

TRANSITION-METAL CATALYZED CO₂ FIXATION FOR THE SYNTHESIS OF CARBOXYLIC ACIDS

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Introduction

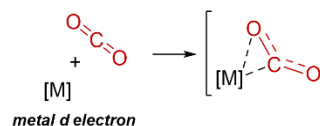
Carbon dioxide (CO₂) is an ideal C1-synthon for organic synthesis. In addition to its non-toxicity, CO₂ is a cheap and abundant feedstock chemical of which annual production is making a huge surplus in global CO₂ market. Utilization of CO₂ into fine chemicals has a great significance in terms of high-value creation. Not surprisingly, in the least ten years, much progress in the effort to incorporate CO₂ into fine chemicals have been accomplished. CO₂ fixation into organic framework to yield carboxylic acids is the most representative transformation in this context, not only because carboxylation via CO₂ fixation is the most atom-efficient approach to install the moiety, but also because carboxylic acid is one of the most prevalent functionalities in a vast array of medicinally important natural products and small-molecule pharmaceuticals.

The challenges in CO₂ fixation come from thermodynamic stability of CO₂. CO₂ is a low-energy gaseous molecule which makes its conversion energy-demanding. Traditional methods of CO₂ carboxylation utilize highly reactive nucleophiles, such as Grignard reagents or phenoxide salts. However, these processes suffer from poor chemoselectivity and limited scope. To complement these traditional methods, transition metal-catalyzed carboxylation has been developed which utilizes much more diverse precursor functionalities and uses much less polarized metal-carbon bonds resulting in higher chemoselectivity.

Based on the mechanism, transition-metal catalyzed CO₂ fixation can be categorized into four subsets: 1) Direct activation of CO₂ by transition metal, 2) Insertion of CO₂ into metal-carbon bonds, 3) Carboxylation of nucleophilic metalallyl complex, and 4) Oxidative cyclization with unsaturated hydrocarbons.

Direct activation of CO₂ by transition metal

Transition metal can activate CO₂ by donating its d electrons into antibonding π^* orbital of CO₂ (Figure 1). Based on this



metal d electron

Figure 1 Direct activation of CO₂ by transition metal

principle, a few methods have been developed, including the seminal example of organozinc carboxylation using Ni- η^2 -CO₂ complex.

Insertion of CO₂ into metal-carbon bonds

Although a transition metal-carbon bond is much less polarized than R-Li or R-MgBr bonds, its electron density still lies on carbon side, and transition metal-carbon σ bond can still activate CO₂ as depicted in Figure 2. Based on this principle, it

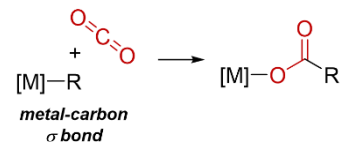


Figure 2 Insertion of CO₂ into metal-carbon bonds

has been shown that transition metal-carbon bonds made from organoboron species, alkenes, alkyl halides, bis- π -allyl complexes, and C-H activation can react with CO₂.

Carboxylation of nucleophilic metalallyl complex

Nucleophilic σ -allyl metal complex can be made from allenes, allylic acetates, and allylic C-H activation. The resulting allylmethyl complexes have been known to fixate CO₂ (Figure 3).

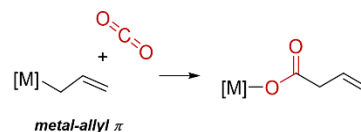


Figure 3 Carboxylation of nucleophilic metalallyl complex

Oxidative cyclization with unsaturated hydrocarbons

CO₂ can also interact with simple alkynes and alkenes in the presence of transition metals via oxidative cyclization as shown in Figure 4. The resulting metallacycle can be transformed into carboxylic acids via protonation, alkylation or reduction.

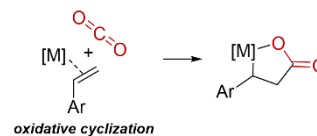


Figure 4 Oxidative cyclization with unsaturated hydrocarbons

Key References:

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