text{Pd}(0)$ complex, allylstannane was first converted into an allyl palladium complex by an oxidative

addition step. Then the insertion of CO_2 into the C–Pd bond gave palladium carboxylate, which further reacted with another allylstannane to yield stannyl carboxylate and regenerated the allyl palladium complex (Scheme 1). This creative strategy provided an important activation mode for the less reactive carbon nucleophiles that would allow their carboxylation by CO_2 . Recently, pincer-type palladium complexes reported by Johansson et al. [12] and (methylallyl) PdL (L = phosphines or NHC) complexes developed by Wu et al. [13] were also shown to be effective catalysts for the carboxylation of allylstannanes by CO_2 . Unfortunately, the industrial application of the carboxylation of allylstannanes is limited due to their toxicity and its ultimately limited substrate scope [14].

Scheme 1. Palladium catalyzed carboxylation of allylstannanes with CO_2 .

1.2 Carboxylation of organoboron reagents

Organoboron reagents are widely used carbon nucleophiles, as certified by the broad application of the Suzuki-Miyaura cross coupling reaction. In 2006, Ukai et al. [15] reported that the carboxylation of aryl- and alkenylboronic esters can be smoothly carried out with $[\text{Rh}(\text{OH})(\text{cod})_2]/\text{dppp}$ (or $(p\text{-MeO})\text{dppp}$) as catalyst and 3 equivalents of CsF as base under an atmospheric pressure of CO_2 in dioxane at 60°C , which afforded various carboxylic acids in high yields (Scheme 2). The suggested mechanism is shown in Scheme 2. First, the rhodium(I) catalyst undergoes transmetalation with the organoboronic ester to form an arylrhodium(I) complex. Then, the insertion of CO_2 into the C–Rh bond of the arylrhodium(I) complex gives a rhodium carboxylate. Next, the transmetalation of rhodium carboxylate with another organoboronic ester regenerates the catalyst and simultaneously forms a new carboxylate.

Scheme 2. Rhodium catalyzed carboxylation of boronic esters with CO_2 .

The acidification of the resulting carboxylate releases carboxylic acid.

Unfortunately, the rhodium catalytic system was shown to be inactive or unsuitable for the carboxylation of bromo, nitro, alkynyl, and vinyl substituted arylboronic esters. To overcome these drawbacks, a further study by Takaya et al. [16] developed a more effective catalytic system that consisted of CuI and bisoxazoline ligands. The copper catalytic system exhibited a broader substrate scope. More important, inexpensive copper salts are particularly attractive for their potential use on a large scale.

Hou and coworkers [17] also established a highly efficient copper-based catalytic system for the carboxylation of organoboronic ester with CO_2 using *N*-heterocyclic carbene as ligand and $\text{Bu}'\text{OK}$ as base (Scheme 3), which also showed a much wider functional group compatibility as compared with the rhodium-based catalytic system. An elegant mechanistic investigation was successfully carried out,

Scheme 3. (IPr)CuCl catalyzed carboxylation of boronic esters with CO_2 .

and two key catalytically active intermediates were isolated in high yields and their molecular structures were unambiguously characterized by X-ray crystallography. This allowed the authors to propose the mechanism in Scheme 3. The metathesis of (IPr)CuCl with $\text{Bu}'\text{OK}$ furnished (IPr)Cu(OBu'), which was followed by transmetalation with organoboronic ester to afford the organocopper complex (IPr)CuR. The insertion of CO_2 into the (IPr)Cu-C bond produced the carboxylate (IPr)Cu(OCOR), which underwent metathesis with another $\text{Bu}'\text{OK}$ to yield the carboxylate RCOOK and regenerated (IPr)Cu(OBu').

In 2011, Ohishi et al. [18] and Ohmiya et al. [19] independently discovered the carboxylation of alkylboron compounds (which were readily generated in situ by the hydroboration of terminal alkenes with 9-borabicyclo[3.3.1]nonane) with CO_2 by a *N*-heterocyclic carbene copper(I) or CuI/1,10-phenanthroline catalyst, which provided a variety of functionalized aliphatic carboxylic acids.

Recently, Riss and coworkers [20] reported an efficient carboxylation of functionalized boronic esters with sub-atmospheric partial pressures of $^{11}\text{CO}_2$ by using CuI as catalyst in the presence of tetramethylethylenediamine (TMEDA), KF, and 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (crypt-222) (Scheme 4). The resulting [^{11}C]carboxylic acid products can be easily converted into ^{11}C -labeled esters and amides, which can be used as excellent positron emission tomography (PET) radiotracers.

Scheme 4. Copper catalyzed carboxylation of boronic esters with $^{11}\text{CO}_2$.

1.3 Carboxylation of organozinc reagents

Organozinc reagents are widely used carbon nucleophiles that show less reactivity than organolithium and Grignard reagents and cannot be directly carboxylated by CO_2 in the absence of a metal catalyst. In 2008, Ochiai et al. [21] reported that the combination of $\text{Ni}(\text{acac})_2$ and a PCy_3 ligand was an efficient catalyst for the carboxylation of alkylzinc iodide-lithium chloride complexes under mild reaction conditions, which afforded a series of aliphatic carboxylic acids in good yields (Scheme 5). Lithium chloride was vital to the

Scheme 5. Nickel catalyzed carboxylation of organozinc reagents with CO_2 .

catalytic efficiency, presumably by facilitating the transmetalation step. However, this catalyst showed poor catalytic activity with aromatic zinc reagents such as $\text{PhZnI} \cdot \text{LiCl}$. It was proposed that the Aresta complex $(\text{PCy}_3)_2\text{Ni}(\eta^2\text{-CO}_2)$ [22] was an important catalytically active intermediate.

Yeung et al. [23] discovered that various electron-rich and electron-poor organozinc reagents were carboxylated by CO_2 in good to excellent yields in the presence of a $\text{Pd}(\text{OAc})_2/\text{PCy}_3$ catalyst (Scheme 6). More important, the relatively cheap and easily accessible nickel complex $(\text{Ni}(\text{PCy}_3)_2)_2(\text{N}_2)$ can also be used as an effective catalyst for the carboxylation of both aromatic and alkyl zinc reagents. It is noteworthy that these catalytic systems are compatible with a variety of functional groups including ketone, ester, and nitrile groups.

Scheme 6. Palladium and nickel catalyzed carboxylation of organozinc reagents with CO_2 .

Unlike transition metal catalyzed carboxylation of organotin and organoboron reagents, palladium or nickel catalyzed carboxylation of organozinc reagents proceed by a different mechanism in which the oxidative addition of CO_2 into the palladium(0) or nickel(0) catalyst initially gives the Aresta complex $(\text{PCy}_3)_2\text{Ni}(\eta^2\text{-CO}_2)$. Subsequent transmetalation with the organozinc compound forms the new C–C bond, which is followed reductive elimination to release the zinc carboxylate and regenerates the palladium(0) or nickel(0) catalyst (Scheme 6). This new pathway provides new possibilities for reactions using CO_2 as a carboxylative reagent.

1.4 Carboxylation of other nucleophiles

Copper or silver alkynylides, which can be easily formed by the reaction of terminal alkynes with copper or silver salts in the presence of a suitable base, have been exten-

sively used as carbon nucleophiles in Sonogashira coupling and other reactions [24]. The insertion of CO_2 into a sp-hybridized carbon–metal bond also occurs under certain conditions. Inoue and coworkers [25] disclosed that alkyl 2-alkynoates can be synthesized by the copper(I) or silver(I)-catalyzed carboxylative coupling reaction of terminal alkynes, alkyl bromides, and CO_2 at 100 °C. However, this methodology can suffer from the formation of direct coupling or dialkyl carbonate byproducts. Anastas and coworkers [26] have reported the silver(I)-catalyzed reaction of phenylacetylene, CO_2 and 3-bromo-1-phenyl-1-propyne, which afforded aryl naphthalene lactones in poor to moderate yields.

In 2010, Zhang et al. [27] used the mechanistic understanding of the carboxylation reaction to develop a convenient method for the highly selective synthesis of functionalized allylic 2-alkynoates by the carboxylative coupling of terminal alkynes, allylic chlorides, and CO_2 in good yields (Scheme 7). The *N*-heterocyclic carbene copper(I) complex $(\text{IPr})\text{CuCl}$ was shown to be a highly selective and active catalyst for this reaction. Also, the catalyst $(\text{IPr})\text{CuCl}$ can be easily recovered in high yield by simple chromatography. The suggested mechanism is shown in Scheme 7. First, the reaction of $(\text{IPr})\text{CuCl}$ with the terminal alkyne and K_2CO_3 generates a copper acetylide complex. Subsequent insertion of CO_2 into the Cu–C bond affords the 2-alkynoate copper complex, which finally reacts with allylic chloride to yield the product allylic 2-alkynoate and regenerates the catalyst $(\text{IPr})\text{CuCl}$. The formation of byproduct by the direct reaction of the copper acetylide complex with allylic chloride without CO_2 insertion is effectively suppressed in this catalytic system.

Later, with a judicious choice of catalyst and base, this

Scheme 7. $(\text{IPr})\text{CuCl}$ catalyzed carboxylative coupling of terminal alkynes, allylic chlorides, and CO_2 .

same group [28] further developed a simple ligand-free Ag(I)-catalyzed direct carboxylation of terminal alkynes with CO₂, which provided a convenient approach to straightforwardly synthesize functionalized propiolic acids in good yields (Scheme 8). Goossen et al. [29] and Yu et al. [30] also reported that a broad scope of terminal alkynes can also be directly carboxylated with CO₂ using the copper/1,10-phenanthroline or *N*-heterocyclic carbene catalyst, which afforded various propiolic acids in good to excellent yields. Interestingly, Cs₂CO₃ was shown to give the best result in this reaction among the bases tested.

Scheme 8. Ag(I) catalyzed direct carboxylation of terminal alkynes with CO₂.

Aryl halides are generally used as electrophiles in many cross-coupling reactions. In 2008, Correa and Martin [31] reported a novel palladium catalytic system that can directly carboxylate the aryl bromides with CO₂ in the presence of 2 equivalents of Et₂Zn, which provided a wide range of substituted benzoic acids bearing both electron-donating and electron-withdrawing groups in moderate to good yields (Scheme 9). The use of PhZnBr as substrate in this catalytic system gave no benzoic acid both in the presence and absence of Et₂Zn. A further mechanistic study revealed that the electrophilic aryl bromide participated in this carboxyla-

Scheme 9. Palladium catalyzed direct carboxylation of aryl bromides with CO₂.

tion reaction in a nucleophilic way. The suggested mechanism is shown in Scheme 9. Oxidative addition of aryl bromide to the palladium(0) catalyst initially gave an aryl palladium intermediate. Subsequent insertion of CO₂ into the aryl C-Pd bond formed the benzoate palladium species, which underwent transmetalation with Et₂Zn to release the zinc benzoate compound. The further reductive elimination of the ethyl palladium intermediate regenerated the palladium(0) catalyst. Alkylation and debromination reactions were effectively inhibited, possibly due to the use of the very bulky biarylphosphine ligand.

2 Carboxylation of a C-H bond

As compared with the carboxylation of nucleophilic organometallic reagents, the direct carboxylation of a C-H bond by CO₂ is a more attractive and economical method to synthesize carboxylic acids and derivatives by avoiding tedious and costly pre-activation steps [32–34]. In 2010, Boogaerts et al. [35] reported that a highly basic gold complex (IPr)Au(OH) was an effective catalyst for the carboxylation of a series of heteroatom-containing aromatic and halogenated aromatic C-H bond (pK_a < 30) by CO₂, which provided a variety of valuable carboxylic acids (Scheme 10). C-H carboxylation is regioselective because the reactions occur at the most acidic C-H bond. Two important catalytically active intermediates were isolated in high yields in a stoichiometric reaction using oxazole as substrate. Interestingly, the catalyst (IPr)Au(OH) can be recovered by simple extraction and reused without any loss in catalytic activity.

Recently, Zhang et al. [36] and Boogaerts et al. [37] almost simultaneously reported that inexpensive

Scheme 10. Gold catalyzed direct carboxylation of a C-H bond with CO₂.

Scheme 11. Copper catalyzed direct carboxylation of a C–H bond with CO₂.

N-heterocyclic carbene copper(I) complexes are efficient catalysts for the carboxylation of the relatively acidic N–H and C–H bonds (Scheme 11). Since the corresponding carboxylic acids were liable to decomposition by rapid decarboxylation, the products were isolated as carboxylic esters after the carboxylates had reacted with alkyl iodides. Stoichiometric experiments by Zhang and coworkers led to the isolation of the catalytically active benzoxazolylcopper and copper(I) benzoxazolylcarboxylate intermediates, which were characterized by X-ray single crystal diffraction. Based on their experimental observations, the deprotonative reaction mechanism depicted in Scheme 11 was proposed.

Chelation-assisted ortho-metalation, which has been studied extensively in the functionalization of the relatively inert C–H bond, can also be introduced for direct C–H carboxylation. Mizuno and co-workers [38] discovered that the combination of Rh(coe)Cl (5 mol%) with 12 mol% PCy₃ was an efficient catalyst for the direct carboxylation of a C–H bond in an arene bearing a pyridyl or pyrazolyl directing-group in the presence of a methylaluminum reagent (Scheme 12). After extensive screening of the transmetalation reagent, AlMe₂(OMe) was shown to best facilitate the carboxylation reaction.

Scheme 12. Rhodium catalyzed direct carboxylation of a C–H bond with CO₂.

3 Using CO₂ as a cycloaddition partner

Oxidative cycloaddition reactions of low valent metal (esp. nickel(0) and palladium(0)) complexes with CO₂ and unsaturated compounds (alkenes, alkynes, allenes, diynes, and dienes, etc.) form five-membered metallacycles (Scheme 13). This is another major route for the transformation of CO₂ into functionalized carboxylic acids and derivatives [2]. The formation of metallalactones from olefins and CO₂ suggests a possible synthesis route to acrylic acid in a straightforward manner, which remains an important challenge currently facing catalytic chemists [9].

Scheme 13. Formation of metallacycles by oxidative addition.

Pioneering studies by Hoberg and other groups revealed that the reaction of stoichiometric nickel(0) complexes, CO₂ and various unsaturated compounds using tetramethylethylenediamine (TMEDA) or bipyridyl (bpy) as ligand afforded a series of oxanickelacyclopentene complexes, which can be isolated and converted into carboxylic acids after acid hydrolysis [39,40]. In 1999, Saito et al. [41] reported that terminal alkynes were carboxylated by CO₂ in a highly regio- and chemoselective manner in the presence of stoichiometric Ni(cod)₂ and 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU), which gave α,β -unsaturated acids in good yields [41]. This reaction can also be extended to conju-

Scheme 14. Nickel mediated regio- and chemoselective carboxylation of alkynes with CO_2 .

gated enyne or diyne substrates (Scheme 14).

Organozinc reagents such as dimethyl or diarylzinc were successfully introduced by Takimoto and coworker [43] into this reaction system to undergo transmetalation with the oxanickelacycles formed (Scheme 15). Arylative carboxylation of 1,3-dienes and alkylative (or arylative) carboxylation of terminal alkynes proceeded in a highly stereoselective manner in the presence of stoichiometric $\text{Ni}(\text{cod})_2$, DBU, and Me_2Zn or arylzinc reagents.

In the above alkylative or arylative carboxylation system, air- and moisture-sensitive and expensive stoichiometric $\text{Ni}(\text{cod})_2$ was used to make the reaction proceed efficiently. In 2002, Takimoto et al. [44] successfully developed the nickel-promoted stoichiometric reactions into nickel-catalyzed reactions. Ring-closing carboxylation of bis-1,3-dienes with CO_2 proceeded smoothly with $\text{Ni}(\text{acac})_2$ as precatalyst and PPh_3 as ligand in the presence of 4.5

equivalents of Me_2Zn or Ph_2Zn , which afforded a range of carboxylic esters in good yields and high regio- and stereo-selectivities (Scheme 16). For the reaction mechanism, the insertion of CO_2 into a bis- π -allylnickel intermediate followed by a transmetalation step with an organozinc reagent was proposed. Further study [45] disclosed that the nickel-catalyzed carboxylative cyclization of bis-1,3-dienes can be readily carried out in a highly enantioselective manner with (*S*)-MeO-MOP as a chiral ligand (Scheme 16).

Based on the success of nickel-catalyzed carboxylative cyclization of bis-1,3-dienes with CO_2 , Shimizu et al. [46] developed nickel-catalyzed alkylative carboxylation of disubstituted alkynes with CO_2 . By tuning the electronic property of the substituent on the disubstituted alkyne, a variety of synthetically important α -silyl- β,β' -dialkyl α,β -unsaturated carboxylic acids were obtained in good yields with high regioselectivity by the reaction of silylated alkyne, CO_2 , and organozinc reagent using a catalytic amount of $\text{Ni}(\text{cod})_2$ in the presence of an excess amount of DBU (Scheme 17).

Pyrones and their derivatives, which are very important intermediates for the preparation of biologically active compounds and other fine chemicals, can be synthesized by [2+2+2] cycloaddition of diynes and CO_2 in an economical way without the use of organometallic transmetalation reagents. The previously developed reaction system had to use rather harsh conditions such as high CO_2 pressures, high temperatures, and had a limited substrate scope [47,48]. A

Scheme 15. Nickel promoted alkylative or arylative carboxylation of alkynes or 1,3-dienes with CO_2 .

Scheme 16. Nickel catalyzed carboxylative cyclization of bis-1,3-dienes with CO_2 .

Scheme 17. Nickel catalyzed alkylative carboxylation of disubstituted alkynes with CO_2 .

major breakthrough was achieved by Louie and co-workers [49,50] who showed that the combination of $Ni(cod)_2$ with an electron-rich and sterically hindered *N*-heterocyclic ligand IPr was a highly efficient catalyst for the [2+2+2] cycloaddition of diynes and CO_2 . A series of pyrones were synthesized in good yields with high regioselectivity under mild reaction conditions (Scheme 18). In this reaction, the alkyne bearing the larger substituent R^L was thought to initially undergo oxidative addition with $Ni(0)$ catalyst and CO_2 regioselectively. This provided the oxynickelacycle, in which the alkyne unit bearing the smaller substituent R^S was

Scheme 18. Nickel catalyzed [2+2+2] cycloaddition of diynes and CO_2 .

coordinated to the nickel, which significantly minimized steric hindrance. Subsequent cycloaddition of the alkyne, and the following reductive elimination formed the pyrone product and regenerated the nickel(0) catalyst (Scheme 18).

4 Hydrocarboxylation

Hydrocarboxylation, which combines the hydrometalation of unsaturated compounds with the carboxylation of the in situ formed organometallic nucleophiles, is another attractive protocol for the synthesis of functionalized carboxylic acids and derivatives that cannot be accessed by the reaction of unsaturated compounds and CO_2 [51,52]. Instead of forming a metallacycle by an oxidative cycloaddition reaction, metal hydride from β hydride elimination from organometallic reagents or metathesis of other hydride donors plays a crucial role in this reaction.

Extending their metal-catalyzed alkylation work, Williams and co-workers [53] discovered that a variety of styrene analogs with electron deficient and neutral ortho, meta, and para substituents underwent hydrocarboxylation in the presence of a catalytic amount of $Ni(acac)_2$ and Cs_2CO_3 under very mild conditions (Scheme 19). With Et_2Zn as hydride donor, this reaction gave the carboxylic acid product in good yield with excellent regioselectivity. Initial mechanistic investigations excluded the involvement of a metallacycle in the reaction. The mechanism proposed a nickel hydride complex as the key catalytically active intermediate. Styrene first inserts into a nickel hydride species

Scheme 19. Nickel catalyzed hydrocarboxylation of styrenes with CO_2 .

to form a benzyl nickel species, which then undergoes direct carboxylation (Scheme 19) or carboxylation, which is followed by carboxylation, to afford the nickel carboxylates species. Transmetalation of nickel carboxylates with Et_2Zn produces zinc carboxylates and releases the ethyl nickel species, which undergoes β hydride elimination to regenerate the nickel hydride species.

Using a silyl pincer-type palladium complex as catalyst, Takaya and co-workers [54] synthesized β,γ -unsaturated carboxylic acid in good yield by the hydrocarboxylation of allenes in the presence of stoichiometric Et_3Al or Et_2Zn (Scheme 20). This hydrocarboxylation gave the β,γ -unsaturated carboxylic acid rather than the α,β -unsaturated carboxylic acid, which was ascribed to the nature of the silyl pincer-type palladium catalyst. The insertion of the allene substrate into the palladium hydride complex resulted in a σ -allyl palladium complex rather than a π -allyl species. Then the coordinated CO_2 inserted into the σ -allyl complex with allylic transposition to afford palladium carboxylate, which was transmetalated with Et_3Al to release the aluminum salt of the β,γ -unsaturated carboxylic acid and finally regenerated palladium hydride complex (Scheme 20). 1,3-Dienes were also suitable substrates for the hydrocarboxylation reaction catalyzed by the same catalyst, which yielded the β,γ -unsaturated carboxylic acid [55].

Fujihara and co-workers [56] developed *N*-heterocyclic carbene copper fluoride complexes as catalysts for the hydrocarboxylation of a wide range of alkynes (including terminal alkynes). Using mild and easy-to-handle hydrosilane as the hydride donor, this hydrocarboxylation reaction afforded a variety of α,β -unsaturated carboxylic acids in moderate to good yields (Scheme 21). The mechanism involves the formation of a copper hydride species by the

Scheme 20. Hydrocarboxylation of allenes with CO_2 catalyzed by a silyl pincer-type palladium complex.

reaction of precatalyst $(\text{NHC})\text{CuF}$ hydrosilane, the syn addition of the copper hydride species to alkyne produced a copper alkenyl species, which was followed by the insertion of CO_2 to provide the copper carboxylate intermediate. This finally underwent σ -bond metathesis with a hydrosilane, affording the corresponding silyl ester and regenerating the copper hydride catalyst (Scheme 21). It is noteworthy that each of the steps in the mechanism were confirmed by stoichiometric reactions.

Recently, Li et al. [57] reported that nickel-catalyzed

Scheme 21. Copper catalyzed hydrocarboxylation of alkynes with CO_2 .

syn-hydrocarboxylation of a wide range of alkynes proceeded smoothly with high regio- and stereoselectivities in the presence of stoichiometric Et_2Zn and CsF (Scheme 22). It is important that the hydrocarboxylation of alkynyl amine using this catalytic system afforded (*E*)-amino acids exclusively in excellent yield with high regio- and stereoselectivities. This offers a convenient approach to synthesize 3-alkylideneoxindole and α -alkylidene- γ -butyrolactam in a highly regio- and stereoselective manner. With respect to the mechanism, experimental investigations implied that the hydrocarboxylation reaction occurs through two sequential nickel-catalyzed reactions: hydrozincation and carboxylation. Nickel-catalyzed hydrozincation of alkynes forms the 1-alkenyl zinc species with high regio- and stereoselectivity. This is followed by the carboxylation of the less active 1-alkenyl zinc species, which is similar to Dong's carboxylation of arylzinc reagents (Scheme 22). CsF plays an important role in accelerating both reactions.

Scheme 22. Nickel catalyzed hydrocarboxylation of alkynes with CO_2 .

Subsequently, Li et al. [58] successfully developed nickel(0)-catalyzed highly regio- and stereoselective methyl-carboxylation of homopropargylic alcohols with ZnMe_2 and CO_2 , which afforded a variety of α -alkylidene- γ -butyrolactones in good yields.

5 Transition metal-free or organocatalytic reactions

Transition metal-free or organocatalytic transformation of CO_2 into valuable chemicals has attracted considerable attention in the past decade. This protocol provides an important strategy for the synthesis of carboxylic acids and de-

rivatives using CO_2 that is complementary to the transition metal-catalyzed process.

In 2011, Chen et al. [59,60] reported the intramolecular carboxylative addition reactions of 2,3-allenamides and 3-aryl-2-alkynamides using atmospheric CO_2 as carboxylative reagent in the presence of K_2CO_3 (Scheme 23). The transition metal-free reactions offer efficient protocols for the synthesis of the biologically important 1,3-oxazine-2,4-diones and oxazolidine-2,4-diones.

Scheme 23. Reaction of CO_2 with 2,3-allenamides or 3-aryl-2-alkynamides.

It is well known that the reaction of primary or secondary amines with CO_2 readily forms unstable carbamic acids, while the carboxylative coupling reaction of amine, CO_2 and alkyl halides suffered from the formation of non-carboxylative direct coupling byproducts as the major reaction. In 2001, Salvatore et al. [61] developed a highly chemoselective carboxylative coupling reaction of amine, CO_2 and alkyl halides using Cs_2CO_3 as base and tetrabutylammonium iodide as additive (Scheme 24). This transition metal-free reaction system effectively suppressed the direct *N*-alkylation and overalkylation of the carbamate produced, therefore, various functionalized carbamates were synthesized in high yields. In 2009, Hooker et al. [62] reported an efficient synthesis of [^{11}C]carbamate by a carboxylative coupling reaction of amine, $^{11}\text{CO}_2$ and benzyl chloride using DBU as both a trapping reagent and a catalyst (Scheme 24).

Scheme 24. Synthesis of carbamates by the reaction of amine, CO_2 and alkyl halides.

Arynes are highly reactive intermediates that are extensively used in modern organic synthesis. In 2006, Yoshida et al. [63] developed a transition metal-free three-component reaction of arynes, imines, and CO_2 to give benzoxazinone

Scheme 25. Reaction of arynes with CO₂.

derivatives in a straightforward way (Scheme 25). Subsequently, they also disclosed that a three-component reaction of secondary amines, arynes, and CO₂ directly gave anthranilic acid derivatives [64].

In the CO₂ and alcohol system, the carbonic acid monoalkyl esters formed cannot be easily converted into other compounds due to their instability. In 2010, Minakata and coworkers [65] developed a transition metal-free electrophilic iodocyclization reaction system using Bu^tOI as iodinating reagent to trap carbonic acid monoalkyl esters. A variety of olefinic and acetylenic alcohols were then converted into iodo-substituted cyclic carbonates under mild conditions (Scheme 26).

Scheme 26. Electrophilic iodocyclization reactions containing CO₂.

Compared with the transition metal-catalyzed direct carboxylation of C–H bond with CO₂, transition metal-free carboxylation of a C–H bond offers a more facile and inexpensive access to carboxylic acids and derivatives. Using Cs₂CO₃ as base, Vechorkin et al. [66] and Yu et al. [67] independently discovered the transition metal-free direct carboxylation of aromatic heterocycles and terminal alkynes with CO₂, which afforded the corresponding heteroaryl carboxylic esters and functionalized propiolic acids in high yields with good functional group tolerance (Scheme 27).

Scheme 27. Transition metal-free carboxylation of aromatic heterocycles or terminal alkynes with CO₂.

Recently, Cantat et al. [68,69] developed an organocatalytic formylation of N–H bonds with CO₂ using 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) or *N*-heterocyclic carbene as catalyst and silanes as reductants, which provided an attractive and efficient method to make various formamides (Scheme 28). When IPr (a widely used

Scheme 28. Organocatalytic formylation of N–H bonds using CO₂ and silanes.

N-heterocyclic carbene) was employed as organic catalyst, this reaction was readily carried out under 0.1 MPa pressure of CO₂ and room temperatures using very cheap poly-methylhydrosiloxane as reductant.

6 Conclusions

Using carbon dioxide as a carboxylative reagent, with CO₂ as an electrophile or cycloaddition partner, a broad range of carboxylic acids and their derivatives have been synthesized by the homogeneous reactions of various carbon and other nucleophiles, reactions of the relatively active C–H bond, and reactions of unsaturated compounds with CO₂. At present, this strategy is one of major approaches to the catalytic transformation of CO₂ into high value-added fine chemicals. Due to the importance of CO₂ utilization, it can be anticipated that more new reactions using carbon dioxide as a carboxylative reagent will be developed in the future. Attention should be paid to the elucidation of the reaction mechanism to further develop highly efficient catalyst systems for the economic production of these carboxylic acids and their derivatives. Computational methods have contributed to the understanding of the mechanistic aspects of many organic reactions. This approach will play an increasingly important role in understanding the reactions, and thus aid in developing new catalysts.

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