# Modular synthesis of β-amino acids from alkenes, amines, and CO₂ via photoredox/copper dual catalysis

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# Modular synthesis of $\beta$-amino acids from alkenes, amines, and CO$_2$ via photoredox/copper dual catalysis

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The conversion of industrial waste into value-added chemicals represents a compelling approach to bolster sustainability efforts. Among the primary components of greenhouse gases, carbon dioxide (CO$_2$) stands as an ideal C1 source owing to its abundance, renewability, and non-toxic nature. The precise conversion of CO$_2$ into value-added chemicals is of great significance in advancing the utilization of renewable resources [1]. Meanwhile, alkenes play a pivotal role as synthetic precursors in organic synthesis, and their functionalization reactions serving as crucial methodologies for the efficient and rapid construction of complex molecules. In recent decades, various noteworthy methods have been documented for synthesizing complex carboxylic acids and their derivatives

under mild conditions through alkene difunctionalization with CO$_2$ [2,3]. However, these reports predominantly centered around monocatalytic systems including photocatalysis, metal catalysis or electrocatalysis, resulting primarily in carboxylated products with α-selectivity (Figure 1(a)). The more challenging β-selective carboxylation, despite its considerable value, has received much less attention [4]. Therefore, the development of novel strategy to achieve the $\beta$-selective carboxylative difunctionalization of alkenes with CO$_2$ stands as a promising avenue for research.

In a recent article by Ye, Yu and co-workers, an innovative strategy involving dual catalysis was devised to address the unique selectivity challenge [5]. The authors postulated that an alkene radical anion intermediate, generated through single-electron reduction within the

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2

photocatalytic system, reacted with $CO_2$ for the $\beta$-selective carboxylation (Figure 1(b)). Subsequently, the synergistic utilization of a metal catalyst would trap the radical adduct, resulting in carboxylative difunctionalization of alkenes with excellent chemo- and regioselectivity. They proposed that the compatibility between the strongly reductive photocatalytic system and high-valent metal-mediated bond-forming processes is the key to achieve this orthogonal difunctionalizing carboxylation of alkenes. However, the highly negative reduction potential of alkenes and the reactivity of amines with $CO_2$ emerge as two primary challenges to be addressed in their investigations.

Inspired by the strong reducing capabilities observed in photoexcited closed-shell phenolates [6,7] and the proven effectiveness of copper catalysts in facilitating C−N bond formation [8-10], the authors introduced a novel approach for aminocarboxylation of alkenes using a combination of binaphthol derivative (ArOH) as the photocatalyst and CuCl as the metal catalyst (Figure 1(c)). This dual catalytic system demonstrated remarkable versatility in accommodating a wide range of substrates, including various anilines, diarylamines, indoline, and hydrazines within the realm of amines, as well as styrenes, gem-difluoroalkenes, and acylates within the domain of alkenes. Notably, the method also enabled the general hydroamination of alkenes when methanol was used as the proton source.
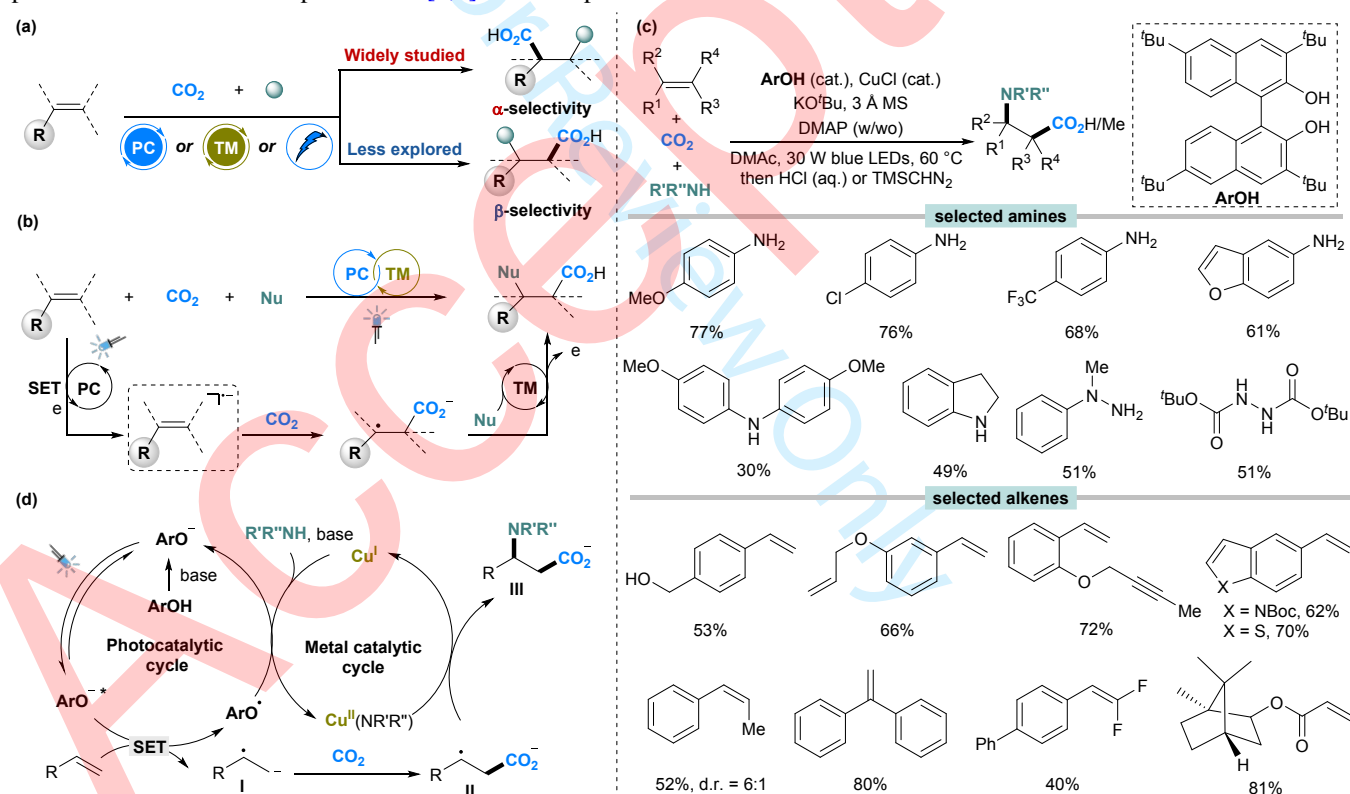


**Figure 1** (a) Monocatalytic carboxylative 1,2-difunctionalization of alkenes with $CO_2$. (b) Reaction design for the $\beta$-selective carboxylation. (c) Reaction scheme and substrate scopes. (d) The proposed mechanism of the metallaphotoredox-enabled aminocarboxylation.

Mechanistic studies revealed that the deprotonated form of ArOH exhibited absorption in the visible-light region. Additionally, Stern-Volmer experiments unveiled that the photo-excited $ArO^{-*}$ was quenched by activated alkenes.

Furthermore, radical trapping experiments supported the formation of the key alkene radical anion and the occurrence of radical-radical cross-coupling processes.

The proposed mechanism is depicted in Figure 1(d).

2

Under visible-light irradiation, the deprotonated photocatalyst (ArO⁻) is excited to generate the highly reductive ArO⁻* (-2.82 V vs SCE), which subsequently undergoes single-electron transfer (SET) with alkenes to produce alkene radical anion **I** and phenoxyl radical (ArO•). A nucleophilic attack by radical anion **I** to $CO_2$ leads to the formation of radical intermediate **II**. Meanwhile, ArO• undergoes reduction by Cu(I) catalyst with concomitant ligand substitution with amine, resulting in the formation of Cu(II)NR'R'' and the regeneration of ArO⁻. Finally, the Cu(II) species engages with radical **II** to facilitate C−N bond formation, yielding the desired $\beta$-amino acid derivatives and regenerating the Cu(I) catalyst.

In conclusion, Ye, Yu and co-workers have introduced a remarkable metallaphotoredox dual catalytic system, enabling the aminocarboxylation of alkene using $CO_2$ and amines to generate valuable $\beta$-amino acid compounds. The discovery of this synergistic catalytic approach is expected to serve as a significant source of inspiration for future advancements, diverging from the conventional reliance on

precious metal photocatalysts. Moreover, we anticipate that these findings will broaden the prospects of $CO_2$ chemistry and pave the way for the future developments in this field.

**Conflict of interest** The authors declare no conflict of interest.

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