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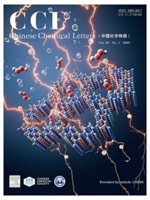

Editorial

EDA-complexes-enabled photochemical synthesis of α-amino acids with imines and tetrabutylammonium oxalate

The synthesis of α-amino acid from imines with different carbonyl sources is attractive for both synthetic organic and medicinal chemistry communities. Imines, which were easily available from the corresponding ketones and amines, were employed as one of the most ideal precursors. Traditionally, cyanation and subsequent hydrolysis were required to install the carboxyl group [1]. In these cases, the toxicity of the cyanation reagents limited its further synthetic applications in organic chemsitry. Besides, metal activation of imine substrates to make the organometallic intermediate and trap CO_2 to give the desired α-amino acid were also developed by many groups (Scheme 1A). The utilization of stoiochiometric amounts of metal reagents was required to realize the transformation. Recently, Yu reported a novel photocatalytic reductive carboxylation protocol for synthesis of α-amino acid from imines with CO_2 as the carbonyl source [2]. In the same year, Walsh and co-worker reported similar work, where Ir(ppy)$_2$(dtbpy) was employed as the photocatalyst [3]. Both reactions used atmospheric CO_2 as the C1 source for carboxylation and teteriary amines as the sacrifical electron donors (Scheme 1B). To date, development of sustaninable protocols for imines reductive carboxylation with stable, easily available, and versatile solid C1 source under redox-neutral conditions has never been realized.

Oxalic salt could be oxidized easily *via* single-electron-transfer and subsquential homolytic cleavage of the C–C bond to produce $CO_2^{\bullet-}$ and CO_2 molecules (Scheme 1C). Interestingly, $CO_2^{\bullet-}$ ($E_{ox} = -2.21$ V *vs.* SCE) has the unique reduction potential, which is more negative than the typical photocatalysis. As a strong reductant, $CO_2^{\bullet-}$ might be able to realize the single-electron-reduction of imines and the *in-situ* generated CO_2 could potentially be used as the carbonyl source.

Very recently, Zhu and co-workers disclosed a photocatalyst-free redox-neutral protocol for synthesis of unnatural α-amino acids promoted by formation of EDA (electron-donor-acceptor) complexes between *N*-Bz-imines and oxalate (Scheme 1D) [4].

In this reaction, oxalate worked as both the carbonyl source and the reductant. It is worthy to note, this method reveals a new way for $CO_2^{\bullet-}$ generation in the absence of any photo-sensitizers. During the optimization of reaction conditions, the authors showcased the details when imines reacted with $(^{n}Bu_4N)_2C_2O_4$ to give the desired product with or without photocatalysts. The reaction could occur in the presence of photocatalysts to give amino ester product in excellent yield. Interestingly, the reaction could still ocurr smoothly to give the desired product in moderate yield, which indicated that a new photocatalyst-free mechanism to initiate the electron transfer and subsequential homolytic cleavage of the C–C bond in oxalate to generate $CO_2^{\bullet-}$ and CO_2 might be involved.

During the substrate scope investigation, in most cases, the desired products could be isolated in moderate yields. Zhu and co-workers suggested that the benzoyl group on nitrogen atom was crucial for formation of the EDA complexes. In order to gain more understandings of the mechanism, several control experiments were conducted, such as D-labeling experiment, radical inhibition experiment, UV–vis absorption experiment. The red-shift of the absorption band and the color changed when imine substrate *N*-(diphenylmethylene)benzamide was combined with tetrabutylammonium oxalate. Moreover, the chemical shifts of the aromatic protons also changed as the oxalic dianion donated electrons to the imine substrate. These results provided solid evidences to indicate formation of the EDA complexes in the reaction.

The authors proposed that electron poor imine substrate and oxalate could form an EDA complex, which could be directly exited under visible-light irradiation. After that, electron transfer from oxalate to the substrate gave oxalate radical anion and imine radical anion. Additionally, the oxalate radical anion underwent homolysis of the C–C bond to generate the $CO_2^{\bullet-}$ and CO_2. Meanwhile, the imine radical anion would fix the CO_2 molecule to give the stable intermediate **II**, which was further reduced by the $CO_2^{\bullet-}$ to give the anion intermediate **III**. The second molecule of CO_2 was released and reacted with intermediate **III** to give the α-amino acid intermediate **IV**. After treatment with MeI and acidic workup, the desired amino ester product could be obtained.

In summary, Zhu and coworkers have successfully synthesized a range of unnatural α-amino acid derivatives by formation of an EDA complex between substrate and oxalate. The redox-neutral process with oxalate as both the carbonyl source and the reductant provide new insights for $CO_2^{\bullet-}$ chemistry and carboxylation reactions. This approach presents a novel pathway for the $CO_2^{\bullet-}$ species generation *via* the EDA complexs formation in the absence of any photocatalyst.

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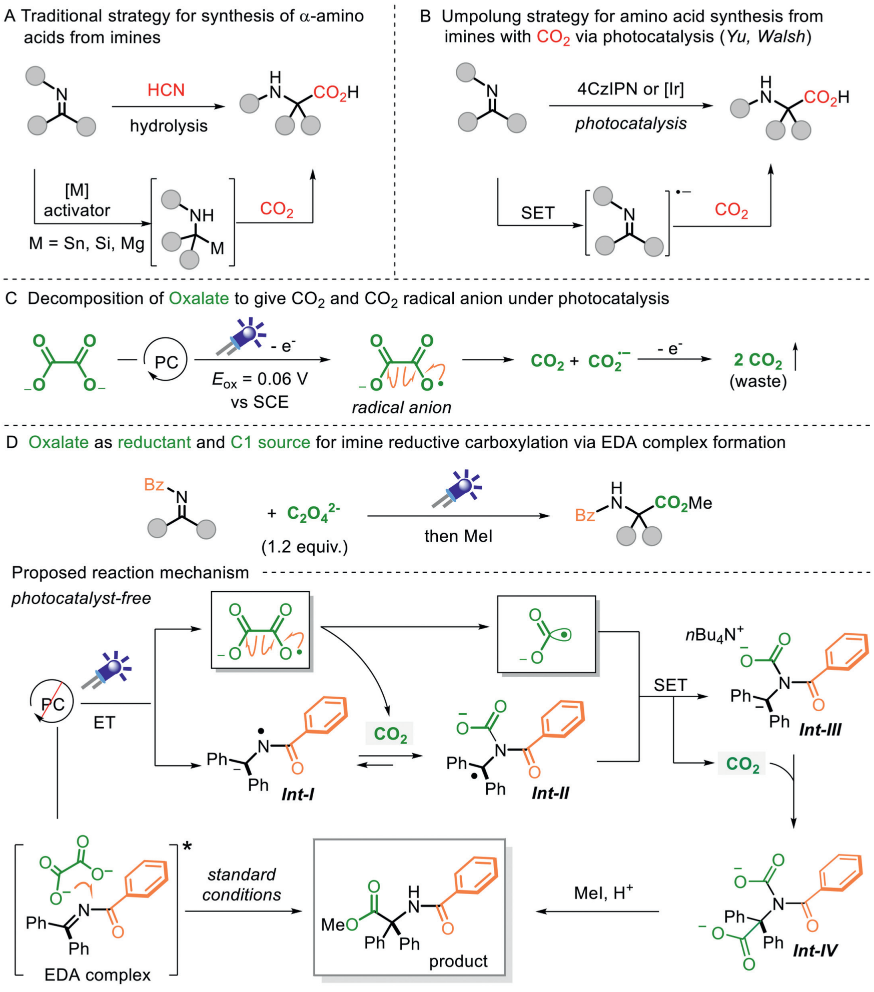

Scheme 1. Photochemical synthesis of α-amino acid derivatives from imines.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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