Green Chemical Technology

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Review

Progress in Chemical Transformations of Glyoxylic Acid as C1 and C2 Synthon

Wanqiang Wang, Jiaxin Yang, Jing Guo, Ting Pang, Jing He, Liang Xu, Chuntian Li and Ping Liu *

School of Chemistry and Chemical Engineering/State Key Laboratory Incubation Base for Green Processing of Chemical Engineering, Shihezi University, Shihezi 832003, China; 20222007045@stu.shzu.edu.cn (W.W.); 20242007022@stu.shzu.edu.cn (J.Y.); 20242007073@stu.shzu.edu.cn (J.G.); pangting@stu.shzu.edu.cn (T.P.); hejing@shzu.edu.cn (J.H.); xuliang4423@shzu.edu.cn (L.X.); lict@shzu.edu.cn (C.L.)

* Corresponding author. E-mail: liuping@shzu.edu.cn (P.L.)

Received: 5 May 2026; Revised: 3 September 2026; Accepted: 16 September 2026; Available online: 8 October 2026

ABSTRACT: Glyoxylic acid, the simplest α-keto acid, contains both aldehyde and carboxyl groups in its molecule and exhibits the reactivity of both. This compound features low toxicity, low cost, ease of storage and handling, and has become a highly valuable C1 and C2 synthon in organic synthesis. In recent years, new reactions based on decarboxylative coupling, condensation, and cyclization strategies of glyoxylic acid have emerged, providing green and efficient routes for the construction of aldehydes, carboxylic acids, amines, heterocycles, and other structural motifs. This review systematically summarizes representative advances in the past five years in the chemical transformations of glyoxylic acid as a C1 synthon (formyl source, carboxylic acid source, methylene source) and as a C2 synthon (participating in Petasis reaction, Morita-Baylis-Hillman reaction, and cyclization reactions), with emphasis on reaction design, substrate scope, functional group compatibility, and mechanistic features. Future directions are also discussed.

Keywords: Glyoxylic acid; C1 synthon; C2 synthon; Decarboxylative coupling; Formylation; Multicomponent reaction

1. Introduction

Glyoxylic acid (OHC-COOH) is the structurally simplest α-keto acid, containing both an aldehyde and a carboxyl group, and is highly reactive [1]. It possesses low toxicity, good stability, low cost, and ease of handling and storage, and has thus gained wide attention in the pharmaceutical, agrochemical, fragrance, and fine chemical industries [2,3]. From an industrial perspective, the main synthetic routes include: catalytic oxidation of glyoxal (heterogeneous noble metal catalysis, homogeneous nitric acid or hydrogen peroxide oxidation, electrochemistry, and enzymatic methods), ozonolysis of maleic acid, oxidation of glycolic acid (enzymatic or chemical), as well as alternative processes such as electroreduction of oxalic acid and pyrolysis of haloacetic acid derivatives [4–8]. Among them, the nitric acid oxidation of glyoxal and the ozonolysis of maleic acid are the mainstream industrial routes, but they suffer from NOx pollution and the need for high-pressure equipment, respectively. In synthetic chemistry, glyoxylic acid can participate in transformations either as a one-carbon unit (C1 synthon) or as a two-carbon unit (C2 synthon). As a C1 synthon, glyoxylic acid often provides a formyl group (–CHO) or a methylene bridge (–CH_2–) via

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decarboxylation, used for constructing aldehydes, formamides, methylene-bridged heterocycles, *etc.* As a C2 synthon, glyoxylic acid retains its full carbon skeleton and participates in Petasis reactions, Morita-Baylis-Hillman reactions, and cyclizations to afford α-amino acids, α,β-unsaturated acids, quinolines, naphthoquinones, and other important structural units. In recent years, the rapid development of visible-light photocatalysis, electrochemistry, transition-metal catalysis, and metal-free green strategies has greatly expanded the range of reaction types and substrates for glyoxylic acid [9]. Based on the dual role of glyoxylic acid in organic synthesis, this review classifies reactions according to C1 and C2 synthons, summarizes the main research progress in this field over the past five years, and comments on the design concepts, limitations, and future directions of key reactions.

2. Glyoxylic Acid as a C1 Synthon

2.1. Glyoxylic Acid as a Formyl Source

In 2017, Wang et al. [10] reported a novel organocatalytic strategy that utilizes aryl or alkenyl boronic acids with glyoxylic acid in a Petasis reaction, followed by oxygen-promoted oxidative decarboxylation, to efficiently synthesize a variety of aromatic, heteroaromatic, and α,β-unsaturated aldehydes (Figure 1). This method, for the first time, achieves the catalytic formylation of boronic acids without transition metals, featuring mild conditions, simple operation, good atom economy, and environmental friendliness. The innovation lies in using *N*-alkylaniline derivatives such as tetrahydroquinoline or indoline as organocatalysts. Their low oxidation potential allows them to be oxidized by oxygen via single-electron transfer, thereby driving the oxidative decarboxylation of the α-amino acid intermediate. The process tolerates a wide range of functional groups, including halogens, nitro, and triflate groups, and enables selective formylation at the non-C3 position of indole. Mechanistic studies suggest that the Petasis adduct first undergoes single-electron transfer to generate an aminium radical cation, which rapidly decarboxylates to form an α-amino radical, then is oxidized to an iminium ion; hydrolysis releases the desired aldehyde and regenerates the amine catalyst. The generated hydrogen peroxide may yield small amounts of phenolic byproducts, but increasing the temperature suppresses this process (Scheme 1).

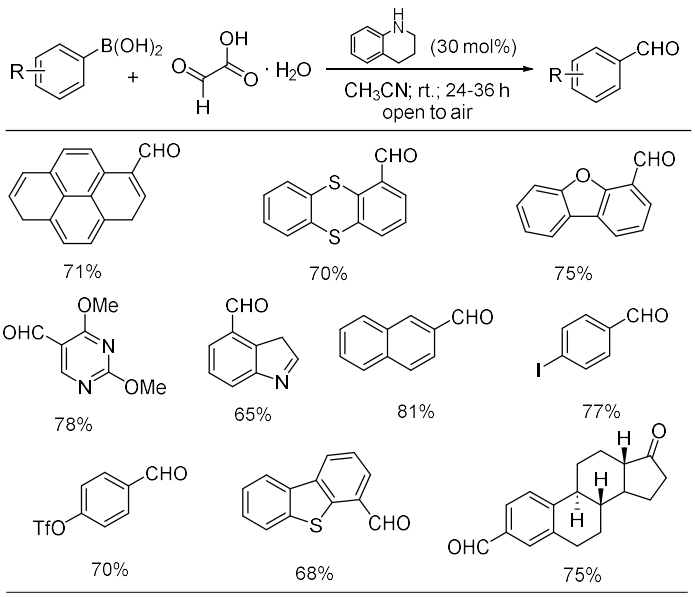
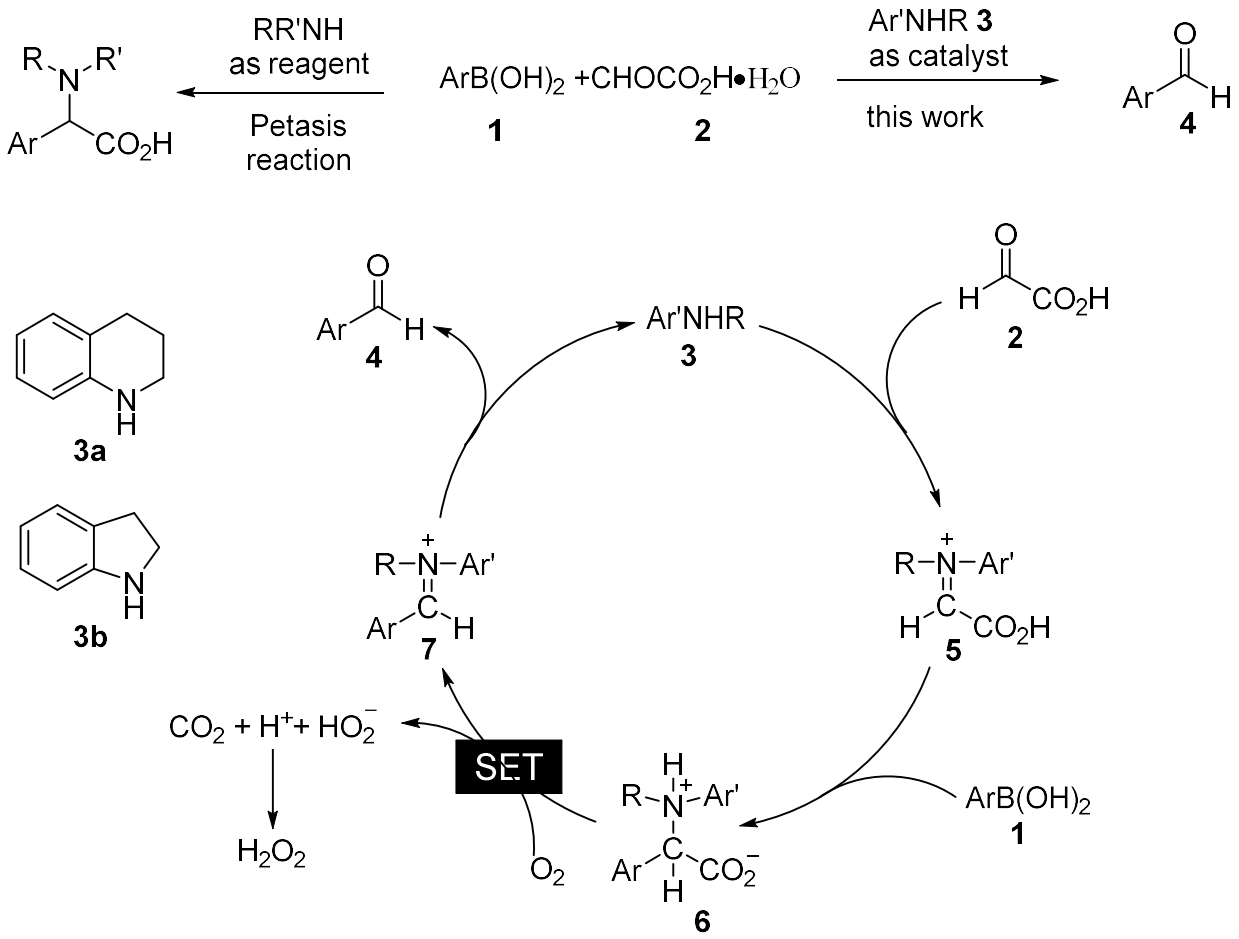


Figure 1. Tetrahydroquinoline-catalyzed formylation of arylboronic acids with glyoxylic acid.



Scheme 1. Plausible reaction mechanism.

In 2018, Huang's group reported the first synthetic method for electrochemical *N*-formylation of amines via decarboxylation of glyoxylic acid, ref. [11] which enables the construction of formamide compounds. Using glyoxylic acid as the formyl source, the reaction was carried out in an undivided cell at a constant current of 5 mA at room temperature. Under standard conditions, copper(II) acetate dihydrate and nickel(II) chloride hexahydrate were employed as additives, cesium carbonate as the base, sodium perchlorate as the electrolyte, and dimethyl sulfoxide as the reaction solvent. Reaction-optimization results demonstrated that the base and electric current were essential for this transformation. Only the trace product was detected in the absence of base, and no reaction occurred without an electric current. The addition of copper and nickel salts could effectively improve product yields. Secondary aromatic amines and cyclic amines, including indoline, piperazine, tetrahydroisoquinoline, and morpholine, were compatible with this protocol (Figure 2). Mechanistically, the authors proposed a plausible reaction pathway based on a set of verification experiments. Glyoxylic acid is converted into a carboxylate anion in the presence of cesium carbonate, which subsequently condenses with an amine to form an intermediate. This intermediate is oxidized by Cu(II), followed by decarboxylation, further one-electron oxidation, and deprotonation to afford the target formamide product. The Cu(II) species is regenerated at the anode, whereas protons are reduced to hydrogen gas at the cathode. Proceeding smoothly under ambient conditions, this electrochemical transformation provides a new sustainable synthetic route for *N*-formylation of amines. The authors noted that further investigations on mechanistic details and synthetic applications were ongoing in their laboratory (Scheme 2).

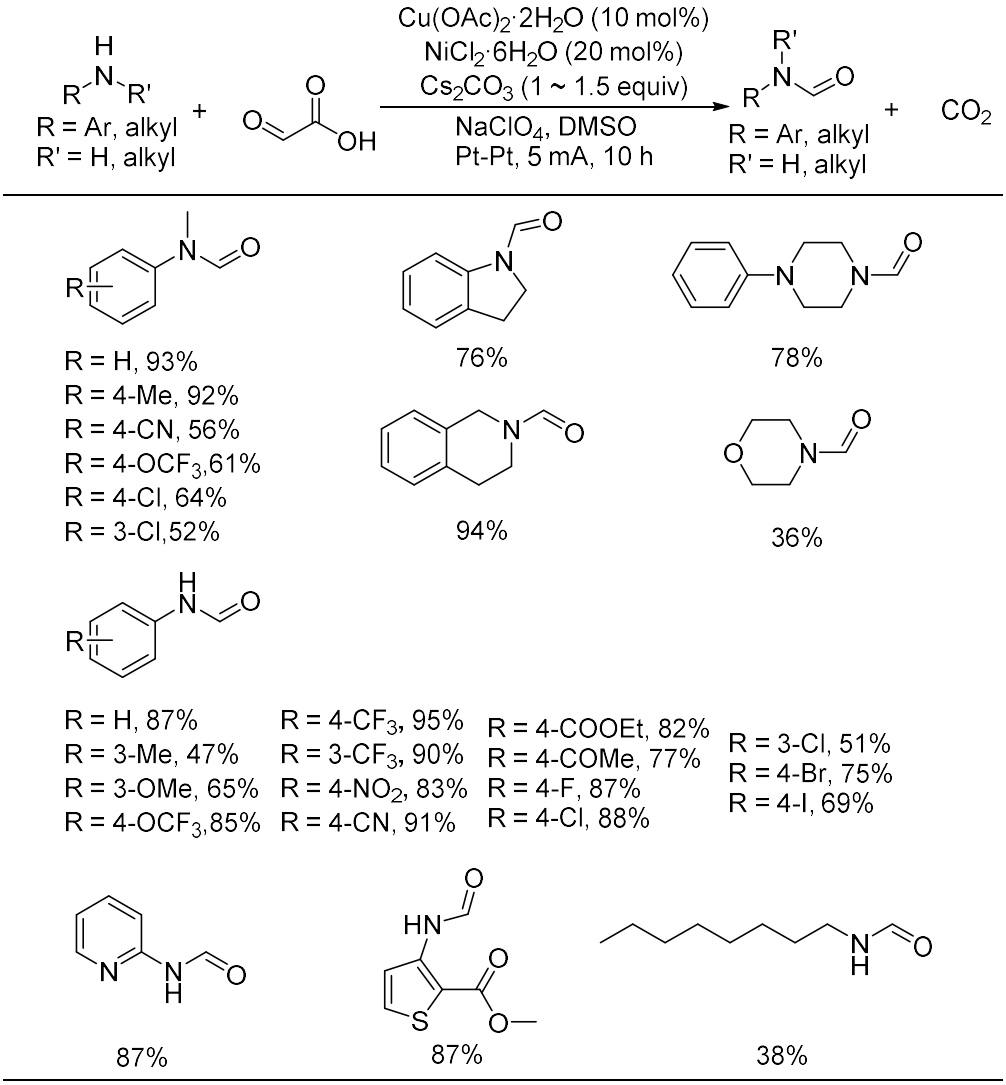
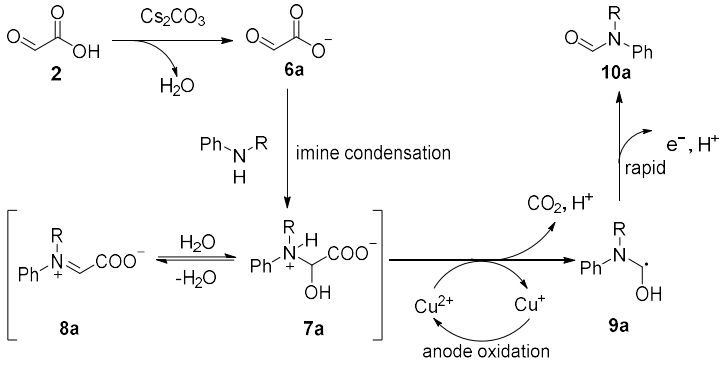


Figure 2. Glyoxylic-acid-involved *N*-formylation.



Scheme 2. Plausible reaction mechanism.

In 2018, Zhao et al. [12] reported a decarboxylative formylation of aryl halides with glyoxylic acid via synergistic photoredox/palladium catalysis (Figure 3). Using the organic dye 4CzIPN as a photocatalyst together with a phosphine-ligated palladium catalyst under blue light irradiation, they successfully achieved a mild transformation with glyoxylic acid monohydrate as the formylating reagent. The conditions are simple and applicable to a variety of aryl and heteroaryl iodides and bromides, tolerating halogens, cyano, nitro, ester, boronate, and other functional groups. Late-stage modification of natural amino acid derivatives

and steroid complex molecules was also realized. Mechanistic studies indicate that the reaction may proceed via photocatalytic oxidative decarboxylation to generate a formyl radical, which then combines with an arylpalladium species from the palladium catalytic cycle, followed by reductive elimination to give the aldehyde product (Scheme 3). This method provides a green and efficient route to functionalized aromatic aldehydes and extends the application of photoredox/palladium synergistic catalysis in decarboxylative coupling reactions, demonstrating the potential of glyoxylic acid as a practical formyl source for the modification of complex molecules.

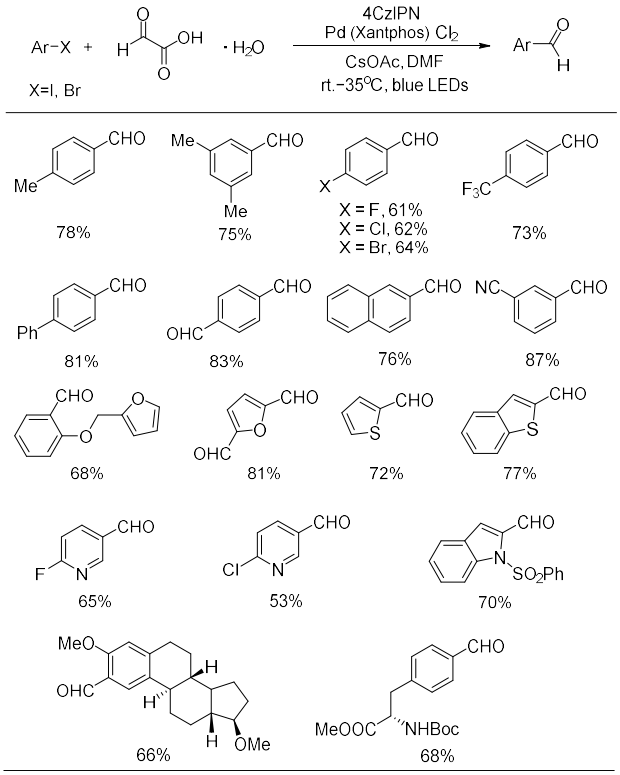
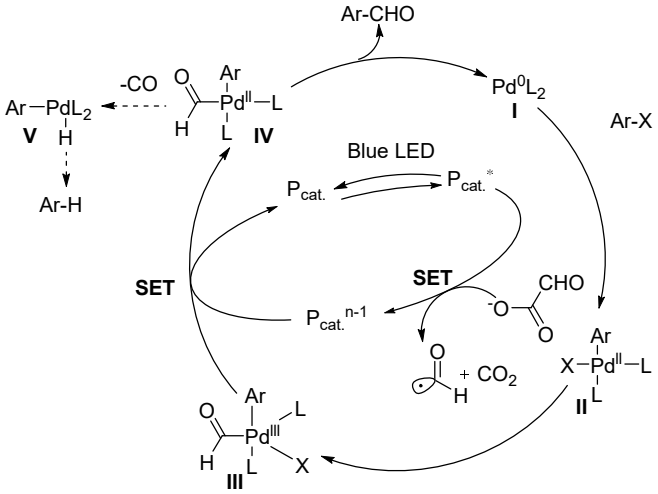


Figure 3. Palladium-catalyzed formylation of aryl halides with glyoxylic acid.



Scheme 3. Plausible reaction mechanism.

In 2018, Wu et al. [13] reported a nickel-catalyzed dehydrogenative-decarboxylative formylation of indoles with glyoxylic acid (Figure 4). This method achieves direct C3-formylation of indoles for the first

time, using a $Cu(OAc)_2/Ag_2CO_3$ oxidation system with $Ni(OAc)_2 \cdot 4H_2O$ and $FeCl_3$ bimetallic catalysis in DMSO at 130 °C, converting various indoles to the corresponding 3-formylindoles. The strategy cleverly combines dehydrogenative and decarboxylative coupling processes, using cheap and readily available glyoxylic acid as the formyl source. The reaction exhibits excellent functional group compatibility: indoles bearing either electron-donating (methyl, methoxy) or electron-withdrawing groups (halogen, nitro, ester) on the benzene ring afford the target products in moderate to good yields. Notably, no *N*-formylation byproduct was detected, indicating good chemoselectivity. Mechanistic studies suggest that the dehydrogenation and decarboxylation steps may occur cooperatively, with a copper salt as the terminal oxidant, a silver salt for recycling the catalytic cycle, and an iron salt promoting indole activation (Scheme 4). This method provides a new, step-economical route to 3-formylindoles, an important class of pharmaceutical intermediates, without the need for prefunctionalization.

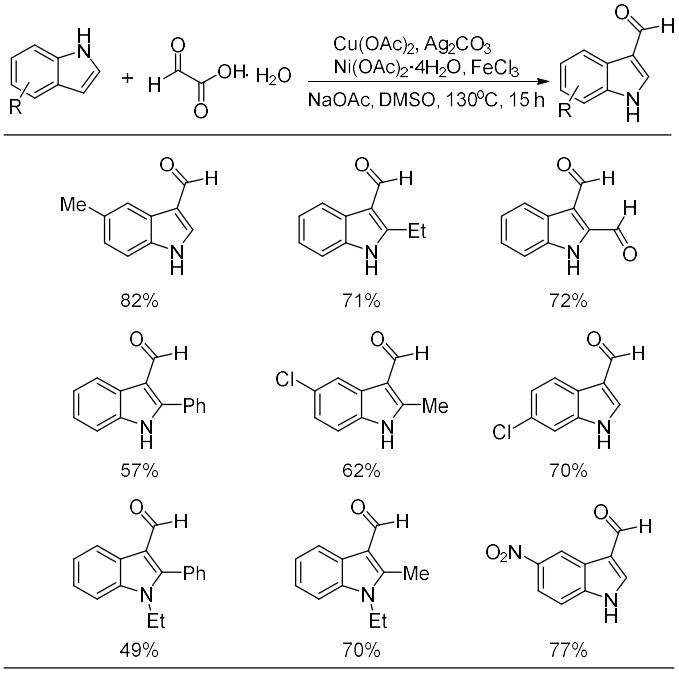
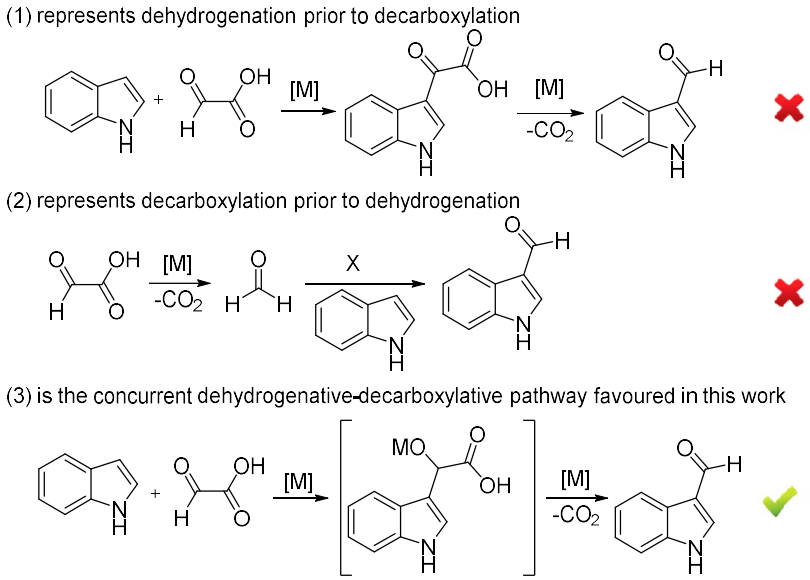


Figure 4. Four-metal-salt catalyzed formylation of indoles with glyoxylic acid.



Scheme 4. Plausible reaction mechanism.

In 2018, Liu's group [14] reported a palladium-catalyzed hydroformylation of terminal arylacetylenes using glyoxylic acid as the formyl source. Under syngas-free conditions, using $PdCl_2(PPh_3)_2$ as a catalyst with common bidentate ligand dppp and monodentate ligand PPh_3, they efficiently and stereoselectively synthesized various (E)-α,β-unsaturated aldehydes under mild conditions (Figure 5). Mechanistically, the authors proposed a catalytic cycle involving the formation of a cationic palladium hydride species, which inserts into the alkyne to give a vinylpalladium intermediate, followed by hydrogenolysis with glyoxylic acid to release the product and regenerate the catalyst (Scheme 5). This method avoids the need for high-pressure equipment and hazardous syngas in traditional hydroformylation, providing a convenient laboratory route to these valuable building blocks.

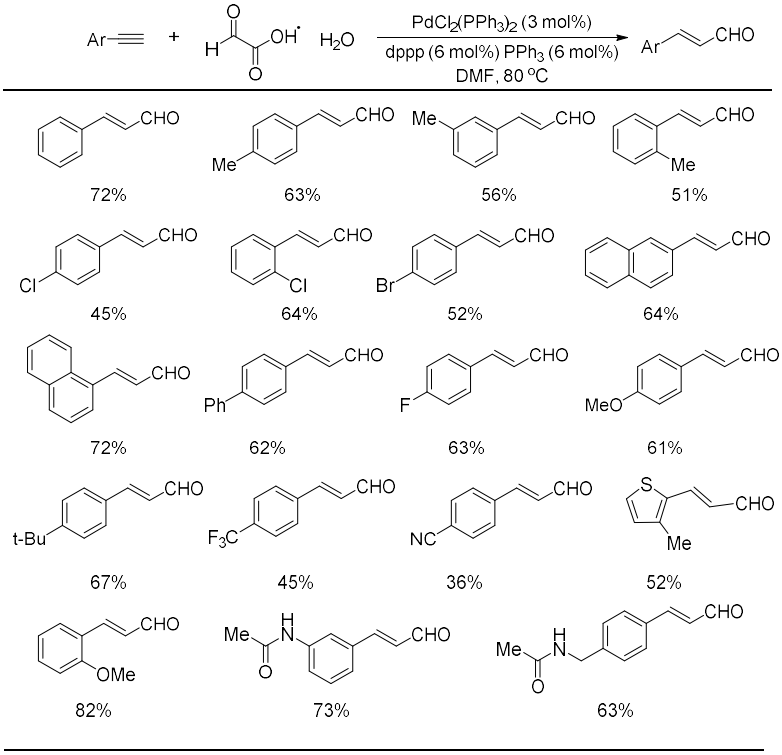
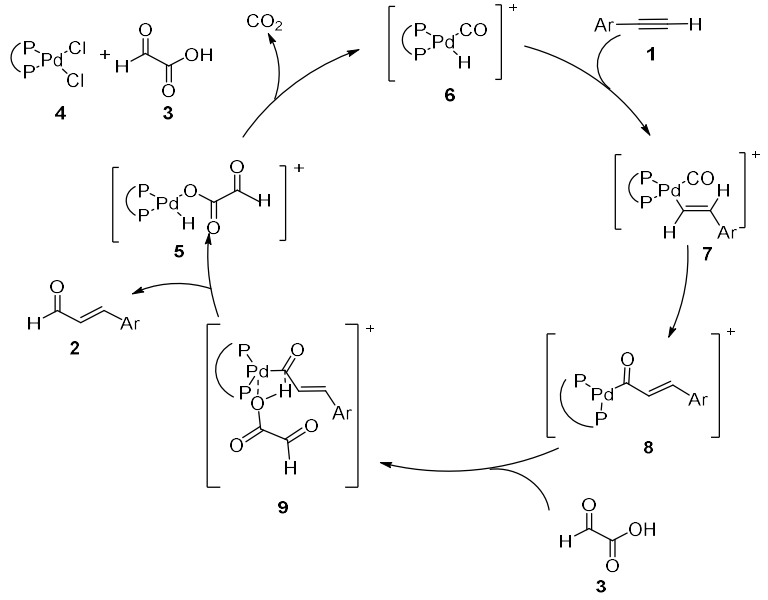


Figure 5. Palladium-catalyzed hydroformylation of terminal arylacetylenes with glyoxylic acid.



Scheme 5. Plausible reaction mechanism.

In 2019, Huang's group [15] reported an efficient electrochemical method for C3-formylation of indoles (Figure 6). Using an amine as a dual-function organocatalyst, they achieved direct formylation of indoles with glyoxylic acid under mild electrochemical conditions. The reaction was carried out at room temperature in an undivided cell with platinum electrodes, requiring only 1 mol% dimethylamine solution or 10 mol% aniline as a catalyst, under very mild conditions. The method exhibits excellent functional group tolerance, works for various *N*-substituted and free NH indoles, and accommodates methyl, methoxy, halogen, nitro, ester groups on the benzene ring. The key strategy is that the amine first condenses with glyoxylic acid to form an α-iminocarboxylate, which is more prone to oxidative decarboxylation at the anode; the resulting active intermediate is then attacked by indole, and finally hydrolyzed to give 3-formylindole while regenerating the amine catalyst (Scheme 6).

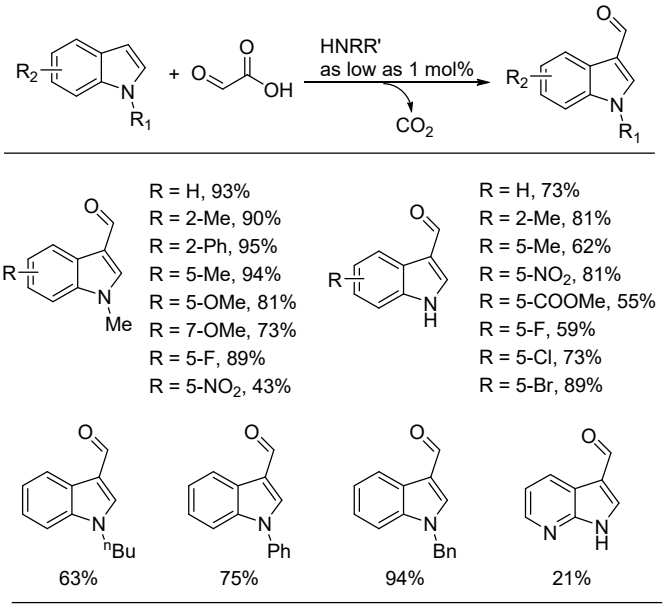
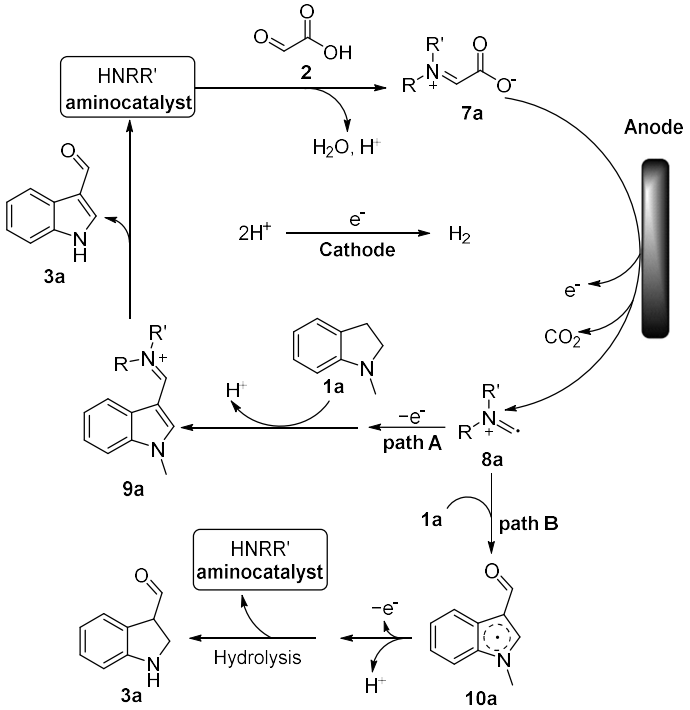


Figure 6. Amine-catalyzed electrochemical formylation of indoles with glyoxylic acid.



Scheme 6. Plausible reaction mechanism.

In 2020, Cao et al. [16] reported a radical/palladium synergistic decarboxylative formylation of aryl halides with glyoxylic acid under an oxygen atmosphere (Figure 7). Using glyoxylic acid monohydrate as the formyl source, $PdCl_2(PPh_3)_2$ as catalyst, Et_3N as base, AIBN as radical initiator, and oxygen (1 atm) in DMF at 110 °C, they efficiently synthesized aromatic aldehydes. The conditions are suitable for a variety of aryl and heteroaryl iodides and bromides, tolerating methyl, methoxy, acetyl, ester, halogen, and other functional groups, giving moderate to good yields. Electron-deficient or *ortho*-substituted substrates showed lower activity, reflecting steric and electronic effects. The proposed mechanism involves a synergistic radical/palladium cycle: AIBN generates isobutyronitrile radicals, which are converted to peroxy radicals by oxygen, possibly promoting oxidative decarboxylation of glyoxylic acid to form a formyl radical; the formyl radical is then captured by an arylpalladium(II) species, followed by reductive elimination from a palladium(III) intermediate to give the aldehyde (Scheme 7). This work provides a new route for formylation without photoirradiation and highlights the unique role of oxygen in modulating radical-metal synergistic reactions.

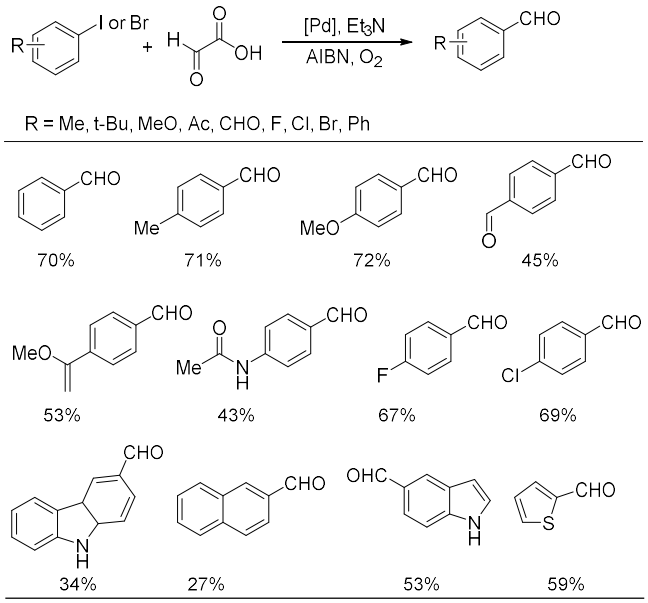
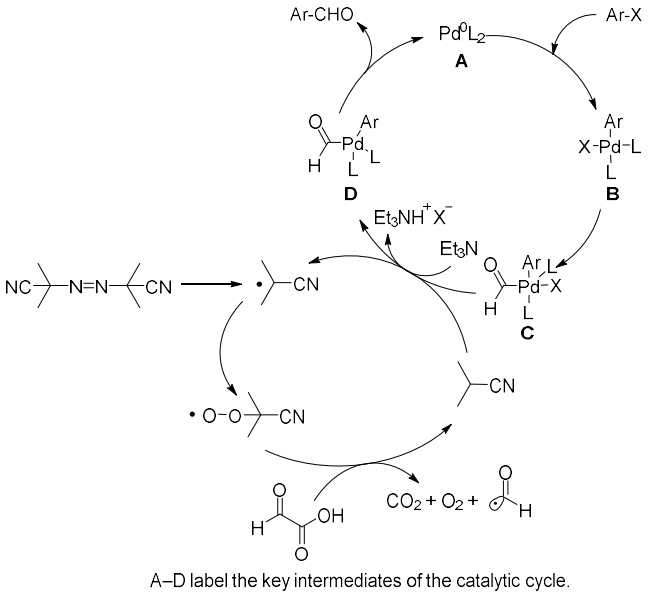


Figure 7. Palladium-catalyzed formylation of aryl halides with glyoxylic acid.



Scheme 7. Plausible reaction mechanism.

In 2022, Wang et al. [17] reported a metal-free, external oxidant-free visible-light photocatalytic strategy using deuterated glyoxylic acid directly as the formyl source to achieve highly selective C3-deuterated formylation of indoles (Figure 8). Using air (O_2) as the terminal oxidant, under visible light irradiation without an external photocatalyst, they efficiently synthesized C1-deuterated 3-formylindoles with 95–99% deuterium incorporation. The method is mild, shows excellent functional group compatibility, works for various *N*-substituted and free NH indoles, including those with electron-donating or electron-withdrawing groups, and enables late-stage deuterated formylation of complex bioactive molecules (e.g., nonsteroidal anti-inflammatory drug (NSAID) derivatives, sugars, and dipeptides). Mechanistically, indole and glyoxylic acid first undergo aldol condensation to form an α-hydroxy acid intermediate; meanwhile, a small amount of indole is oxidized to isatin under light and air. The excited state of isatin promotes decarboxylation of the α-hydroxy acid intermediate via single-electron oxidation, generating a carbon radical; this radical combines with O_2 and then fragments to give the target aldehyde and H_2O_2, completing the catalytic cycle (Scheme 8). This strategy provides a green and practical new route to high-value deuterated aldehydes.

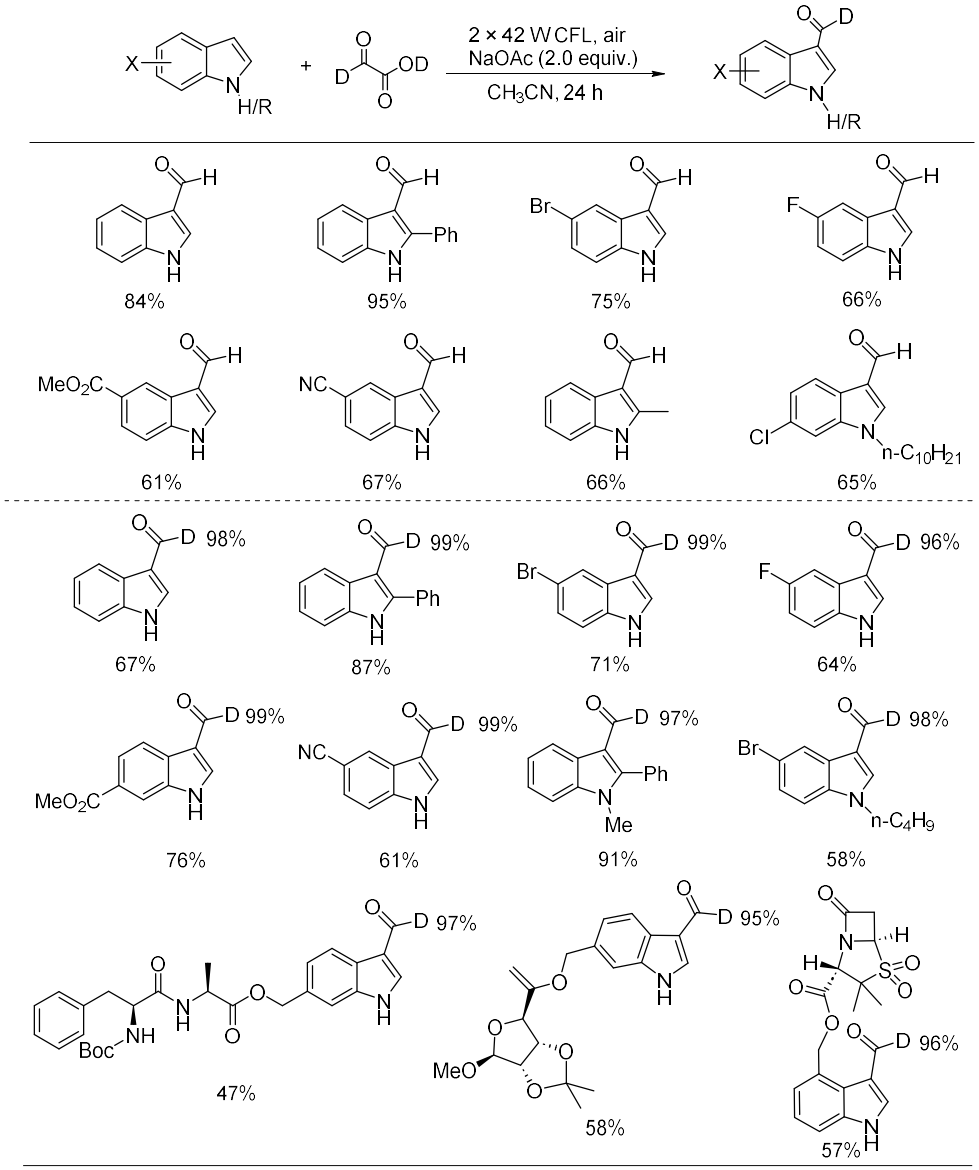
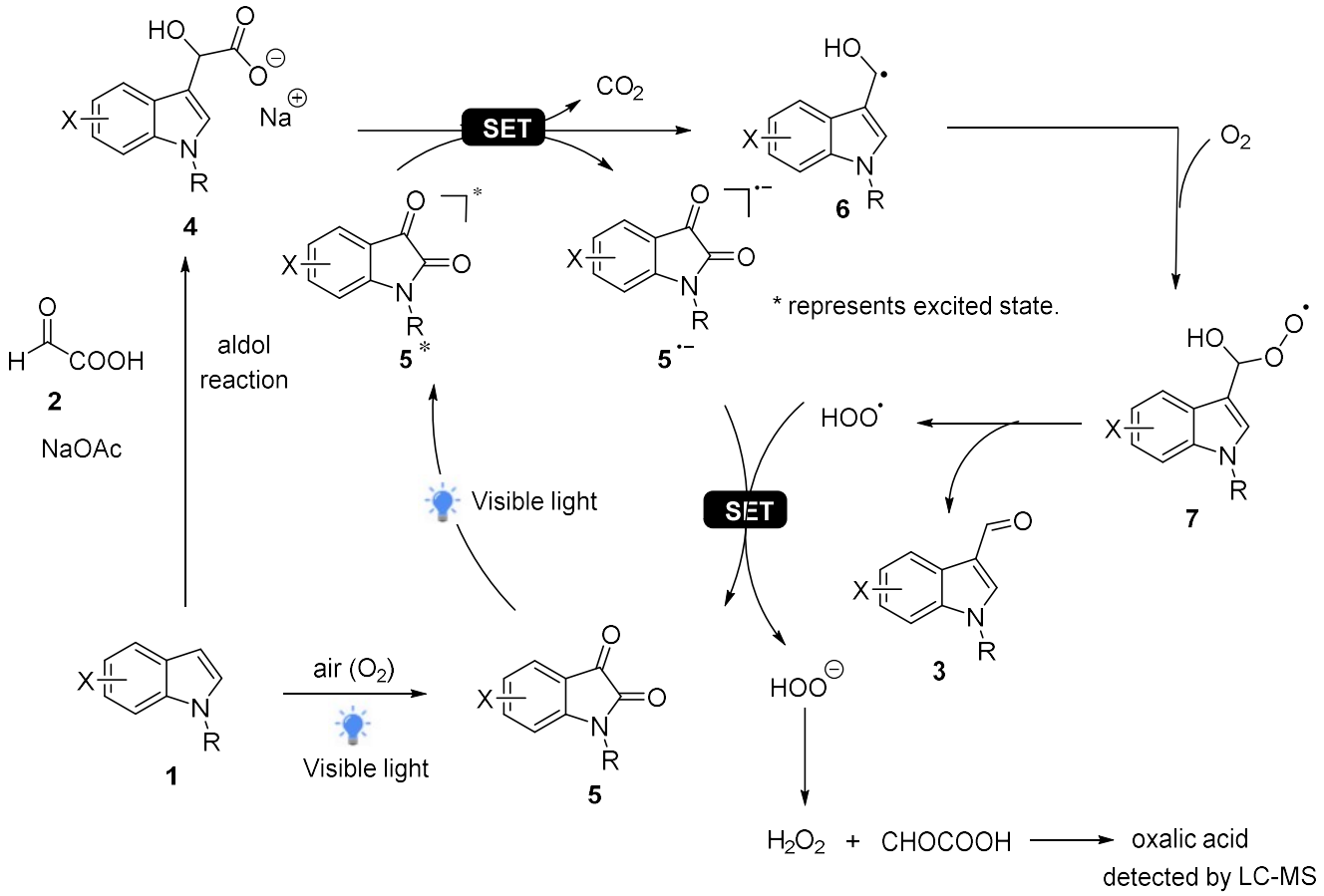


Figure 8. Amine-catalyzed formylation of indoles with deuterated glyoxylic acid.



Scheme 8. Plausible reaction mechanism.

In 2022, Dinesh et al. [18] reported a direct decarboxylative cross-coupling method using ammonium persulfate (APS) as oxidant and α-oxo/keto acids (such as glyoxylic acid, pyruvic acid, phenylglyoxylic acid) as formyl/acyl sources to achieve C–H formylation or acylation of indoles and β-carbolines, giving moderate to good yields (Figure 9). This method was successfully applied to the efficient total synthesis of the indole alkaloids pityriacitrin, eudistomin Y_1/Y_3, and marinacarbolines A–D, demonstrating excellent synthetic utility. Mechanistically, thermal decomposition of APS generates sulfate radical anion ($SO_4^{\cdot-}$), which abstracts a hydrogen atom from the α-keto acid to form an acyloxy radical, which rapidly decarboxylates, releasing CO_2 and forming a formyl or acyl radical. This radical undergoes Minisci-type electrophilic addition to the electron-rich indole or β-carboline, followed by single-electron transfer or hydrogen atom abstraction to give the final carbonyl product (Scheme 9). This strategy offers a green and efficient route to structurally diverse 3-formylindoles and acylated β-carbolines.

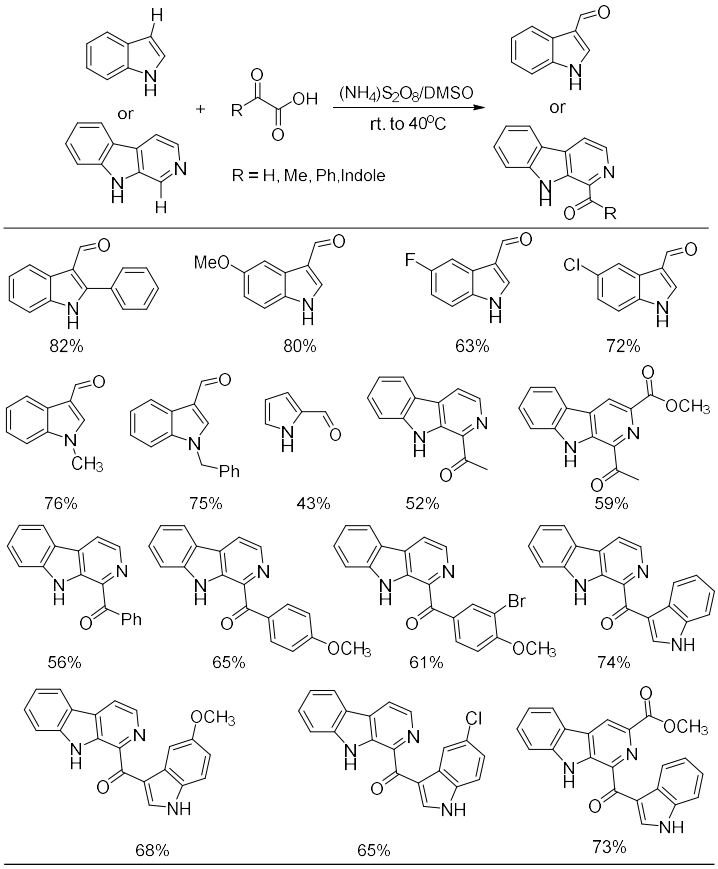
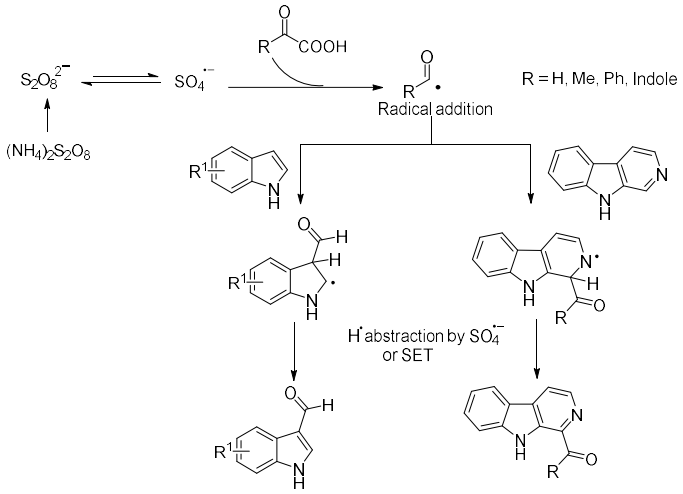


Figure 9. Ammonium persulfate-mediated formylation of indoles or β-carbolines with glyoxylic acid.



Scheme 9. Plausible reaction mechanism.

In 2023, Laha et al. [19] reported a general strategy for site-selective decarboxylative formylation of nitrogen heterocycles and anilines using glyoxylic acid as the formyl source and potassium persulfate as the oxidant (Figure 10). Under mild neutral conditions, this method simultaneously achieves *C*-formylation of indoles, azaindoles, pyrroles, and *N*-formylation of anilines. Furthermore, the method can be extended to tandem reactions for one-pot construction of quinazolinones, benzimidazoles, and other heterocycles, and successfully synthesized a key intermediate of the anticancer drug vemurafenib and the natural product luotonin F, demonstrating its potential for practical application. Mechanistically, the authors proposed two possible pathways: Path 1 involves thermal decomposition of persulfate to generate sulfate radical, which abstracts a hydrogen from glyoxylic acid and induces decarboxylation to form a formyl radical, followed by

Minisci-type addition to the substrate and oxidative deprotonation to give the product; Path 2 involves initial aldol condensation to form an α-hydroxy acid intermediate, which then undergoes sulfate radical-induced single-electron oxidation, decarboxylation, and radical recombination to yield the target aldehyde (Scheme 10).

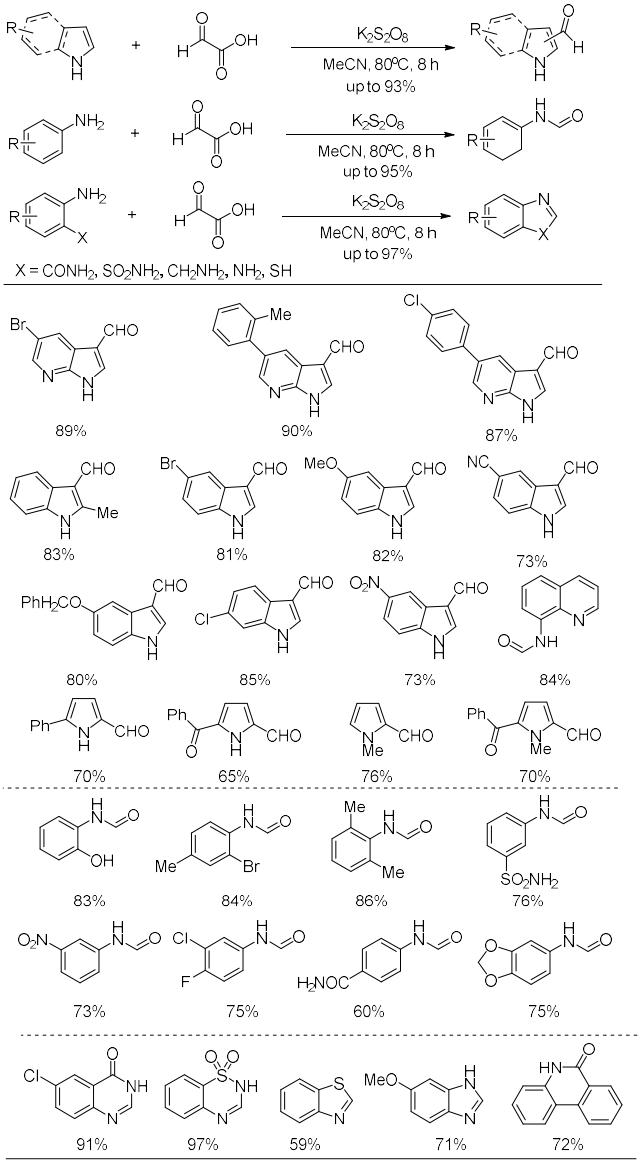
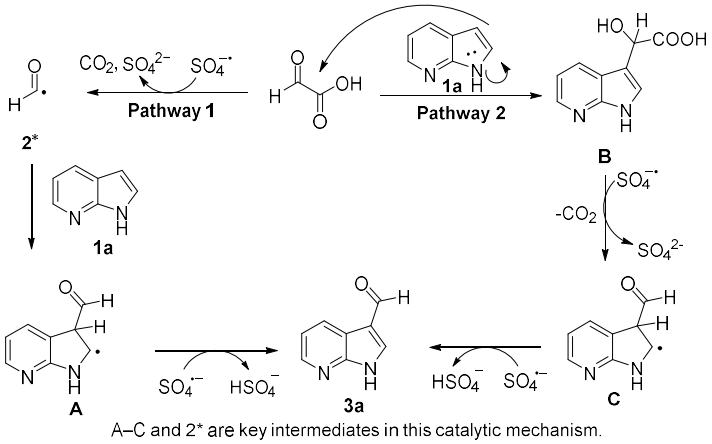


Figure 10. $K_2S_2O_8$-catalyzed formylation of *N*-heteroarenes and anilines.



Scheme 10. Plausible reaction mechanism.

In 2023, Wu et al. [20] reported a hydrogen peroxide (H_2O_2)-promoted decarboxylative *N*-formylation method using glyoxylic acid as the formyl source, under metal-free, base-free, room-temperature conditions, to efficiently synthesize formamides. The substrate scope covers various substituted anilines, heterocyclic amines, benzylamines, and alkylamines, with moderate to excellent yields (up to 97%), and gram-scale synthesis and chemoselective transformations (e.g., monoformylation of *p*-phenylenediamine) were also achieved (Figure 11). The innovation lies in the first use of H_2O_2 as a green oxidant to drive the decarboxylative formylation of amines with glyoxylic acid, avoiding metal catalysts, strong bases, or high temperatures in traditional methods, and featuring simple operation and environmental friendliness. Mechanistic studies suggest that H_2O_2 undergoes homolysis to generate hydroxyl radicals *OH*, which first react with the intermediate (carboxylate salt) formed in situ from glyoxylic acid and amine, inducing decarboxylation via single-electron oxidation to give a carbon-centered radical; further oxidation and intramolecular electron rearrangement ultimately release a proton to yield the formamide product (Scheme 11). This strategy provides a new idea for the sustainable synthesis of formamides.

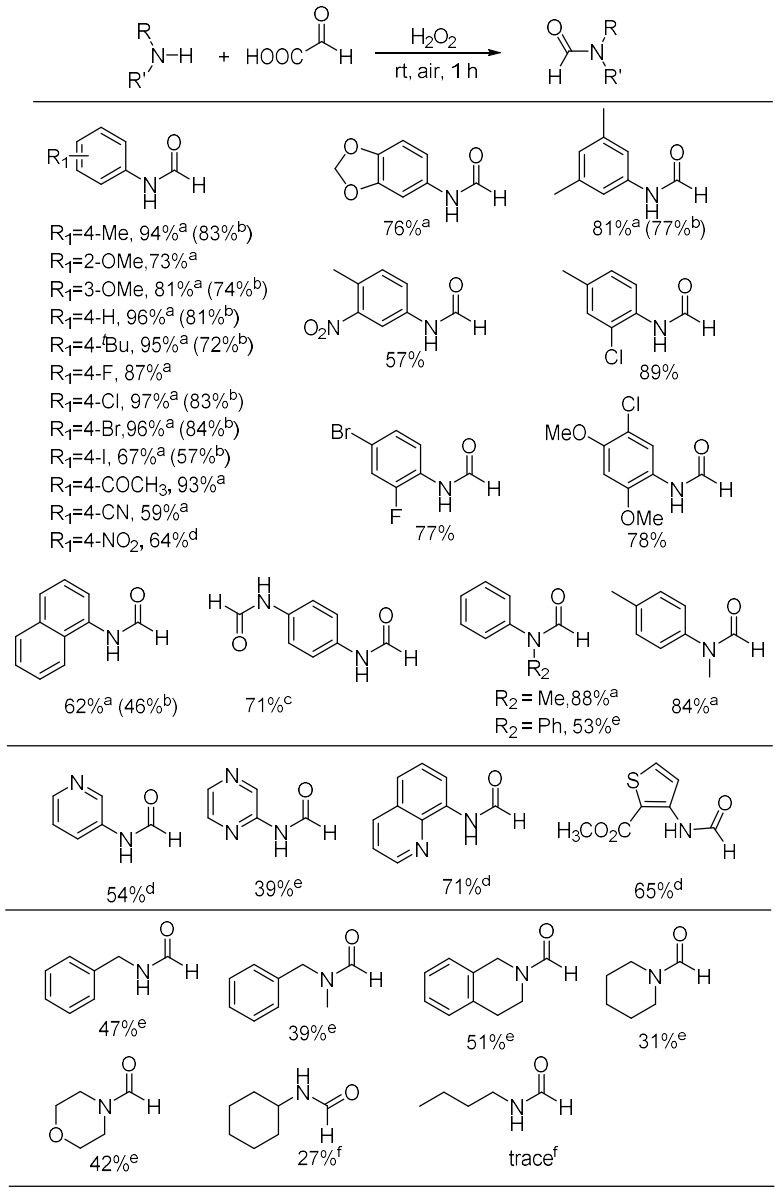
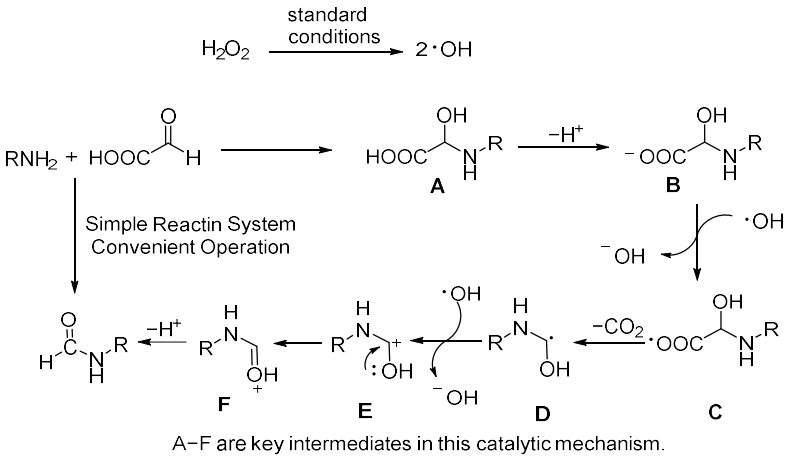


Figure 11. Synthesis of formamides. [a] Reaction conditions: **1** (0.3 mmol), **2a** (0.3 mmol, 50% in water), H_2O_2 (2.0 equiv, 30% in water), DMSO (1.5 mL), at rt under air for 1 h. Yields shown are of isolated products. [b] H_2O as the solvent. [c] 0.6 mmol of **2a**. [d] 60 °C for 3 h. [e] 90 °C for 6 h. [f] 120 °C for 6 h.



Scheme 11. Plausible reaction mechanism.

In 2023, Nagarajan's group developed a transition-metal-free and oxidant-free photochemical decarboxylative formylation strategy [21]. Using 50% aqueous glyoxylic acid as the formyl synthon, C3-selective decarboxylative formylation of indoles was accomplished under 254 nm UV irradiation at room temperature to efficiently construct a series of indole-3-carboxaldehyde derivatives (Figure 12). Traditional protocols for C3-formylation of indoles mainly rely on classic reactions, including Vilsmeier-Haack, Riemer-Tiemann, and Duff reactions, which commonly suffer from environmentally hazardous reagents, harsh reaction conditions, and unsatisfactory selectivity. In contrast, previously reported glyoxylic-acid-mediated indole formylation systems generally require nickel catalysis, electrochemical set-ups, or photoredox catalysts. Different from those precedents, the present system dispenses with transition-metals, external oxidants, exogenous bases, and photoredox catalysts. With acetonitrile serving as the sole solvent, the transformation proceeds under UV irradiation at room temperature, featuring inexpensive starting materials and straightforward operation. Mechanistically, the authors proposed a plausible reaction pathway for this photochemical decarboxylative formylation based on previous literature. A reactive formyl-containing species is generated upon 254 nm UV photoexcitation of aqueous glyoxylic acid, which reacts with indole. Subsequent decarboxylation releases CO_2 and yields indole-3-carboxaldehyde. Notably, no control experiments such as radical-trapping tests or high-resolution mass-spectrometry analysis were carried out in this study, so the proposed mechanism remains to be further validated (Scheme 12). This work provides a concise new photochemical route for the decarboxylative formylation of nitrogen-containing heterocycles.

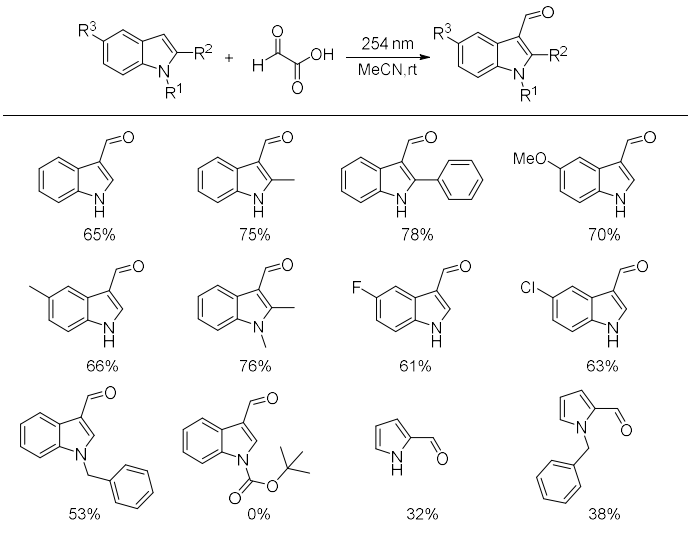
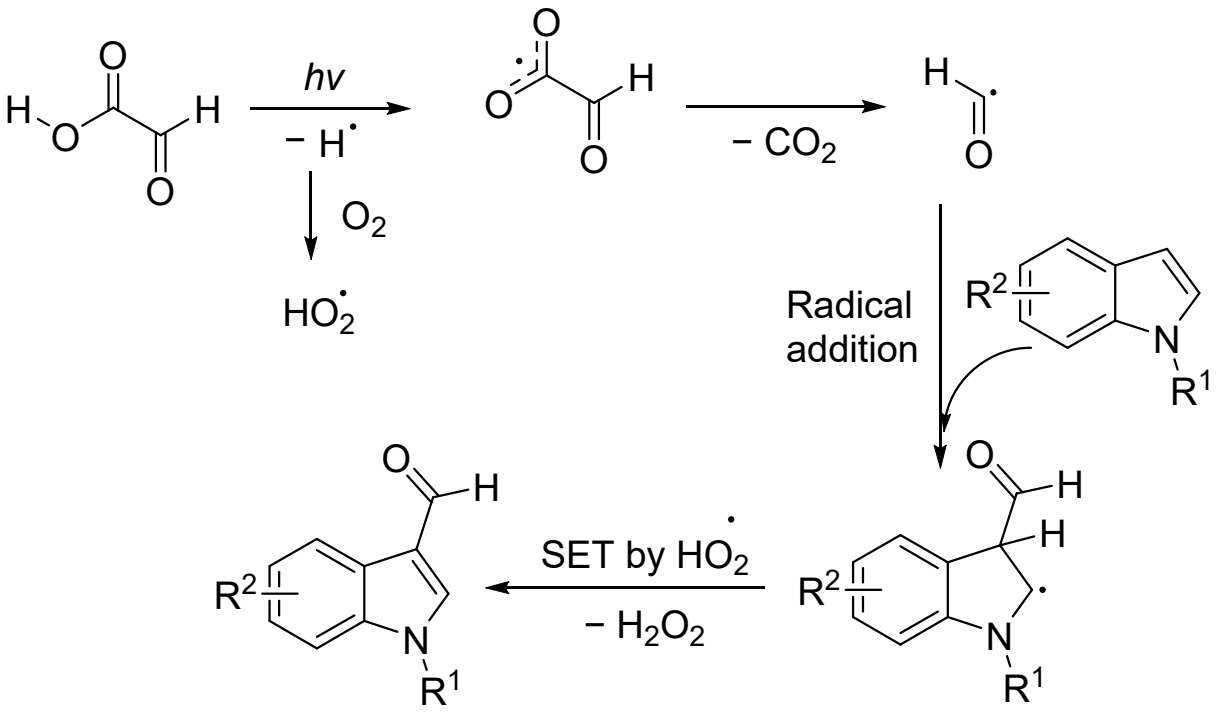


Figure 12. Synthesis of indole-3-carboxaldehyde derivatives.



Scheme 12. Plausible reaction mechanism.

In 2024, Yang et al. [22] reported a visible-light-induced photoredox catalytic reaction using glyoxylic acid acetals and CO_2 as starting materials to achieve formyl/carboxylation of activated alkenes, efficiently synthesizing γ-formyl esters (Figure 13). The reaction applies to a variety of aryl ethylenes and α,β-unsaturated amides. Moreover, the products can be further converted to γ-formyl esters, hemiacetals, and 1,4-diols. Mechanistically, deprotonation of the glyoxylic acid acetal by Cs_2CO_3 is followed by reductive quenching of the excited state photocatalyst 4CzIPN, generating an acetal radical. This radical adds to the alkene, and the resulting intermediate undergoes single-electron reduction to form a carbanion, which then attacks CO_2 to form a carboxylate salt, and finally, methyl esterification gives the target product. Control experiments (TEMPO inhibition, D_2O exchange, benzaldehyde trapping) confirmed the presence of radical and carbanion intermediates (Scheme 13). This strategy provides a green new route to multifunctional molecules containing both aldehyde and carboxyl groups.

In 2025, Kumbhakar et al. [23] developed a sustainable electrochemical strategy for the direct formylation of enamines via anodic decarboxylation of glyoxylic acid, affording a series of formylated enamines in good yields and excellent diastereoselectivity *E*/*Zupto* > 20:1 (Figure 14). The method completely avoids metal catalysts and chemical oxidants, operates at room temperature under air, and an electrolyte-free version was developed, significantly enhancing sustainability. The substrate scope is broad, including long-chain alkyl, allyl, propargyl, aryl, and heterocyclic substituted enamines, and the reaction can be scaled to the gram level, with further conversion to pyrazole derivatives. Mechanistically, cyclic voltammetry and spectroelectrochemical studies indicate that enamine and glyoxylic acid first form a rapid adduct intermediate. This intermediate undergoes anodic single-electron oxidation to generate a radical cation, which undergoes ionic decarboxylation to form a resonance-stabilized allyl radical; subsequent anodic oxidation and deprotonation give the target product. A parallel pathway involves oxidative decarboxylation of a carboxylate intermediate. This work provides a green and efficient new method for the selective functionalization of enamines (Scheme 14).

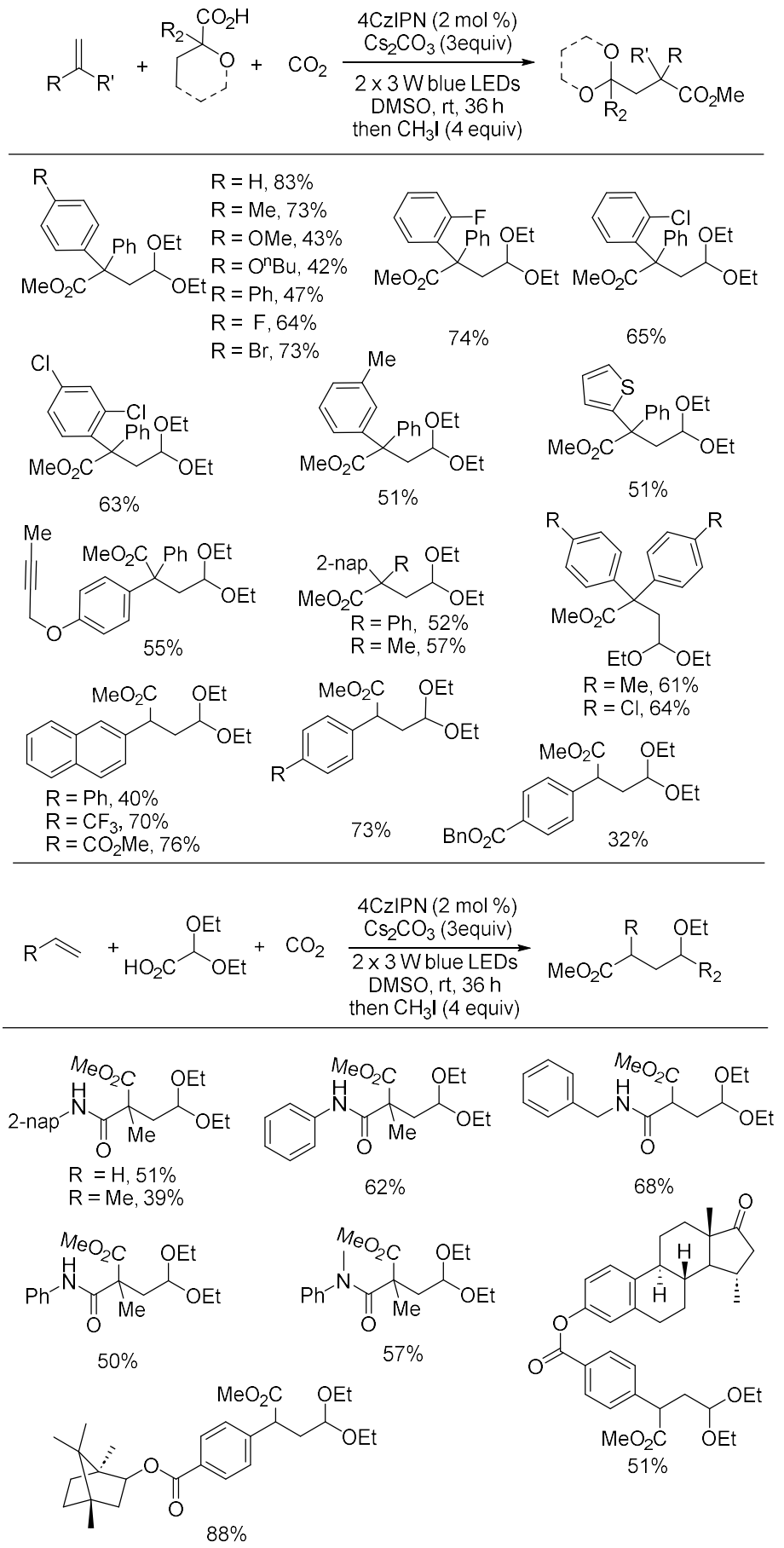
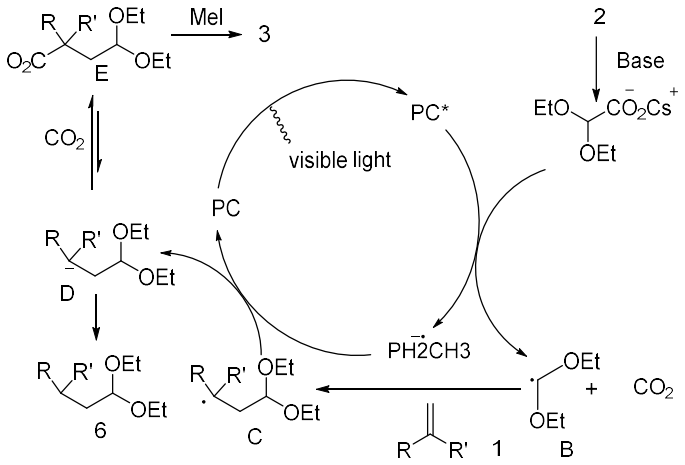


Figure 13. Visible-light-induced photoredox catalytic formylation involving glyoxylic acid.



Scheme 13. Plausible reaction mechanism.

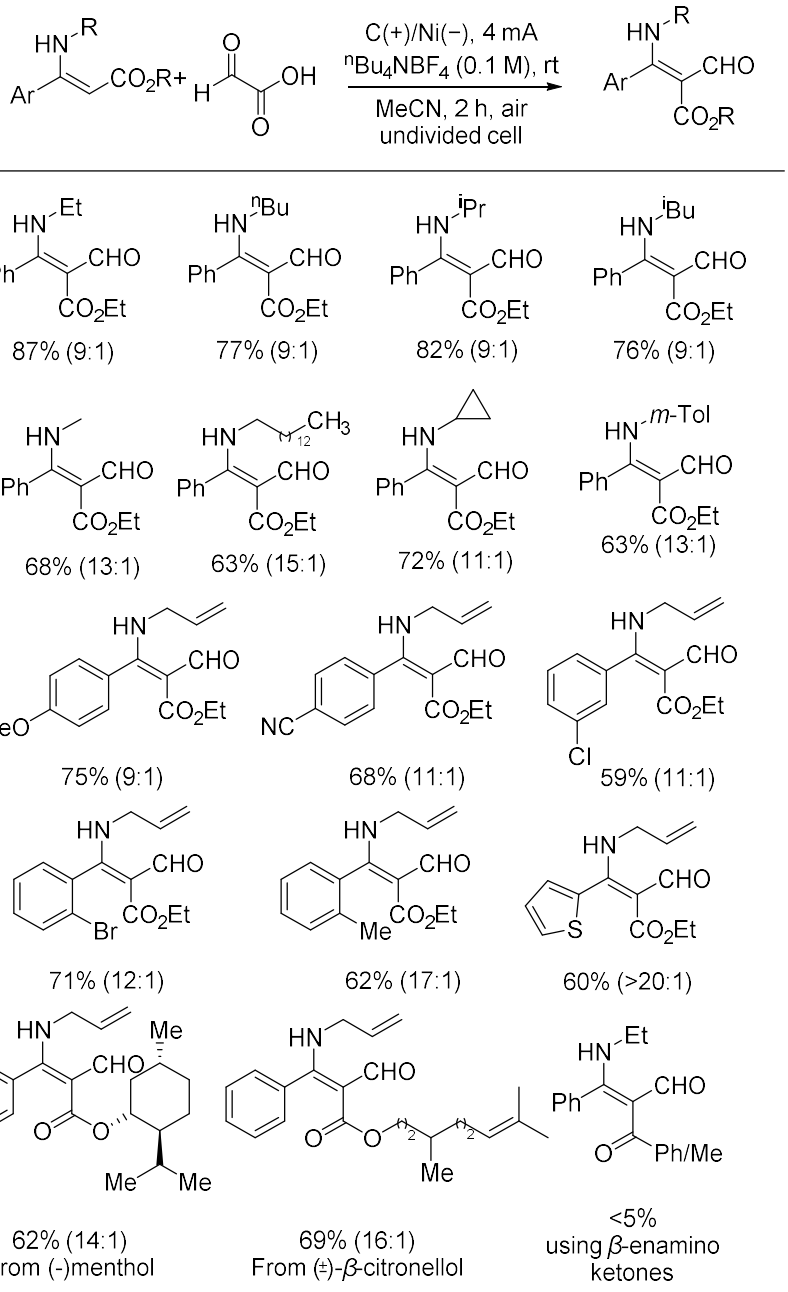
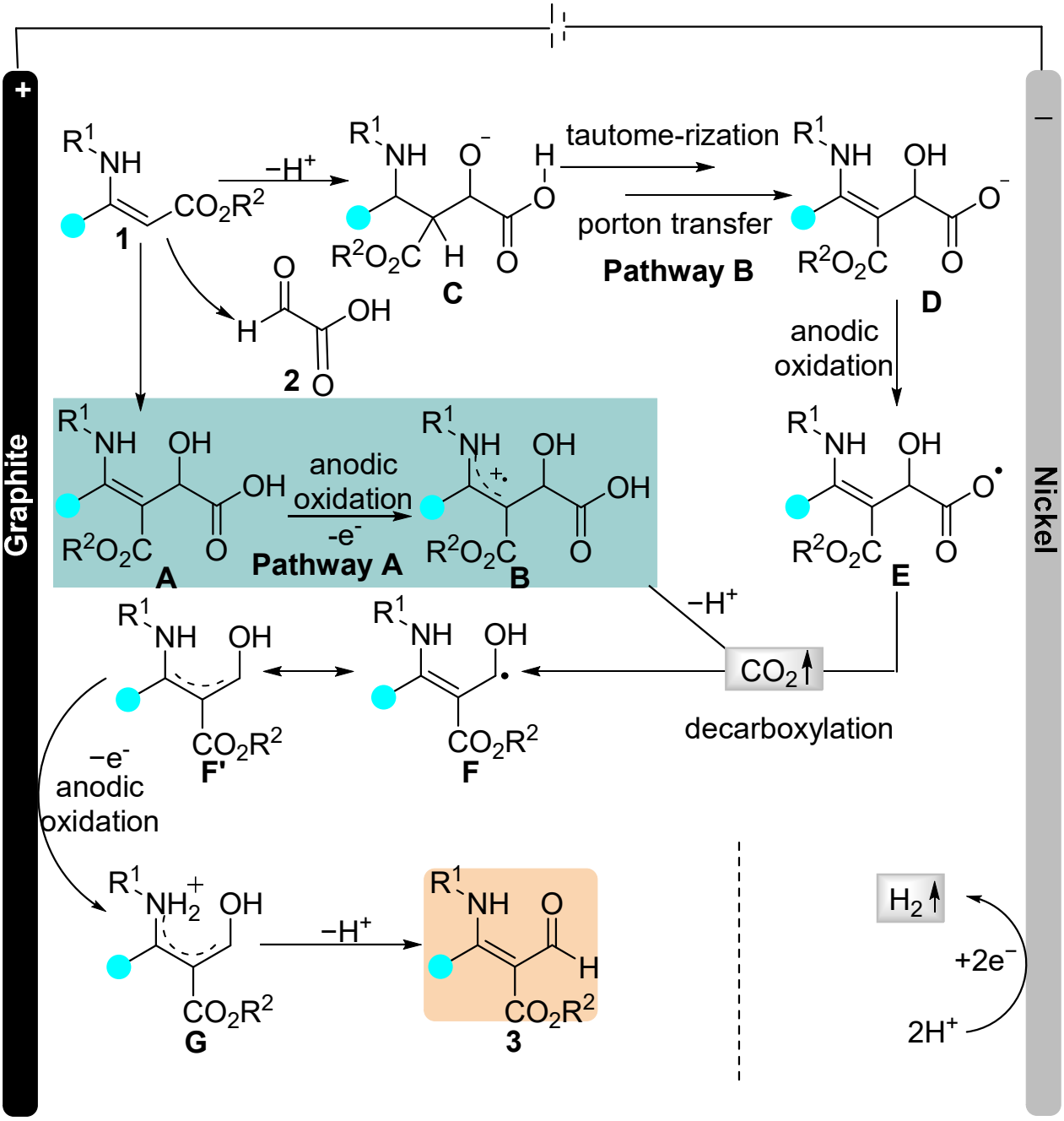


Figure 14. Electrochemically driven formylation using glyoxylic acid.



Scheme 14. Plausible reaction mechanism.

In 2025, Sujat et al. [24] reported a metal-free, mild C3 selective functionalization strategy using cheap and readily available glyoxylic acid as the C1 source and potassium persulfate as the oxidant. By simply switching the reaction solvent and temperature, they achieved hydroxymethylation (DMSO, 80 °C) (Figure 15), methylenation (DMSO, 130 °C, giving a dimeric coupled product) (Figure 16), and formylation (CH_3CN, 80 °C) of the 4H-pyrido[1,2-*a*]pyrimidin-4-one scaffold. Mechanistic studies indicate that persulfate thermal decomposition generates sulfate radical, which reacts with glyoxylic acid to form a hydroxymethyl radical; addition and hydrogen abstraction give the hydroxymethyl product. At higher temperatures, Whereas in acetonitrile, a decarboxylative formylation pathway yields the aldehyde product (Scheme 15), the hydroxymethyl intermediate dehydrates to form a methylene radical, which couples with another substrate molecule to give the methylene-bridged product (Scheme 16). This strategy offers a green and tunable method for constructing diverse heterocyclic derivatives.

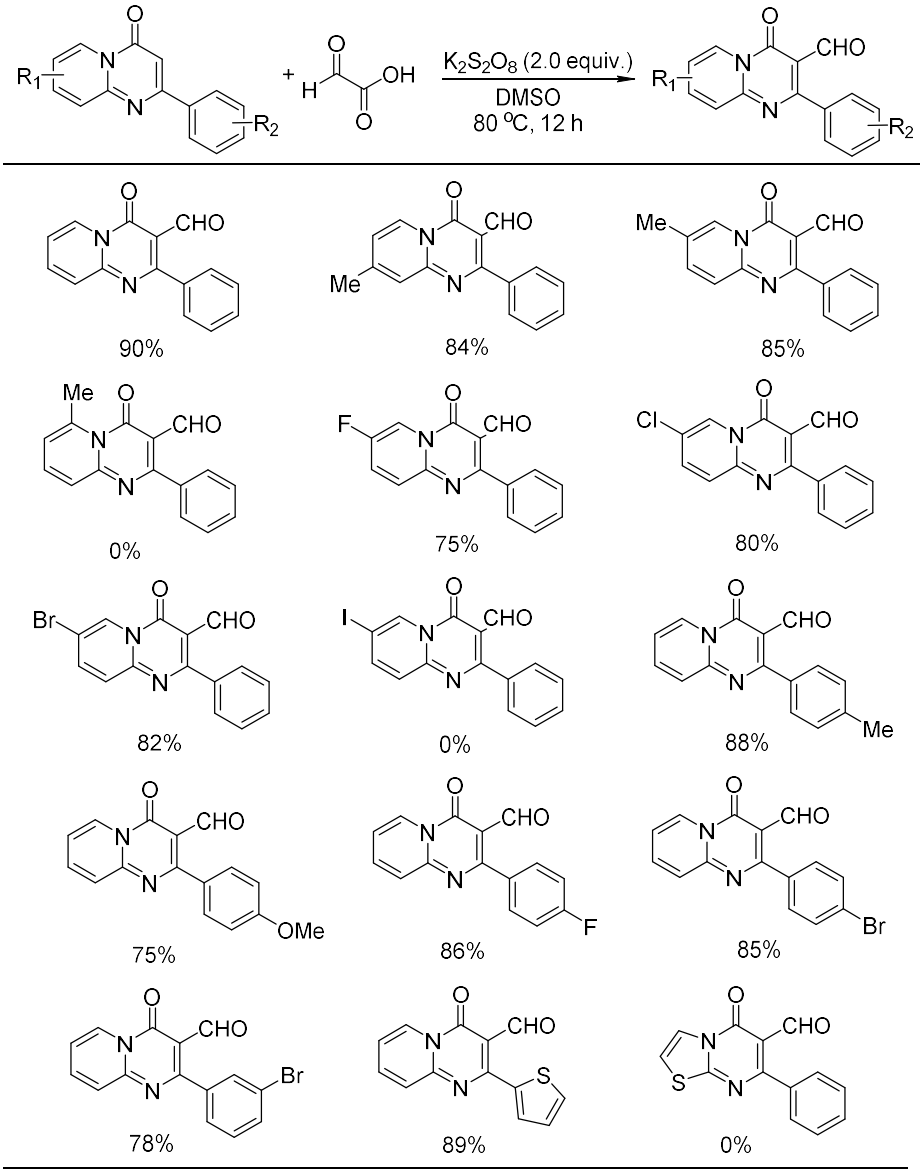
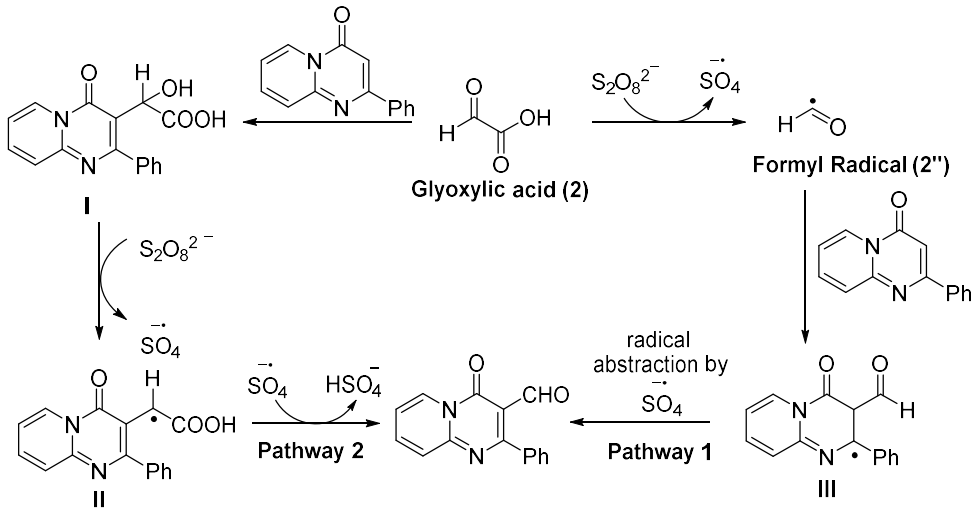


Figure 15. Glyoxylic acid as a hydroxymethyl source.



Scheme 15. Plausible reaction mechanism (formylation pathway).

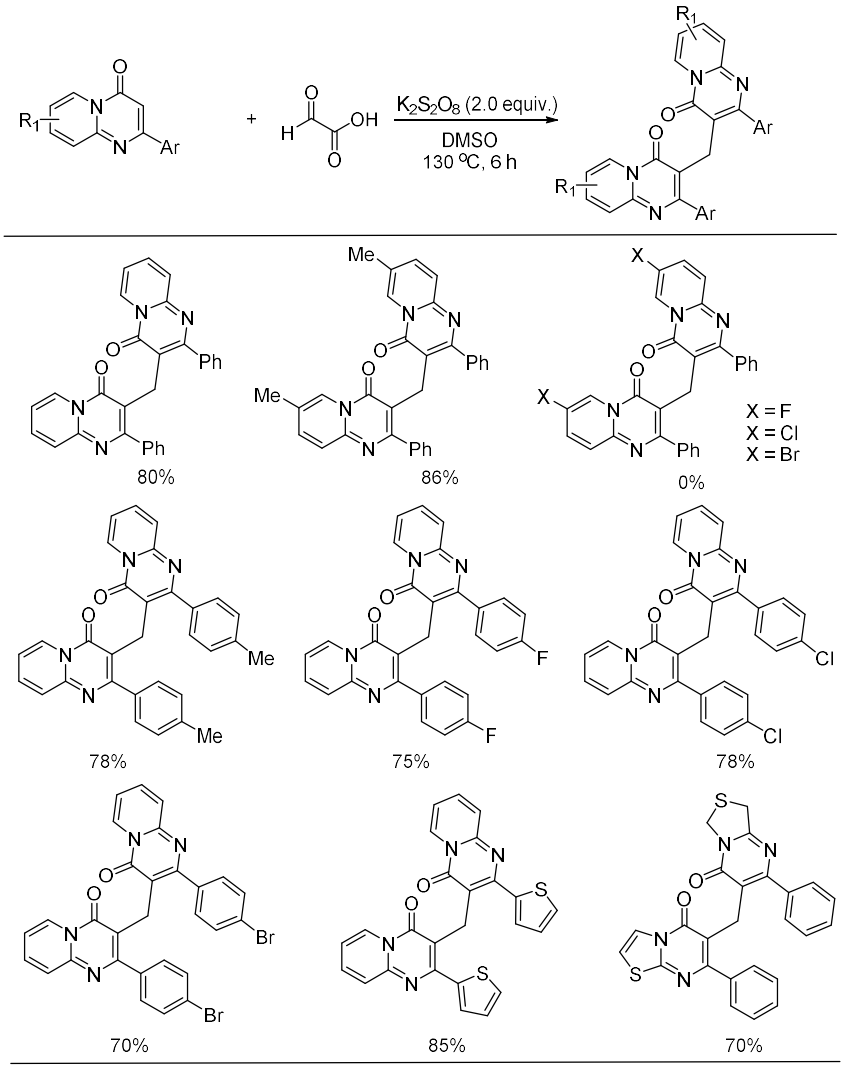
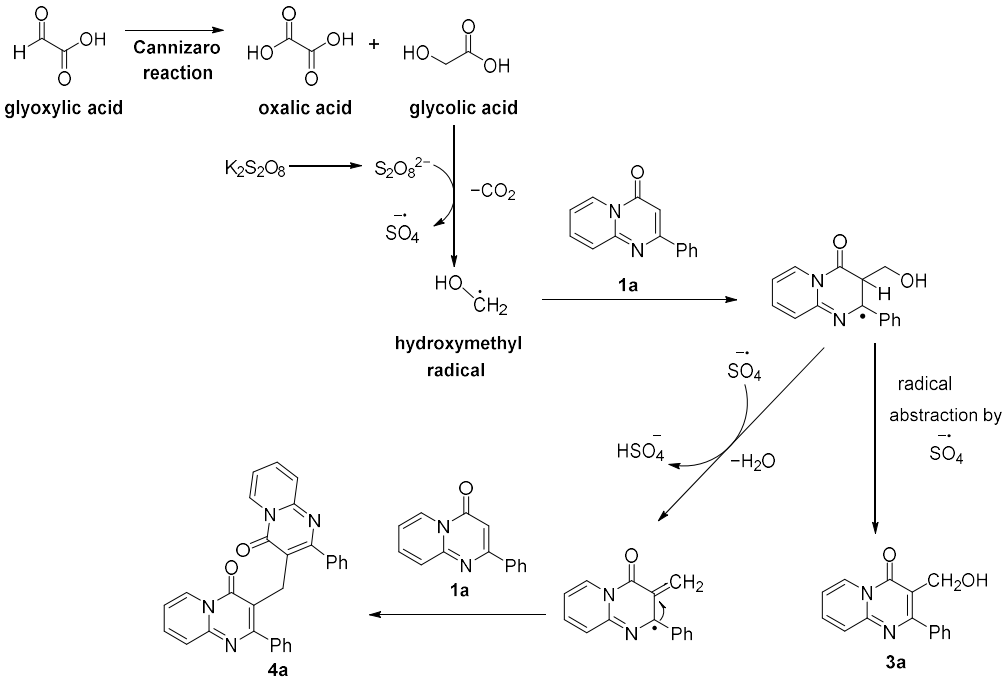


Figure 16. Glyoxylic acid as a methylene source.



Scheme 16. Plausible reaction mechanism (methylenation pathway).

2.2. Glyoxylic Acid as a Methylene Source

In 2008, Kita and co-workers reported a novel oxidative decarboxylation strategy [25]. Using 1,2-diamines and glyoxylic acid monohydrate as substrates, a variety of 2-H-imidazoline compounds were efficiently synthesized via condensation followed by N-bromosuccinimide (NBS)-mediated oxidative decarboxylation (Figure 17). This work achieved the first preparation of 2-H-imidazolines from glyoxylic acid and 1,2-diamines through oxidative decarboxylation, featuring mild reaction conditions (room-temperature operation), simple manipulation, nearly neutral reagents, and good functional-group tolerance. The key innovation lies in employing glyoxylic acid monohydrate as the coupling partner. The carboxyl group within the molecule not only enhances the reactivity of the aldehyde moiety to facilitate aminal formation, but also assists bromide elimination during the oxidation step, thus driving the oxidative decarboxylation of the 2-carboxyimidazolidine intermediate. This transformation tolerates various sensitive functional groups, including ester and nitrile groups, and enables efficient conversion of *N*-alkyl-, *N*-benzyl-, bulky alkyl-, and even quaternary-carbon-substituted 1,2-diamines. Mechanistic studies indicate that 1,2-diamine first condenses with glyoxylic acid to afford 2-carboxyimidazolidine intermediate i. Subsequent bromination at the nitrogen atom furnishes intermediate ii, which rapidly undergoes a concerted decarboxylation-debromination process to deliver the desired 2-H-imidazoline product (Scheme 17).

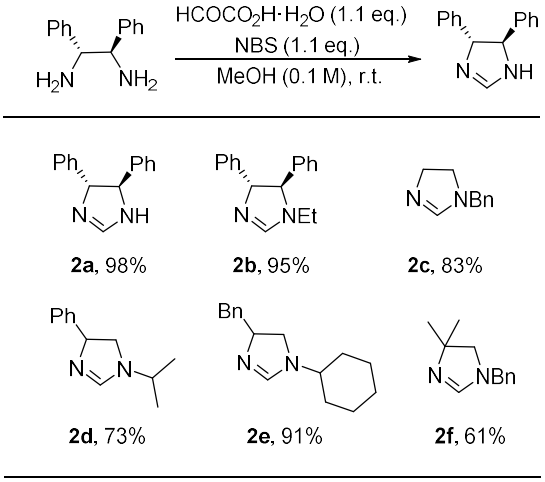
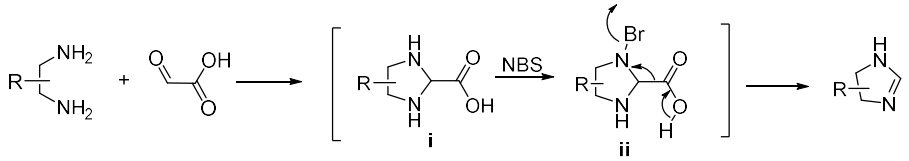


Figure 17. Synthesis of 2-H-imidazoline derivatives.



Scheme 17. Plausible reaction mechanism.

In 2019, Yan and co-workers developed a novel copper-catalyzed synthetic strategy [26]. Using substrates containing dual nitrogen nucleophilic sites and glyoxylic acid as starting materials, a variety of nitrogen-containing heterocyclic compounds, including 1,3,5-triazines, quinazolinones, and quinazolines, were efficiently constructed via oxidative decarboxylative amination (Figure 18). This work firstly realized the copper-catalyzed oxidative decarboxylative amination between glyoxylic acid and dinucleophilic nitrogen substrates, which possesses the advantages of mild reaction conditions, simple operation, high atom economy, and environmental friendliness. The core innovation of this strategy lies in the adoption of low-cost copper(II) triflate ($Cu(OTf)_2$) as the catalyst and di-tert-butyl peroxide (DTBP) as the oxidant. The synergistic effect of the tetramethylethylenediamine (TMEDA) ligand effectively promotes the oxidative

decarboxylation of glyoxylic acid. During the reaction, the aldehyde carbon of glyoxylic acid is incorporated into the heterocyclic skeleton, while the carboxyl carbon is eliminated in the form of carbon dioxide. This synthetic protocol exhibits excellent functional group tolerance toward halogens, trifluoromethyl, methoxy, and methyl groups. Moreover, it can be scaled up to a 10 mmol gram-scale synthesis with an 80% yield, demonstrating promising practical application potential. Mechanistic studies reveal that the reaction proceeds predominantly via Path A. The substrate first condenses with glyoxylic acid to afford intermediate A, which undergoes ligand-exchange with $Cu(OTf)_2$ to form Cu(II) complex B. Complex B releases CO_2 to generate Cu(II) complex C. Upon oxidation and elimination of one molecule of water, complex C is converted into Cu(III) complex D. Finally, reductive elimination of D delivers the heterocyclic product and regenerates the copper catalyst. In addition, control experiments confirm that *in-situ*-generated formaldehyde can act as a minor intermediate and participate in the reaction through a sequential condensation-oxidation process (Path B) (Scheme 18).

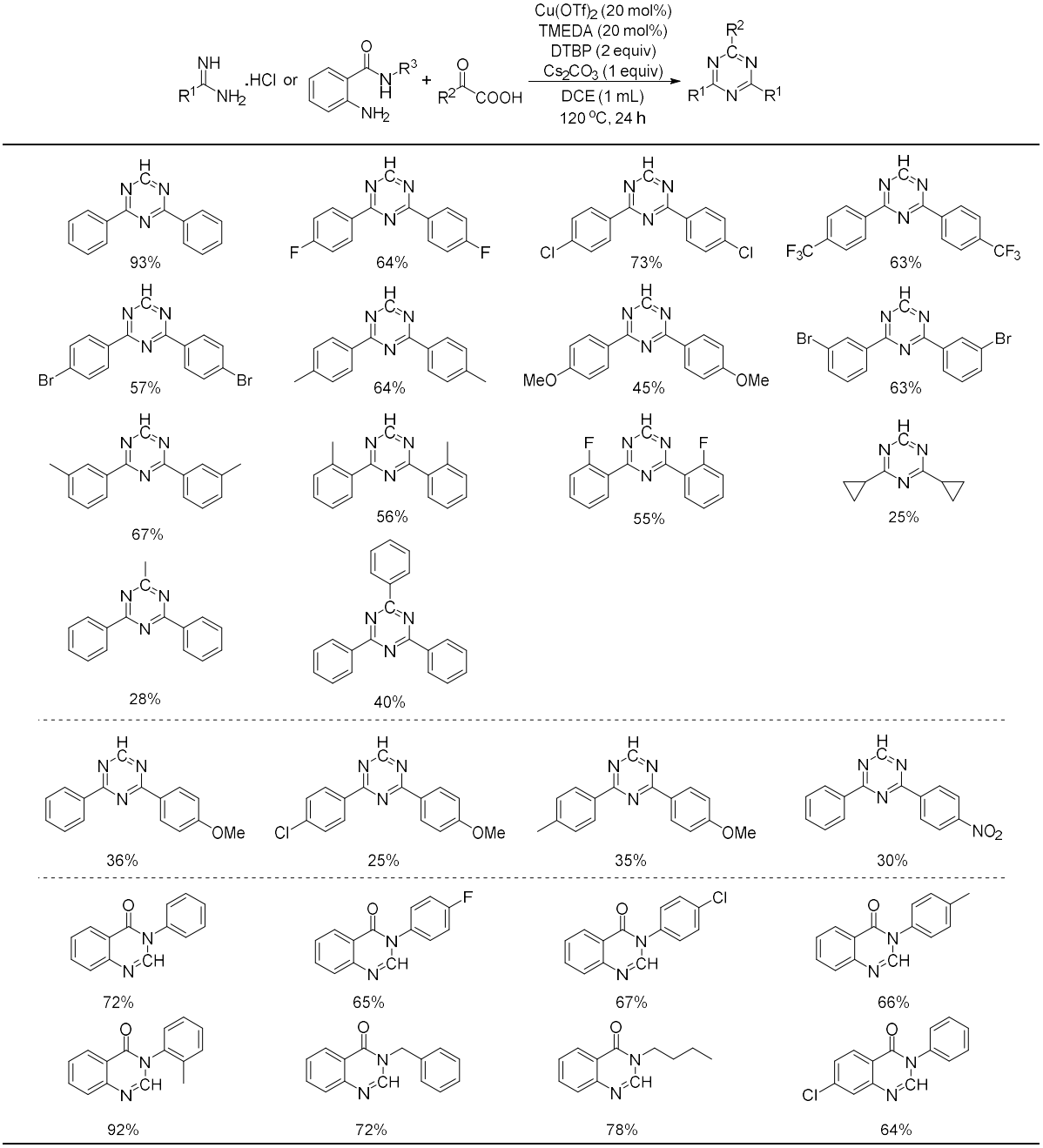
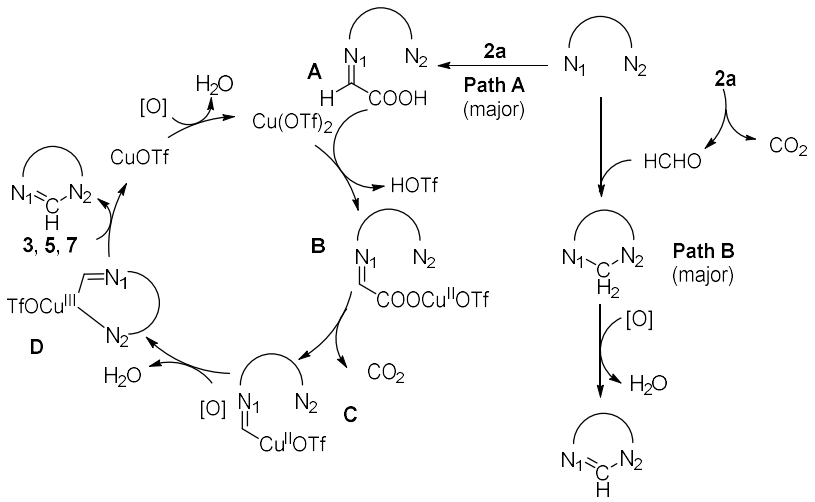


Figure 18. Copper-catalyzed oxidative decarboxylative amination of glyoxylic acid with dinucleophilic amines.



Scheme 18. Plausible reaction mechanism.

In 2021, Feng's group [27] reported a carboxyl-assisted metal-free decarboxylative coupling method using glyoxylic acid monohydrate, secondary amines, and alkynes to synthesize a series of propargylamine derivatives in moderate to good yields (up to 93%) (Figure 19). The innovation lies in using the carboxyl group of glyoxylic acid to activate the sp carbon of the alkyne *in situ*, promoting Michael addition with the iminium ion generated *in situ*, followed by decarboxylation to give the target product, thus avoiding the need for transition metal catalysts (e.g., Cu, Au) in traditional A^3-coupling. The method uses cheap and readily available glyoxylic acid instead of expensive propiolic acid, and the substrate scope includes various *N*-alkylbenzylamines, aliphatic secondary amines, and aryl/alkyl alkynes. Mechanistically, glyoxylic acid condenses with the amine to form an iminium salt intermediate, whose carboxyl group assists the deprotonation or activation of the alkyne via hydrogen bonding or electronic effects, allowing nucleophilic addition to proceed smoothly, giving an unstable intermediate that undergoes metal-free decarboxylation, releasing CO_2 to give the propargylamine (Scheme 19). This strategy provides a green and simple route to the biologically important propargylamine scaffold.

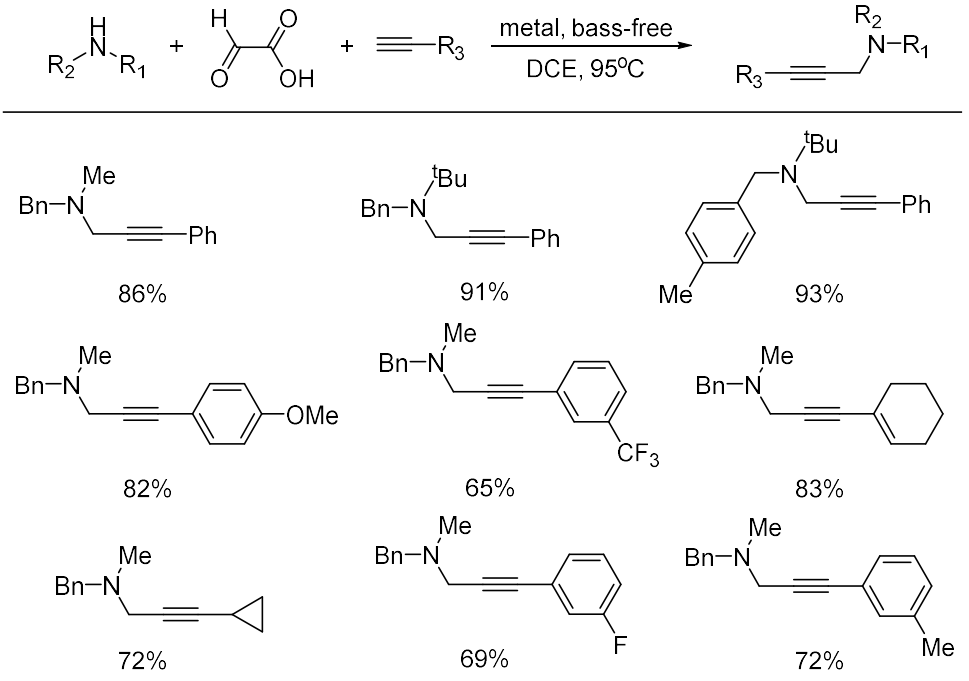
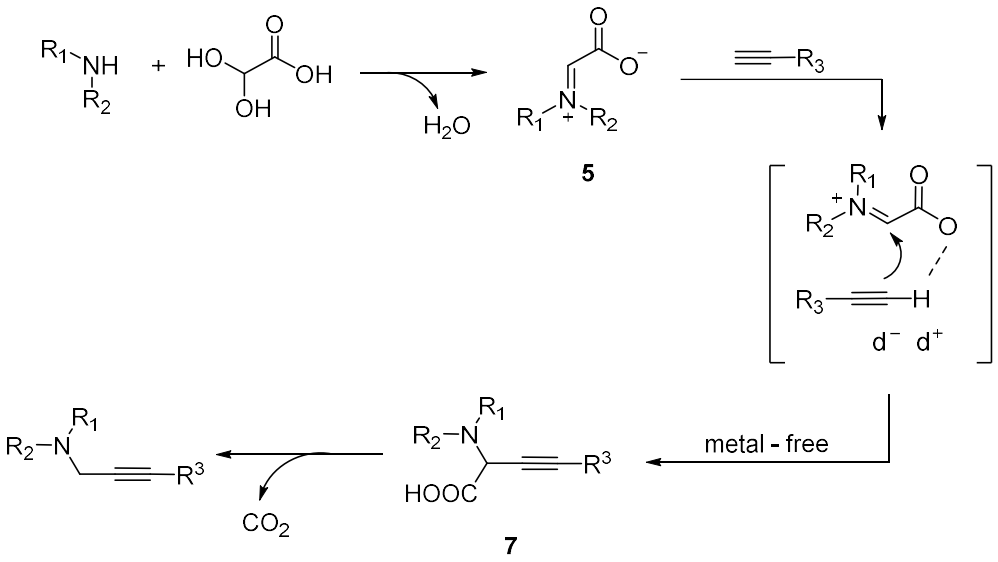


Figure 19. Three-component reaction of glyoxylic acid, secondary amines, and alkynes.



Scheme 19. Plausible reaction mechanism.

In the same year, Lim et al. [28] developed a metal-free double decarboxylative three-component reaction using arylalkynoic acids, glyoxylic acid, and amines at 80 °C to efficiently synthesize propargylamines (Figure 20). In a toluene/DCE mixed solvent, the reaction worked well with various cyclic and acyclic secondary amines (e.g., morpholine, pyrrolidine, diethylamine, *etc.*) and arylalkynoic acids bearing different substituents, giving good yields (up to 95%). Mechanistically, the authors proposed that glyoxylic acid condenses with the amine to form an iminium ion intermediate, while the arylalkynoic acid, assisted by its carboxyl group, promotes decarboxylation to form an alkynyl nucleophile; subsequent nucleophilic addition and a second decarboxylation release CO_2 to give the target product (Scheme 20). Control experiments showed that the carboxyl groups of both the arylalkynoic acid and glyoxylic acid are crucial for reaction efficiency—both are indispensable. This method provides a green route to propargylamines without metal residues.

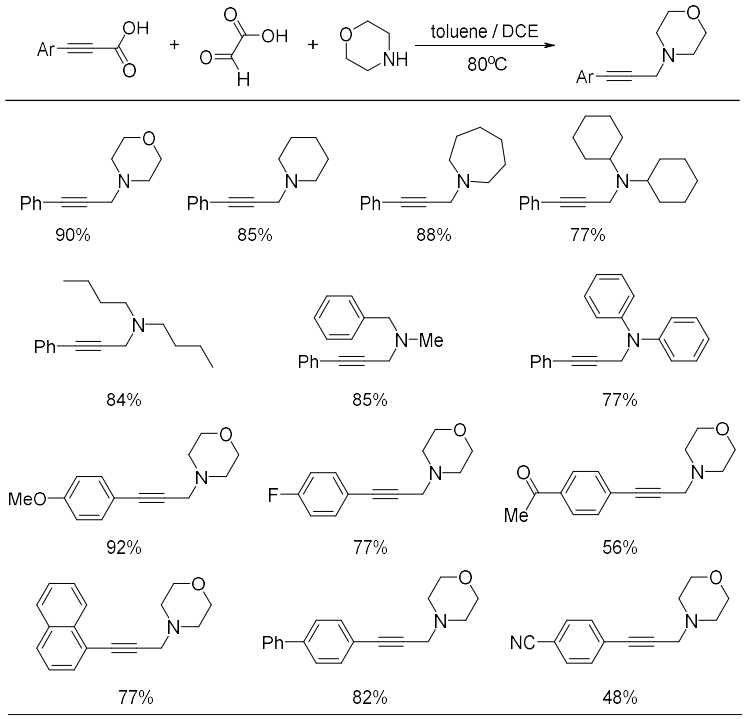
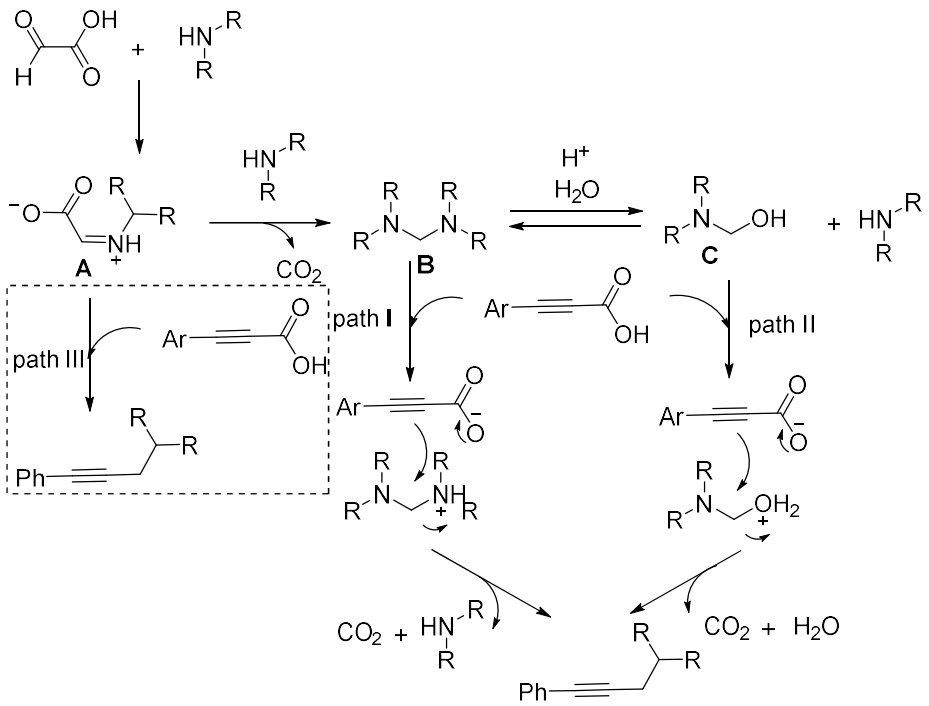


Figure 20. Three-component reaction of glyoxylic acid, arylalkynoic acids, and amines.



Scheme 20. Plausible reaction mechanism.

In 2021, Luo's group [29] reported a copper-mediated [5+1] oxidative cyclization strategy using 2-vinylanilines and glyoxylic acid to efficiently synthesize 4-arylquinoline derivatives in good to excellent yields (Figure 21). This method avoids the dependence on specific ketone substrates in traditional Friedländer-type approaches; the substrate scope is broad, with the aniline ring tolerating electron-donating (tert-butyl, methoxy) and electron-withdrawing (F, Cl, Br, CF_3) substituents, and the alkene part accommodating aryl or methyl groups, providing a new route to diverse 4-arylquinolines. Mechanistically, glyoxylic acid and 2-vinylaniline undergo nucleophilic addition under Lewis acid $Cu(OAc)_2$ catalysis, dehydrating to form an imine intermediate; then a 6π electrocyclization gives a dihydroquinoline; finally, copper-mediated aerobic oxidative aromatization, accompanied by decarboxylation (release of CO_2) yields the target 4-arylquinoline (Scheme 21). This strategy offers a simple and efficient route to the biologically important quinoline scaffold.

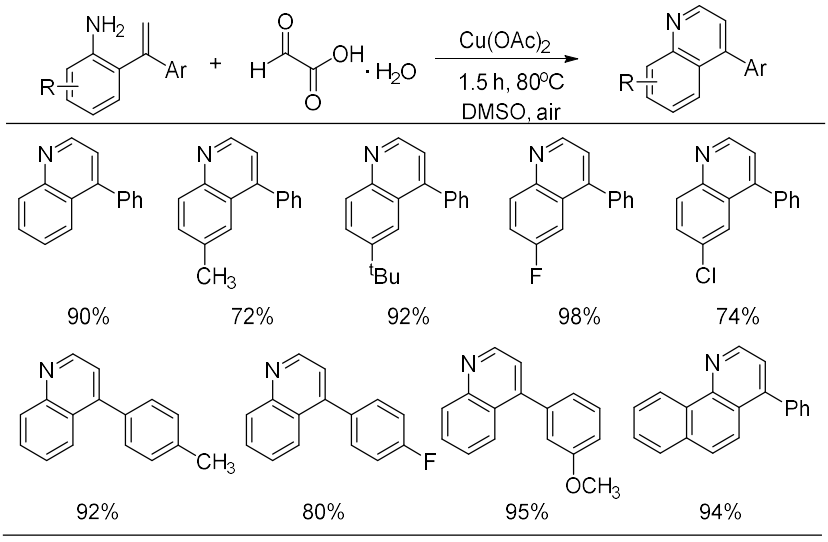
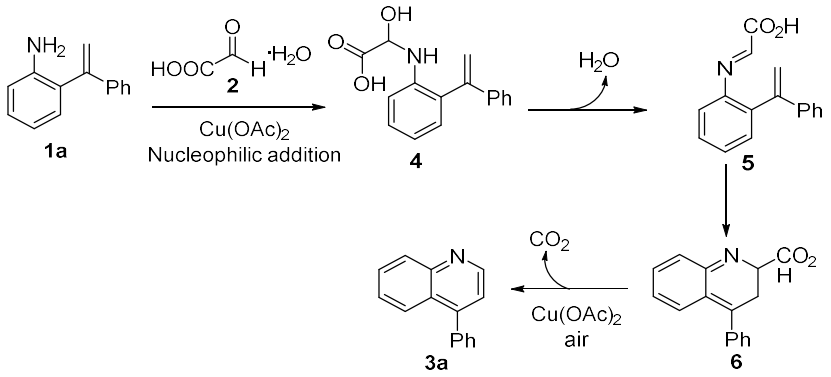


Figure 21. Copper-mediated [5+1] annulation of 2-vinylanilines and glyoxylic acid.



Scheme 21. Plausible reaction mechanism.

In 2022, Tang's group [30] reported a transition metal-free three-component reaction using imidazo[1,2-*a*]pyridine, glyoxylic acid, and sodium sulfinates in aqueous medium to achieve direct C3-sulfonylmethylation of imidazo[1,2-*a*]pyridines (Figure 22). The substrates include various substituted arylsulfinates (with electron-donating, electron-withdrawing, halogen, alkyl groups) and variously substituted imidazopyridines (with aryl, alkyl, heterocyclic, and various substituents on the pyridine ring), and the products can be further converted to 3-alkenylimidazopyridines. Mechanistically, control experiments indicate that glyoxylic acid and imidazopyridine first undergo nucleophilic addition to form an α-hydroxy acid intermediate; after protonation, this intermediate undergoes nucleophilic substitution with the sodium sulfinate to generate a sulfonyl-substituted intermediate; finally, decarboxylation releases CO_2 to give the target product (Scheme 22). This strategy provides a green and efficient route to sulfonylmethylated *N*-heterocycles with potential biological activity.

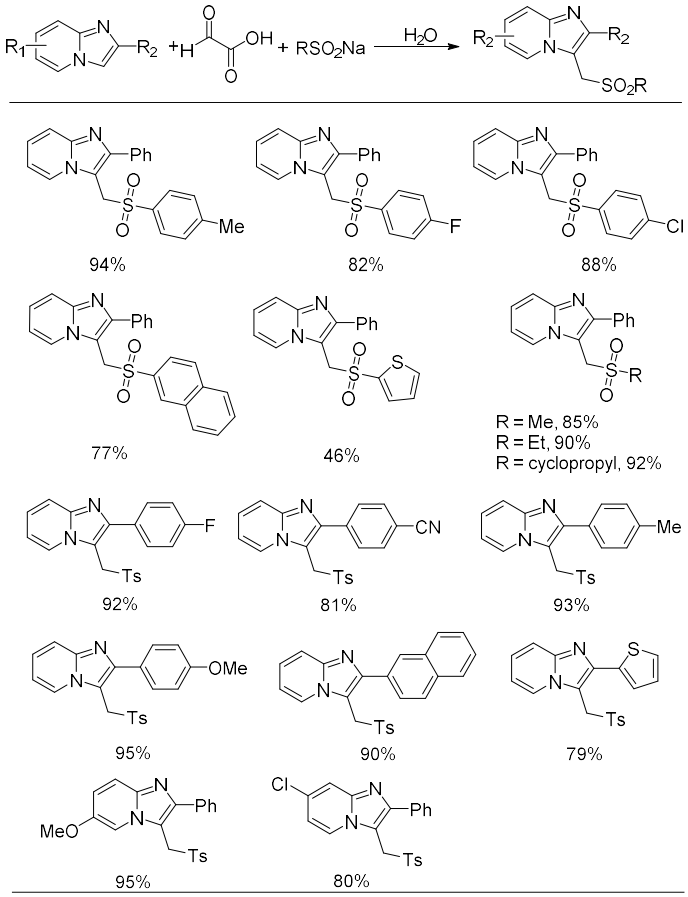
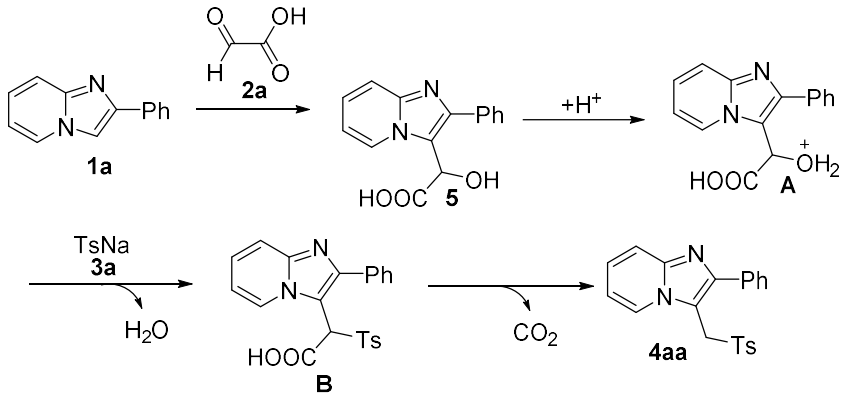


Figure 22. C3-sulfonylmethylation of imidazo[1,2-*a*]pyridines with glyoxylic acid and sodium sulfinates.



Scheme 22. Plausible reaction mechanism.

In 2022, Tang's group [31] developed a new C(sp^2)–H sulfonylmethylation method using glyoxylic acid as the C1 source and sodium sulfinates as the sulfonyl source, achieving highly regioselective C4-sulfonylmethylation of pyrazol-5-amines in aqueous medium, in good to excellent yields (Figure 23). The substrate scope is broad, covering various substituted pyrazol-5-amines, enamines, indoles, and antipyrine, and can be extended to enamine substrates by adding $Sc(OTf)_3$ catalyst and acetonitrile; some products exhibited antiproliferative activity against HeLa, HepG2, and other cancer cell lines. Mechanistically, pyrazol-5-amine first condenses with glyoxylic acid to form an α-hydroxy acid intermediate; after protonation, elimination of an amine gives an imine intermediate, which undergoes nucleophilic addition with sodium sulfinate, followed by decarboxylation, releasing CO_2 to give the target product (Scheme 23). This strategy provides a green and simple route to sulfonylmethylated heterocycles with potential pharmaceutical activity.

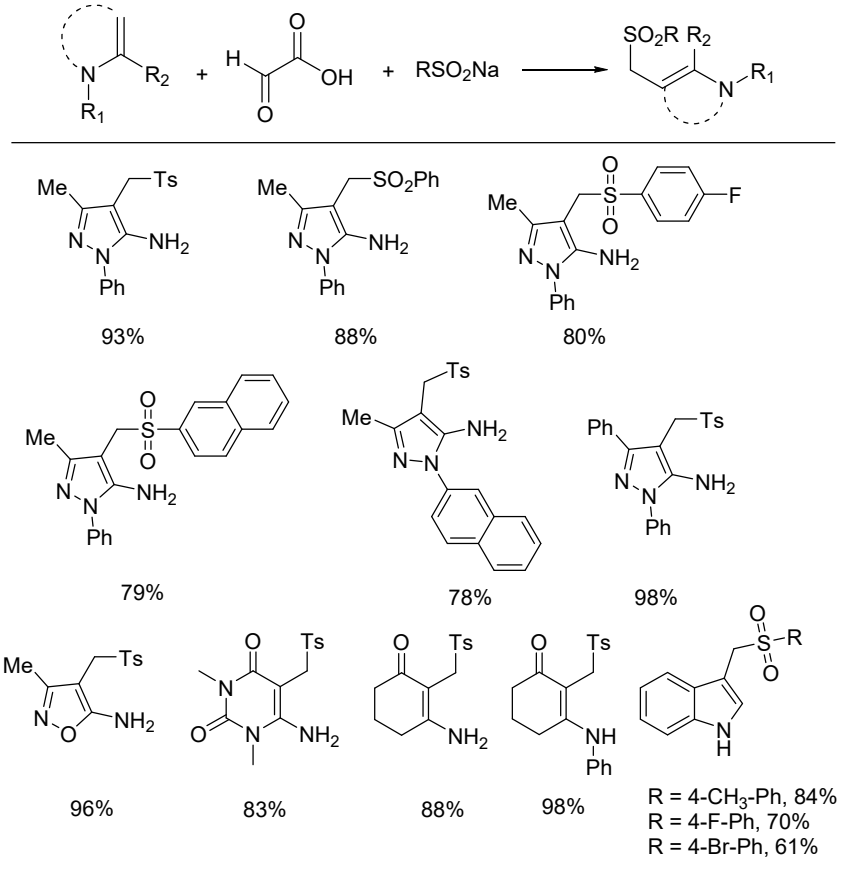
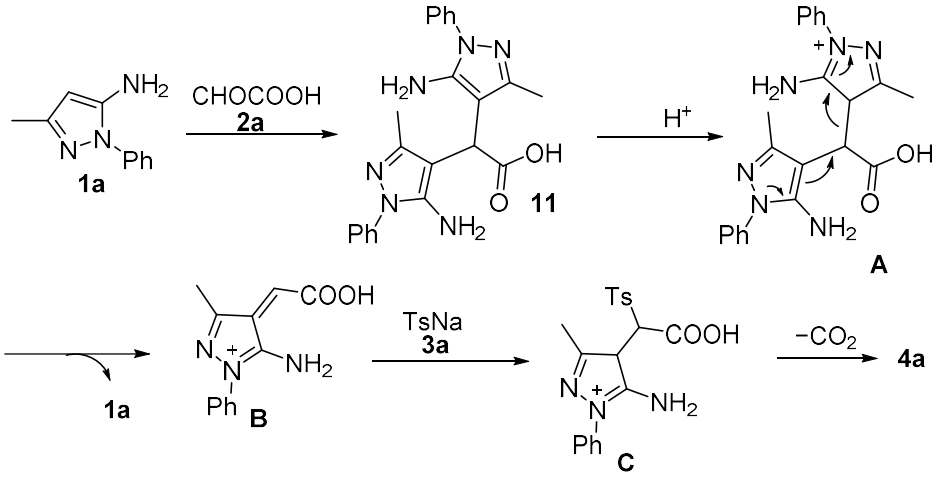


Figure 23. C4-sulfonylmethylation of pyrazol-5-amines with glyoxylic acid and sodium sulfinates.



Scheme 23. Plausible reaction mechanism.

In 2025, Wu's group [32] developed a base-catalyzed ($NaHCO_3$) aqueous methylenation method using glyoxylic acid as the methylene source to achieve methylenation of imidazo[1,2-*a*]pyridines, constructing a series of bis(imidazo[1,2-*a*]pyridin-3-yl)methane derivatives (Figure 24). The system has a broad substrate scope, tolerating both electron-donating and electron-withdrawing substituents, and was successfully extended to cross-coupling with various nucleophiles such as indole, pyrrole, antipyrine, amines, and benzimidazole, giving a variety of functionalized products. Some new compounds exhibited antiproliferative activity against three tumor cell lines. Mechanistically, control experiments showed that glyoxylic acid and imidazo[1,2-*a*]pyridine first undergo nucleophilic addition to form an α-hydroxy acid intermediate, which then decarboxylates and deprotonates under base catalysis to form a nucleophilic carbanion intermediate. This intermediate subsequently undergoes electrophilic substitution with another substrate molecule or direct protonation to give the methylene-bridged product or mono-substituted product, respectively (Scheme 24). This strategy provides a green and simple new route to methylene-bridged bis-heterocyclic scaffolds.

In 2026, Liu's group reported the first catalyst-free selective C3-aminomethylation of 7-aminopyrazolo[1,5-*a*]pyrimidine [33]. Using 7-aminopyrazolo[1,5-*a*]pyrimidine-type substrates and glyoxylic acid monohydrate, this strategy enables direct reaction under mild conditions to efficiently afford a series of C3-aminomethylated pyrazolo[1,5-*a*]pyrimidine derivatives (Figure 25). Conventional Mannich reactions suffer from the drawbacks of using carcinogenic formaldehyde as the methylene source and relying on anhydrous reagents. To address these issues, this work employs industrially accessible and operationally safe glyoxylic acid monohydrate instead of formaldehyde, which not only circumvents the stringent requirement for anhydrous conditions but also greatly improves the safety and operability of the reaction. The key innovation is that no external catalyst is required; the aminomethylation process can be driven merely by the direct interaction between the substrate and glyoxylic acid. Featuring mild conditions and simple operation, the reaction is amenable to gram-scale preparation. Furthermore, the resulting aminomethylated products can undergo diverse downstream functional transformations such as chlorination and C-N cross-coupling, showing excellent synthetic application potential. Mechanistic studies demonstrate that radical reaction pathways can be ruled out on the basis of radical-trapping, stepwise-addition control experiments, and high-resolution mass spectrometry (HRMS) detection of intermediates. The transformation proceeds via two parallel stepwise ionic pathways, which converge to a common carboxyl-substituted intermediate. Final decarboxylation of this intermediate delivers the desired aminomethylated product (Scheme 25). This study provides a mild, green, and efficient synthetic strategy for the construction of C3-aminomethyl pyrazolo[1,5-*a*]pyrimidine derivatives in medicinal chemistry.

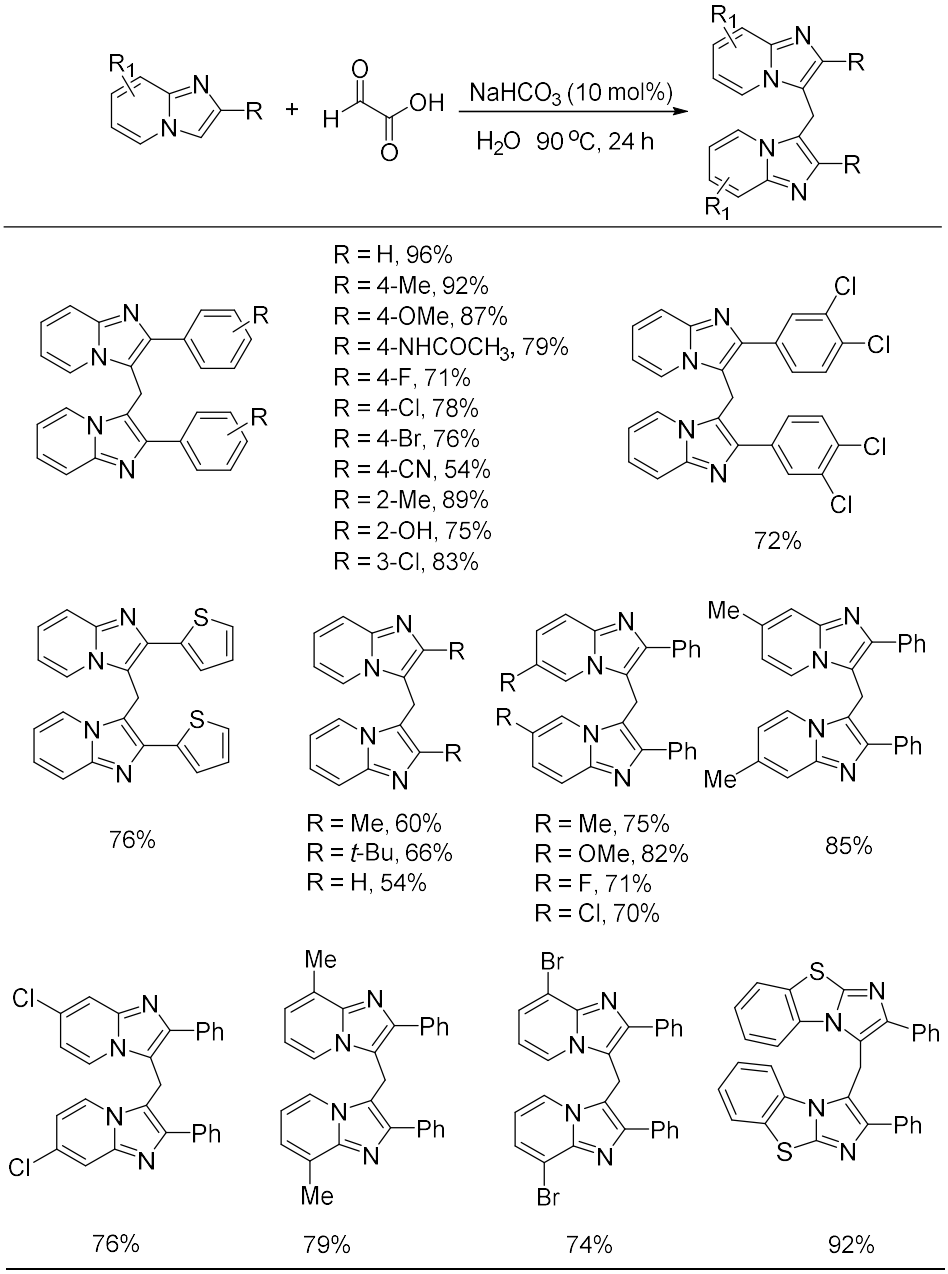
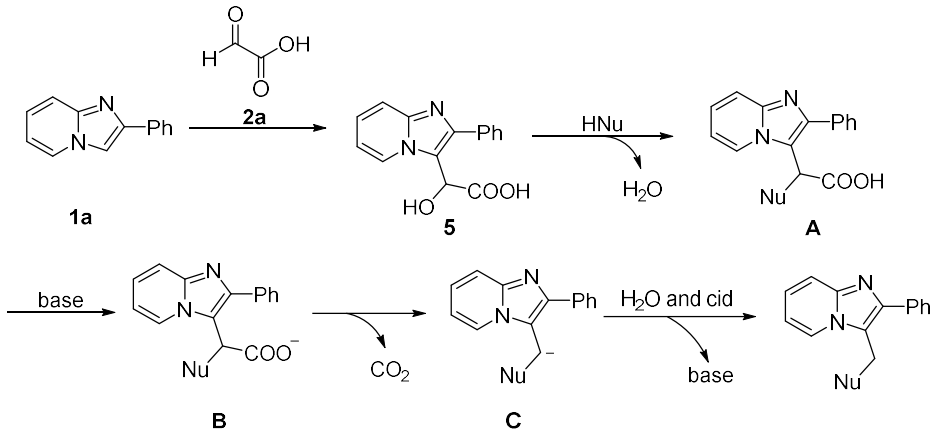


Figure 24. Methylenation of imidazo[1,2-*a*]pyridines.



Scheme 24. Plausible reaction mechanism.

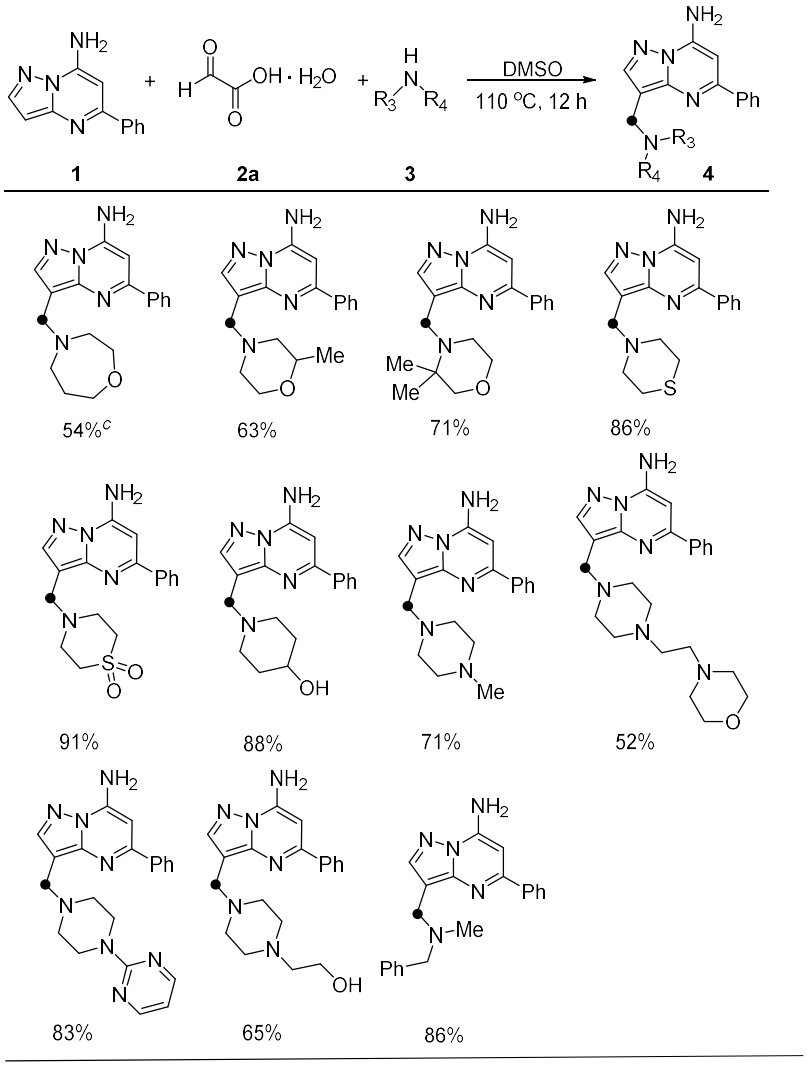
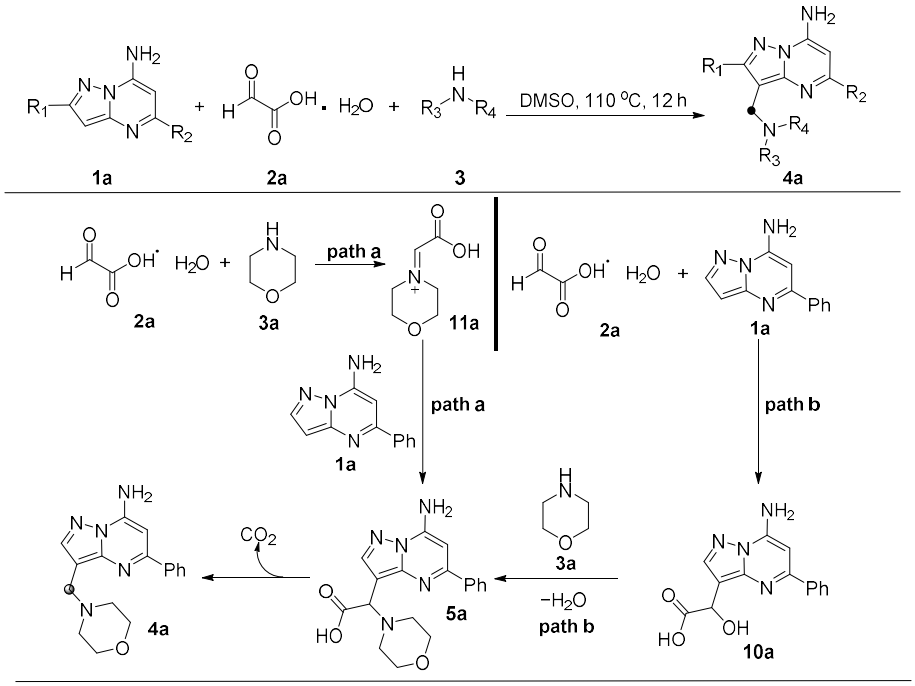


Figure 25. Synthesis of C3-aminomethylated pyrazolo [1,5-*a*] pyrimidines.



Scheme 25. Plausible reaction mechanism.

3. Glyoxylic Acid as a C2 Synthon

In 2016, Amarasekara and Ha [34] reported the acid-catalyzed condensation of levulinic acid with glyoxylic acid. Using concentrated sulfuric acid (20 mol%) as a catalyst under solvent-free conditions at 80 °C for 24 h, they obtained 1-methyl-2,8-dioxabicyclo[3.3.0]oct-4-ene-3,7-dione in 92% yield (Figure 26). The reaction mechanism involves an acid-catalyzed aldol condensation, two lactonizations, and a dehydration cascade (Scheme 26). Under 10% Pd/C catalysis, the unsaturated bislactone can be quantitatively reduced to the saturated bislactone under H_2 (1 atm), or ring-opened in methanol to give 3-acetyl-dimethyl glutarate. The saturated bislactone is an important monomer for polyester synthesis, but traditional routes give low yields; this method uses the biomass platform molecule levulinic acid and renewable glyoxylic acid as starting materials, providing a fully carbon-renewable, efficient, and green route to a polymer precursor. This work expands the application of biomass-derived small molecules in high-value chemicals and polymer monomers.

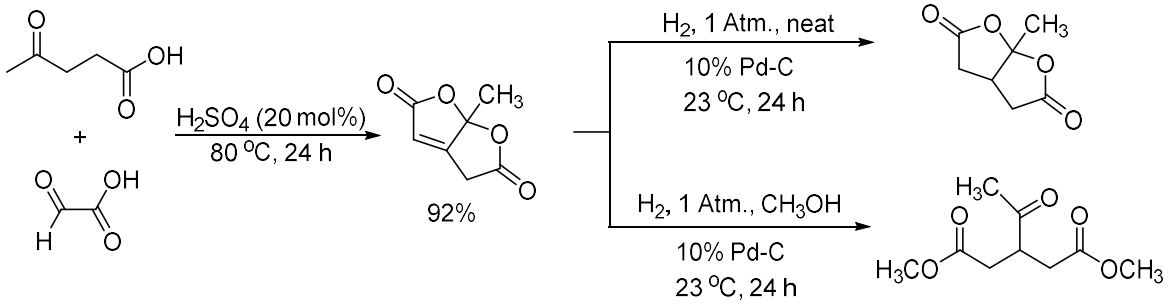
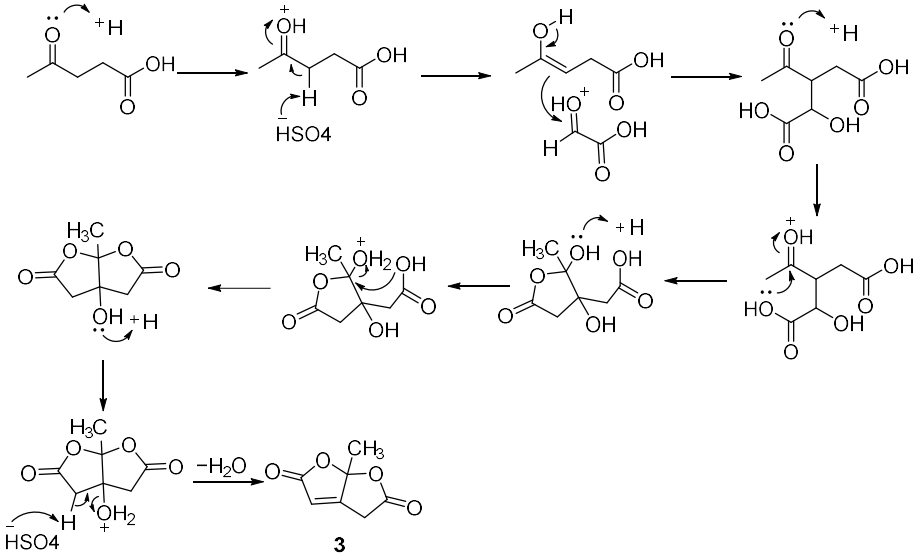


Figure 26. Condensation-cyclization of levulinic acid with glyoxylic acid.



Scheme 26. Plausible reaction mechanism.

In 2017, Zhang's group [35] reported an iridium photoredox-catalyzed decarboxylative Michael addition using glyoxylic acid acetals (e.g., diethoxyacetic acid) as formyl equivalents, reacting with various Michael acceptors under blue LED irradiation. The substrate scope includes α,β-unsaturated amides (secondary and tertiary), acrylates, diethyl maleate, benzylidene diethyl malonate, unsaturated ketones, aldehydes, and nitriles, all of which give the corresponding acetal products in good to excellent yields (Figure 27). Additionally, 2-vinylpyridine, 4-vinylpyridine, and α-arylstyrene can also be used as substrates. The method features mild conditions (room temperature, atmospheric pressure), simple operation, and avoids the need for high-pressure syngas and transition metal catalysts in traditional hydroformylation. The

resulting acetals serve as protected aldehyde forms and have significant synthetic value. Mechanistic studies indicate that the excited state iridium catalyst oxidizes the diethoxyacetate anion, triggering decarboxylation to generate a diethoxymethyl radical; this radical is trapped by the Michael acceptor, and the resulting radical then oxidizes the reduced iridium catalyst to complete the catalytic cycle (Scheme 27). This work extends the application of photoredox catalysis in decarboxylative coupling and provides a new strategy for constructing functionalized acetals and aldehydes.

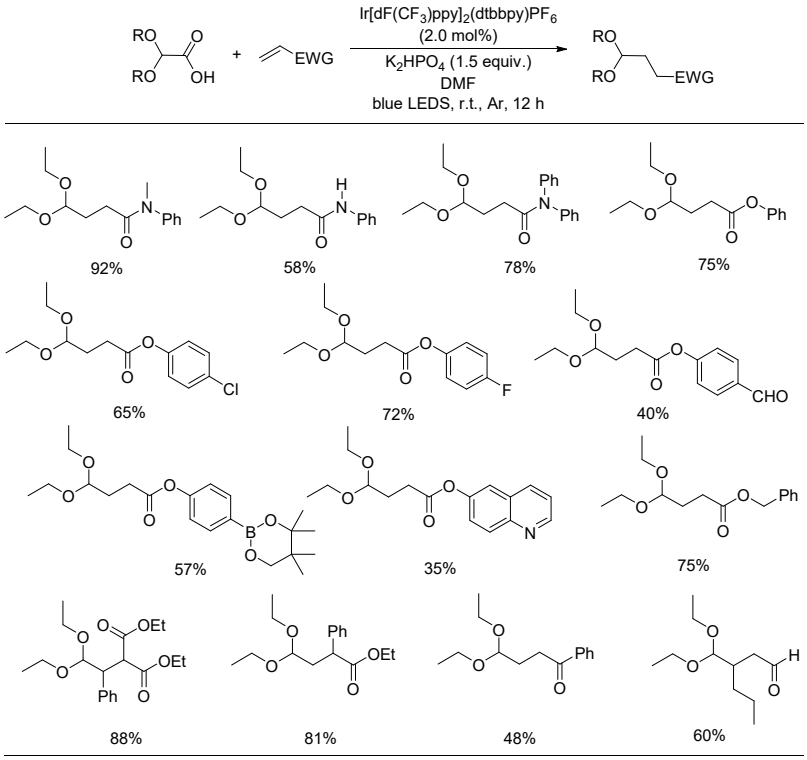
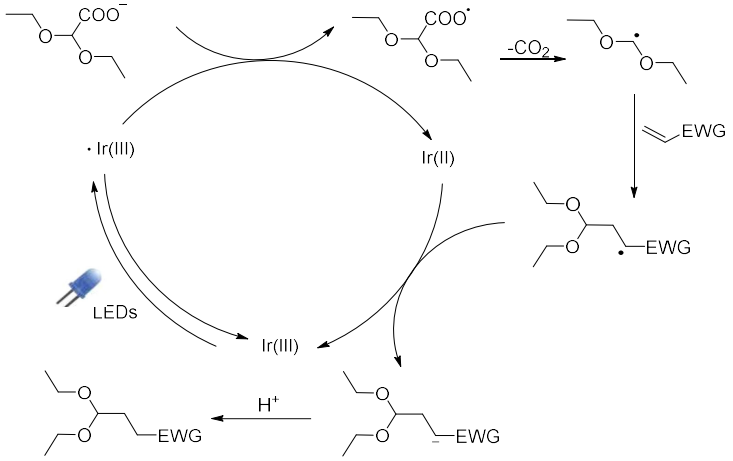


Figure 27. Iridium photoredox-catalyzed decarboxylative Michael addition of glyoxylic acid acetal.



Scheme 27. Plausible reaction mechanism.

In 2021, Uguen et al. [36] developed a microwave-assisted aldol condensation of glyoxylic acid with methyl ketone derivatives to synthesize a series of E-4-oxo-2-butenoic acids (Figure 28). Two optimized conditions were established for aromatic and aliphatic methyl ketones: p-toluenesulfonic acid catalysis for aromatic substrates, and pyrrolidine/acetic acid catalysis for aliphatic substrates. The substrate scope is broad (covering electron-donating, electron-withdrawing, heterocyclic, and ketones with additional enolizable sites), yields are moderate to excellent, reaction times are short, and gram-scale synthesis is

possible. All products were obtained as single E-isomers. Mechanistically, the authors calculated the HOMO energies of the enol and enamine and the LUMO energy of protonated glyoxylic acid. Aromatic ketones have higher enol HOMO energies and a smaller energy gap with the electrophile, so the acid-catalyzed pathway predominates; for aliphatic ketones, the enol HOMO is lower, but the pyrrolidine-derived enamine has a significantly raised HOMO, reducing the energy gap, so the base/amine-catalyzed pathway is more effective (Scheme 28). This work provides a green, general, and scalable route to biologically active 4-oxo-2-butenoic acids.

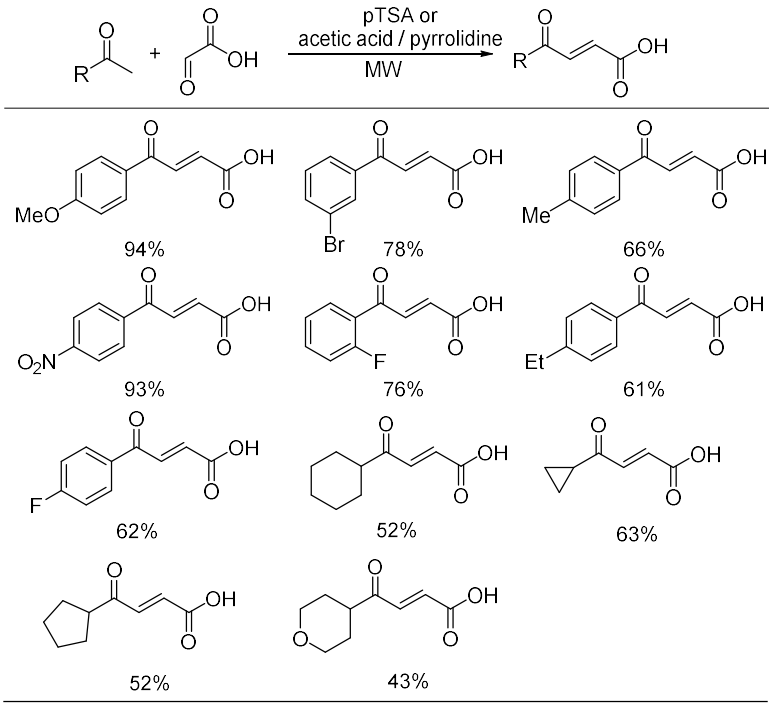
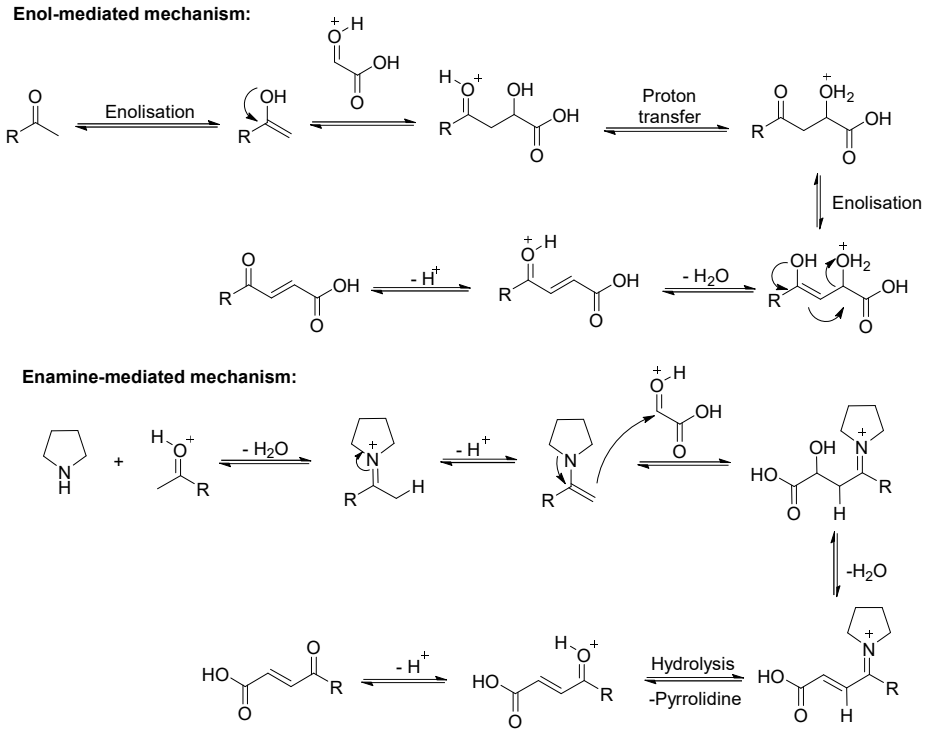


Figure 28. Microwave-assisted aldol condensation of methyl ketones with glyoxylic acid.



Scheme 28. Plausible reaction mechanism.

In 2022, Davioud-Charvet's group [37] reported a safe and economical second-generation route for multigram synthesis of 6-fluoromenadione and its 6-substituted derivatives (Figure 29). Starting from 4′-fluoropropiophenone, the key steps include aldol condensation with glyoxylic acid, catalytic hydrogenation, polyphosphoric acid (PPA)-mediated cyclization to construct 7-fluoro-3-methyltetralone, then bromination, lithium carbonate-promoted aromatization to give a naphthol intermediate, and finally oxidation with (diacetoxyiodo)benzene (PIDA) to give the target product. The route requires only a final purification step, overall yield 50%, and was successfully extended to methoxy, methyl, trifluoromethyl, chloro, bromo, and other substituted derivatives. Mechanistically, the aldol condensation under acidic conditions gives an α,β-unsaturated carboxylic acid (E/Z mixture); hydrogenation reduces the double bond; PPA cyclization proceeds via formation of a carboxylic-phosphoric mixed anhydride, followed by intramolecular Friedel–Crafts acylation; bromination and elimination (dehydrobromination with Li_2CO_3) achieve aromatization; PIDA oxidizes the naphthol to 1,4-naphthoquinone. This method avoids the dangerous lauroyl peroxide and low-yield radical cyclization steps of the first-generation route.

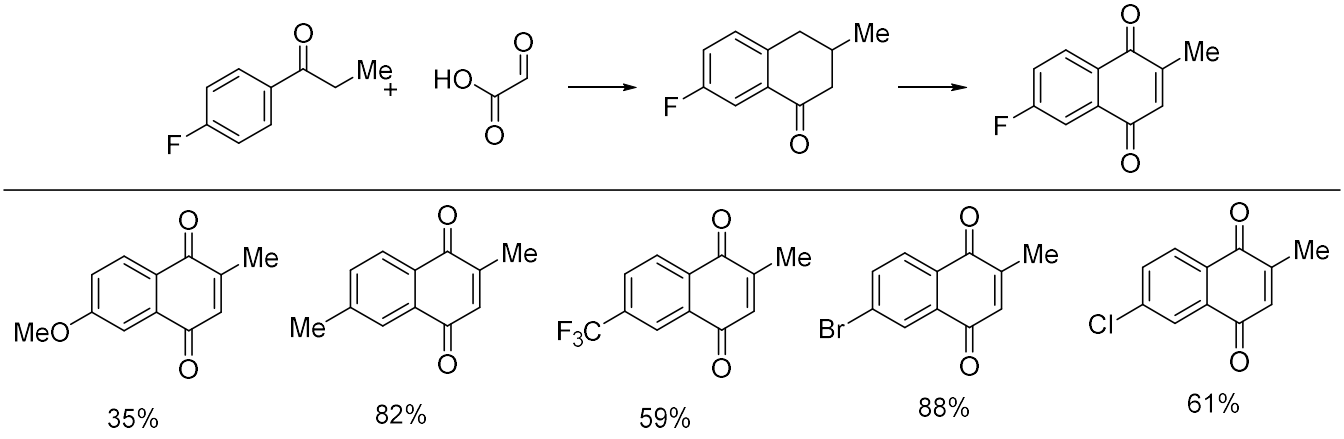


Figure 29. Condensation-cyclization of arylpropiophenones with glyoxylic acid.

In 2023, Jakob et al. [38] reported a palladium-catalyzed asymmetric three-component reaction using glyoxylic acid, sulfonamide, and arylboronic acid to efficiently synthesize α-arylglycine derivatives (Figure 30). Despite the presence of a fast racemic Petasis background reaction, the authors achieved enantioselective control through a carefully designed catalyst system: $Pd(TFA)_2$ with an S,S′-iPrBox chiral ligand, using nitromethane as the solvent and adding 5 equivalents of water as an additive, thereby obtaining moderate to good yields and excellent enantiomeric ratios. The method is applicable to various substituted arylboronic acids (e.g., *p*-tolyl, *p*-fluorophenyl, *p*-chlorophenyl), but electron-rich or sterically bulky boronic acids led to decreased enantioselectivity. The resulting Pbf-protected product can be used directly in peptide synthesis: coupling with L-valine methyl ester hydrochloride, followed by deprotection, gave a dipeptide without racemization. Mechanistic studies indicate two competing pathways: a catalyst-free Petasis pathway (via coordination of the boronic acid to the hydroxyl group of glyoxylic acid to form an ate complex, followed by intramolecular aryl transfer, giving racemic product) and a palladium-catalyzed pathway (transmetalation, enantioselective aryl transfer to the imine, product dissociation). Water plays a key role in the product dissociation step, while nitromethane stabilizes the cationic palladium species (Scheme 29). This strategy provides a green and practical asymmetric route to α-arylglycine-containing peptides and natural products.

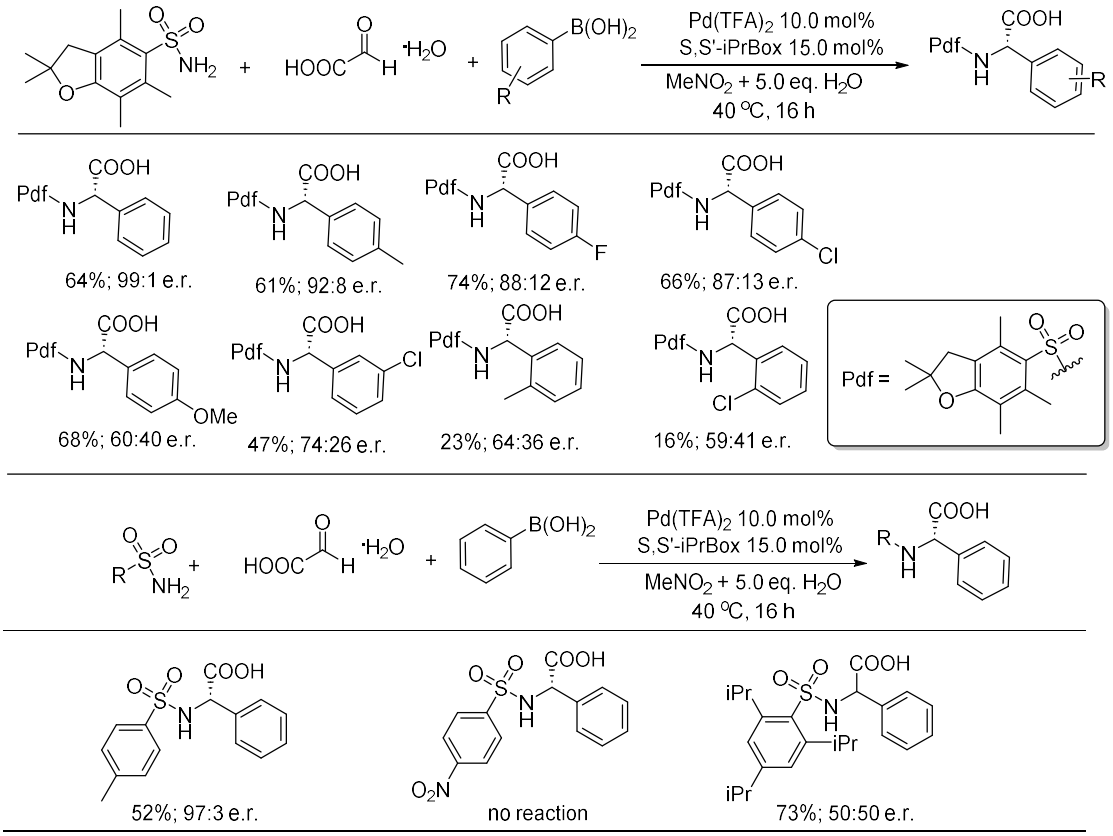
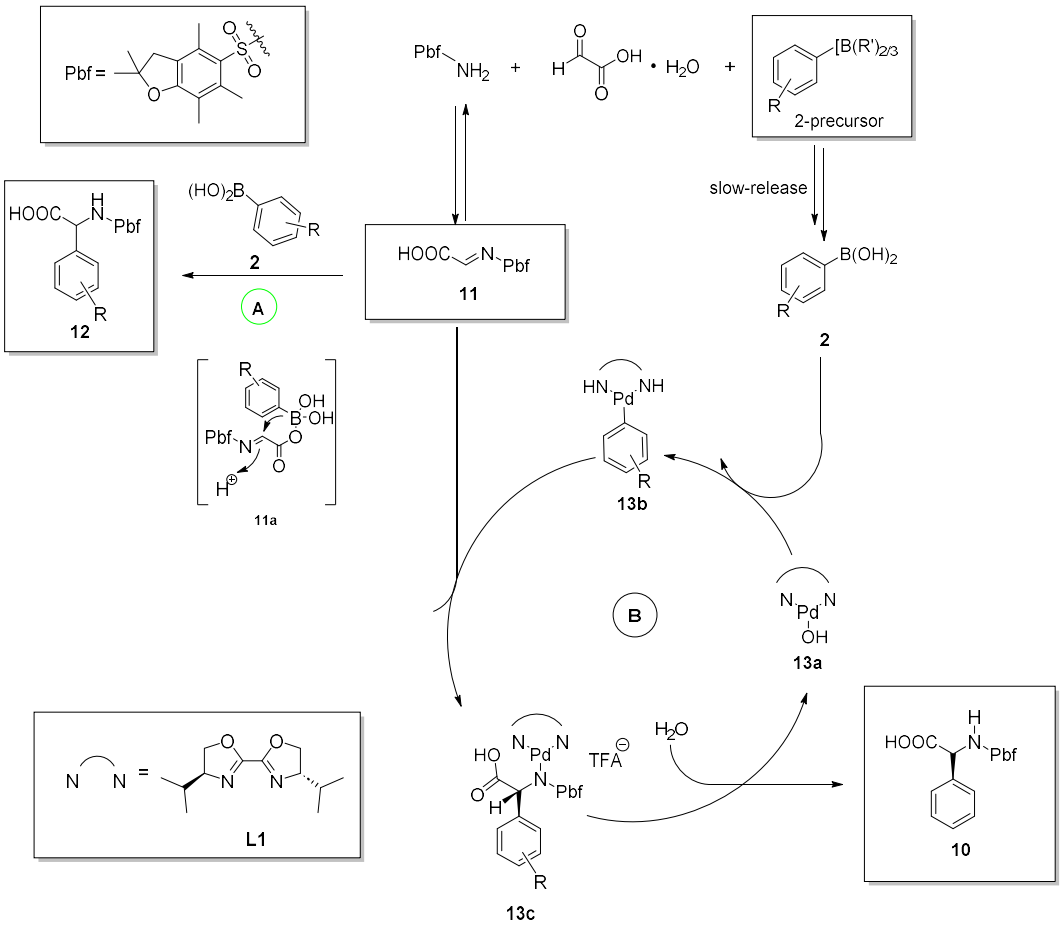


Figure 30. Construction of α-arylglycine scaffold from glyoxylic acid, sulfonamide, and arylboronic acid.



Scheme 29. Plausible reaction mechanism.

In 2025, Yue et al. [39] studied the application of glyoxylic acid in the Morita-Baylis-Hillman (MBH) reaction. By attaching glyoxylic acid, a polar C2 fragment, to alkyl acrylates in a single step, they synthesized a series of new amphiphilic compounds (surfactants) and systematically assessed their physicochemical properties and surface activity (Figure 31). Using 2 equivalents of DABCO, 2 equivalents of acrylate, 4 M concentration, at room temperature for 24 h, GAOn series products n = 6, 8, 10, 12, 14, 16, 18 were obtained, and hydrogenation gave the saturated products GAOnH. This work demonstrates the potential of glyoxylic acid as an electrophilic substrate in the MBH reaction for constructing novel amphiphilic molecules (Scheme 30).

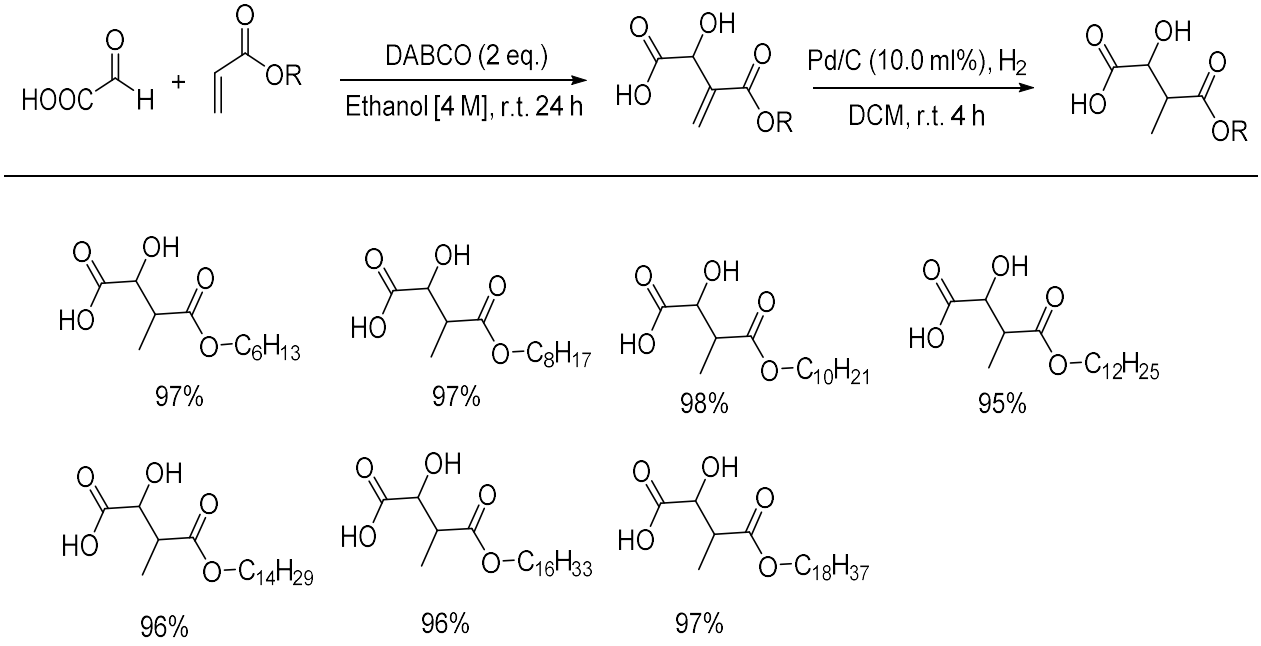
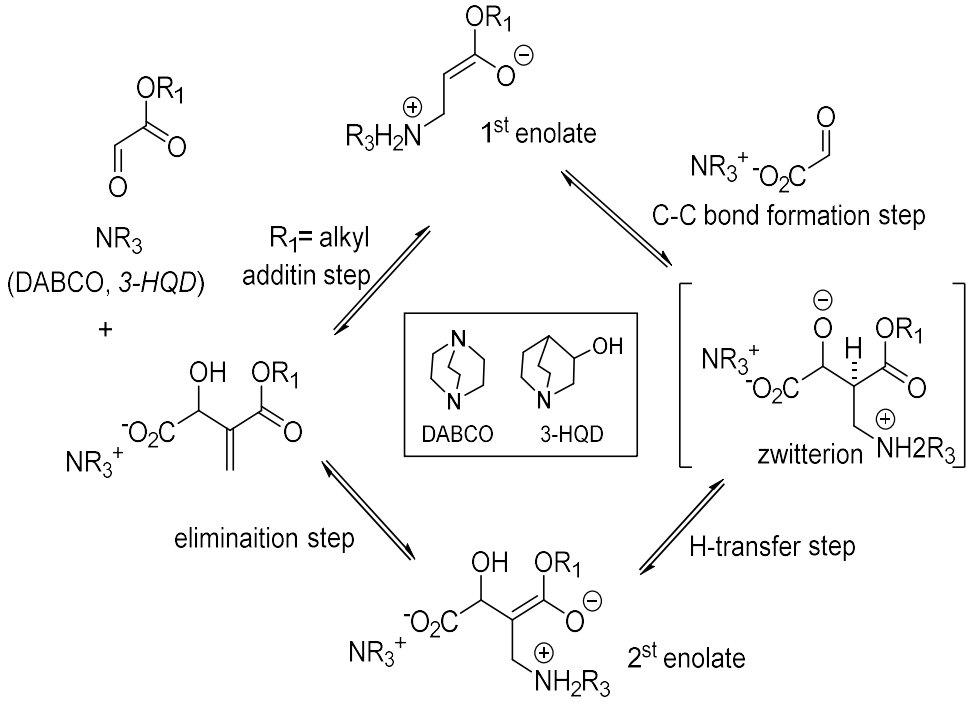


Figure 31. Synthesis of novel amphiphilic compounds using glyoxylic acid.



Scheme 30. Plausible reaction mechanism.

In 2025, Wang et al. [40] reported a hexafluoroisopropanol (HFIP)-promoted three-component cascade cyclization for the efficient construction of α-amino-γ-spirolactones (Figure 32). The method utilizes readily available amines, glyoxylic acid, and unactivated alkenes as starting materials, and proceeds under mild, metal-free, and additive-free conditions via a one-pot condensation/aza-Prins cyclization/lactonization sequence to afford complex spirocyclic frameworks. Regarding the reaction mechanism, HFIP acts as a strong hydrogen-bond donor to stabilize the iminium ion intermediate (Int-I), facilitating its aza-Prins-type addition with the alkene to generate a carbocation intermediate (Int-II), which is subsequently trapped by the pendant carboxylic acid to form the target spirolactone (Scheme 31). The method features broad substrate scope, high functional group tolerance, and excellent sustainability metrics, and has been successfully applied to the late-stage functionalization of drug molecules (Figure 33). Preliminary bioactivity assays show that certain spirolactone derivatives exhibit antiproliferative activity against PC-9 lung cancer cells comparable to that of 5-fluorouracil, along with improved metabolic stability over the parent drugs, highlighting their potential for drug discovery.

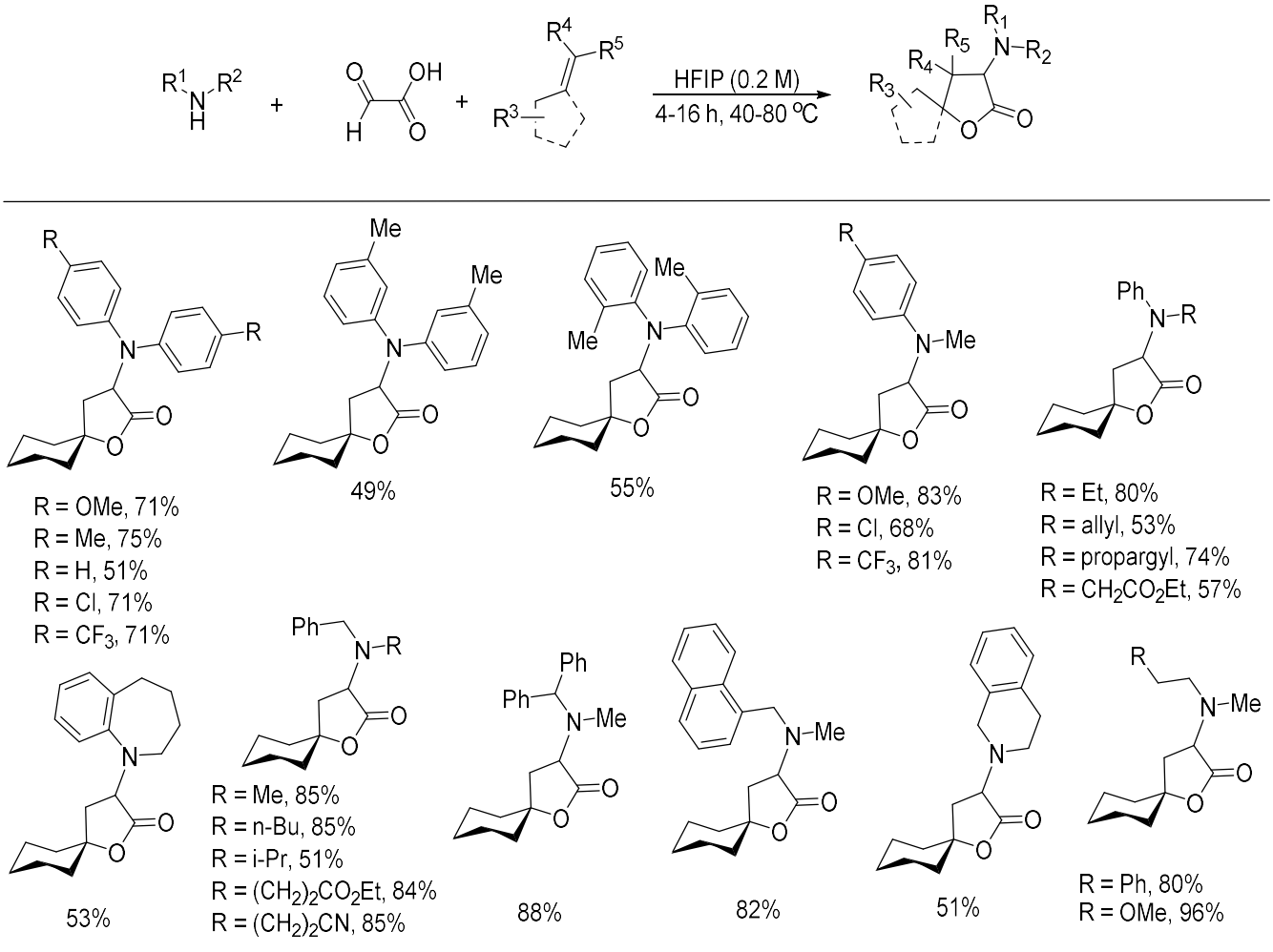


Figure 32. Reactivity of various secondary amines with glyoxylic acid and methylenecyclohexane.

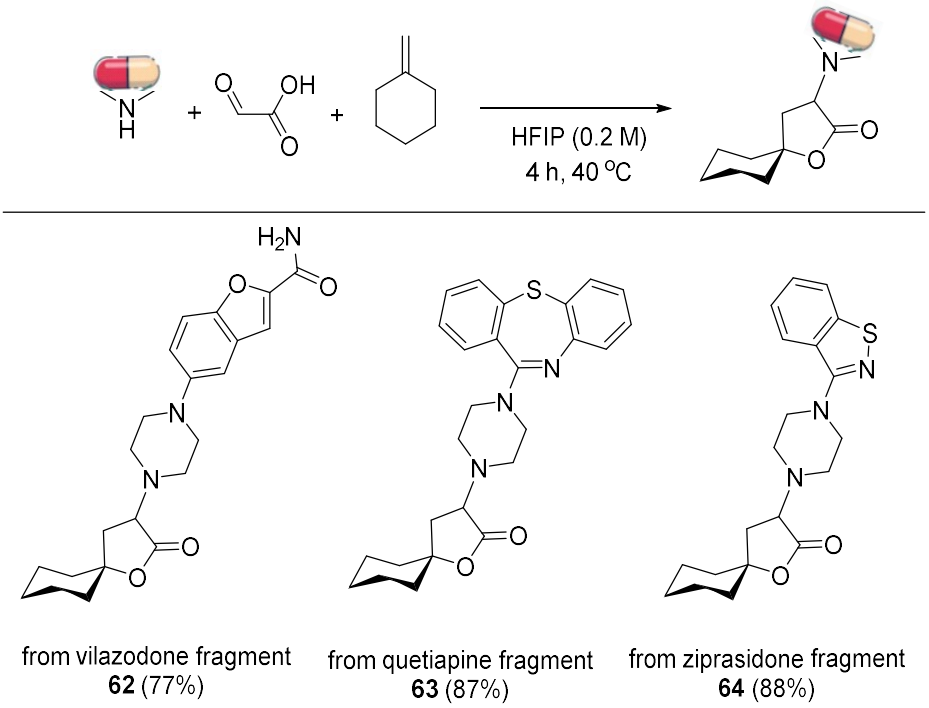
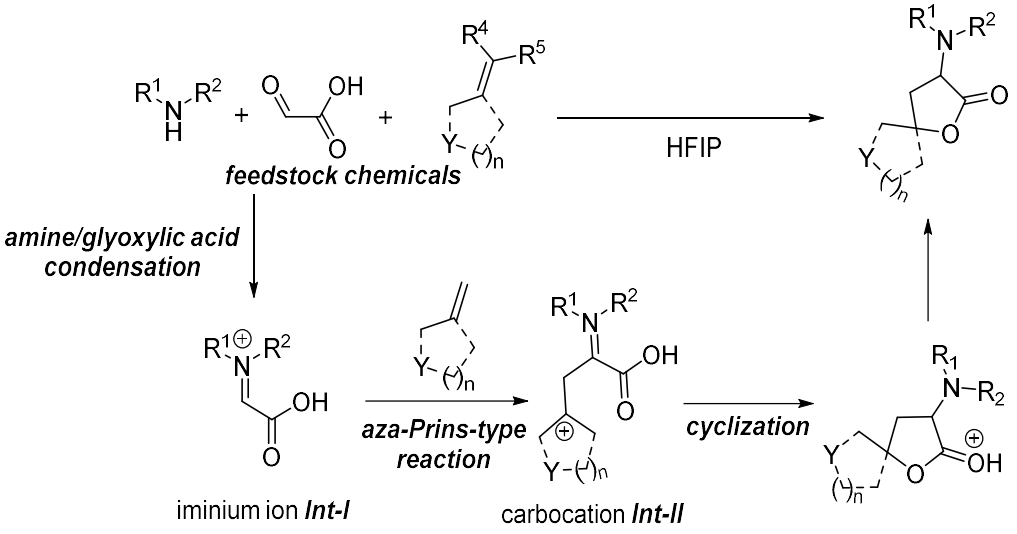


Figure 33. Late-Stage Functionalization of Pharmacophore.



Scheme 31. Plausible reaction mechanism.

Recently, Wang et al. [41] reported a metal-free, hexafluoroisopropanol (HFIP)-mediated three-component cascade reaction of secondary amines, glyoxylic acid, and allenes via a hydroaminoalkylation-aza-Prins process, enabling the efficient construction of structurally diverse α-amino-butenolide frameworks (Figure 34). The reaction simultaneously forms C–N, C–C, and C–O bonds with water as the sole byproduct, featuring excellent atom and step economy. Mechanistically, HFIP acts as a strong hydrogen-bond-donating solvent that significantly stabilizes the electrophilic iminium ion intermediate generated in situ from the amine and glyoxylic acid. This iminium ion then undergoes an aza-Prins addition with the allene to generate a carbocationic intermediate, which rapidly participates in intramolecular O-cyclization to afford the target butenolide (Scheme 32). This mechanism explains the unique superiority of HFIP over other solvents and enables the reaction to accommodate a broad range of substrates under mild conditions and to be applicable to the late-stage functionalization of drug molecules.

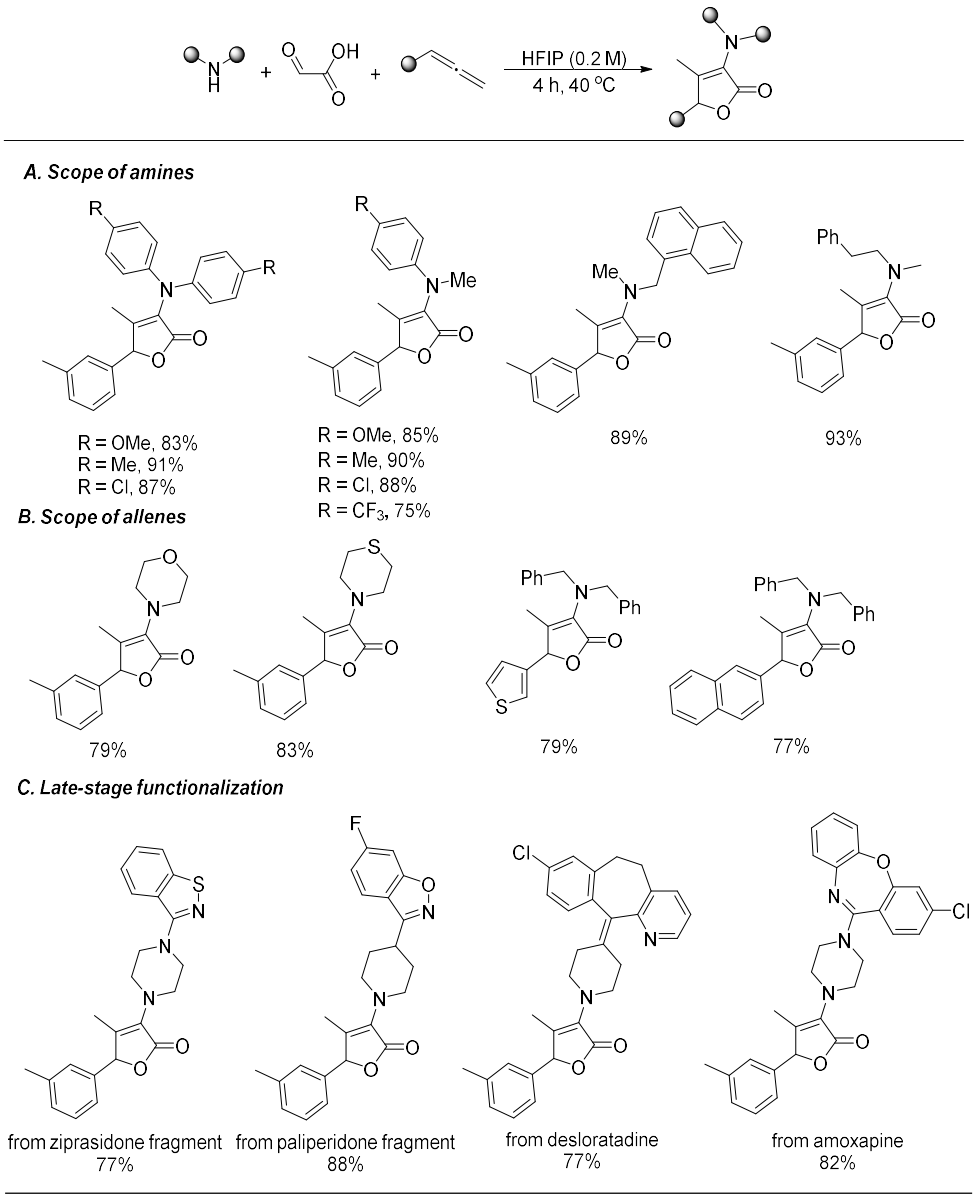
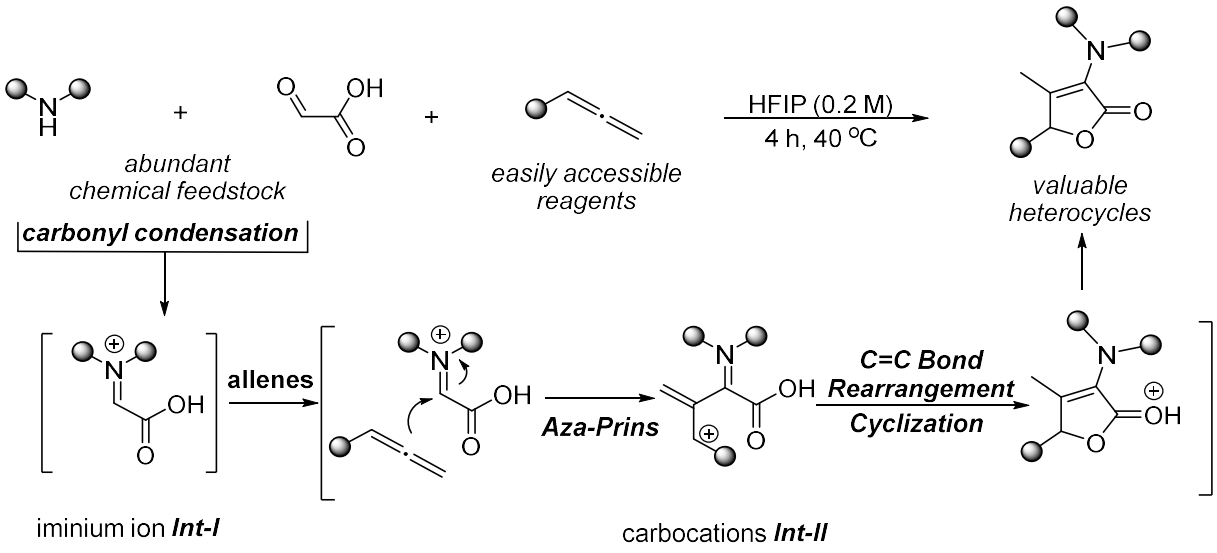


Figure 34. Scope of the hydroaminoalkylation-aza-Prins reaction.



Scheme 32. Plausible reaction mechanism.

4. Glyoxylic Acid as a Promoter

In 2023, Dong's group reported a novel metal-free promotion strategy [42]. Using glyoxylic acid monohydrate as the promoter, the reaction of maleimides, quinones, and sodium sulfinates was realized to efficiently construct C–SO_2 bonds, achieve α-sulfonylation of α,β-unsaturated ketones, and furnish a variety of sulfonylated succinimide and monosulfonylated hydroquinone products (Figure 35). This method is free of transition metals and features mild reaction conditions, short reaction times, good atom economy, and simple operation. The key innovation lies in the adoption of inexpensive and green glyoxylic acid monohydrate as the promoter and sodium sulfinates as sulfonylating reagents. The transformation proceeds via a protonation-nucleophilic addition mechanism. Radical control experiments unambiguously ruled out radical pathways (Scheme 33). This reaction possesses broad substrate scope, tolerates diverse structural skeletons, and can be readily scaled up to the gram scale. Nevertheless, this strategy still exhibits certain limitations toward several substrates, such as sodium triflinate and diethyl maleate. This work provides a new experimental protocol for the synthesis of sulfone compounds.

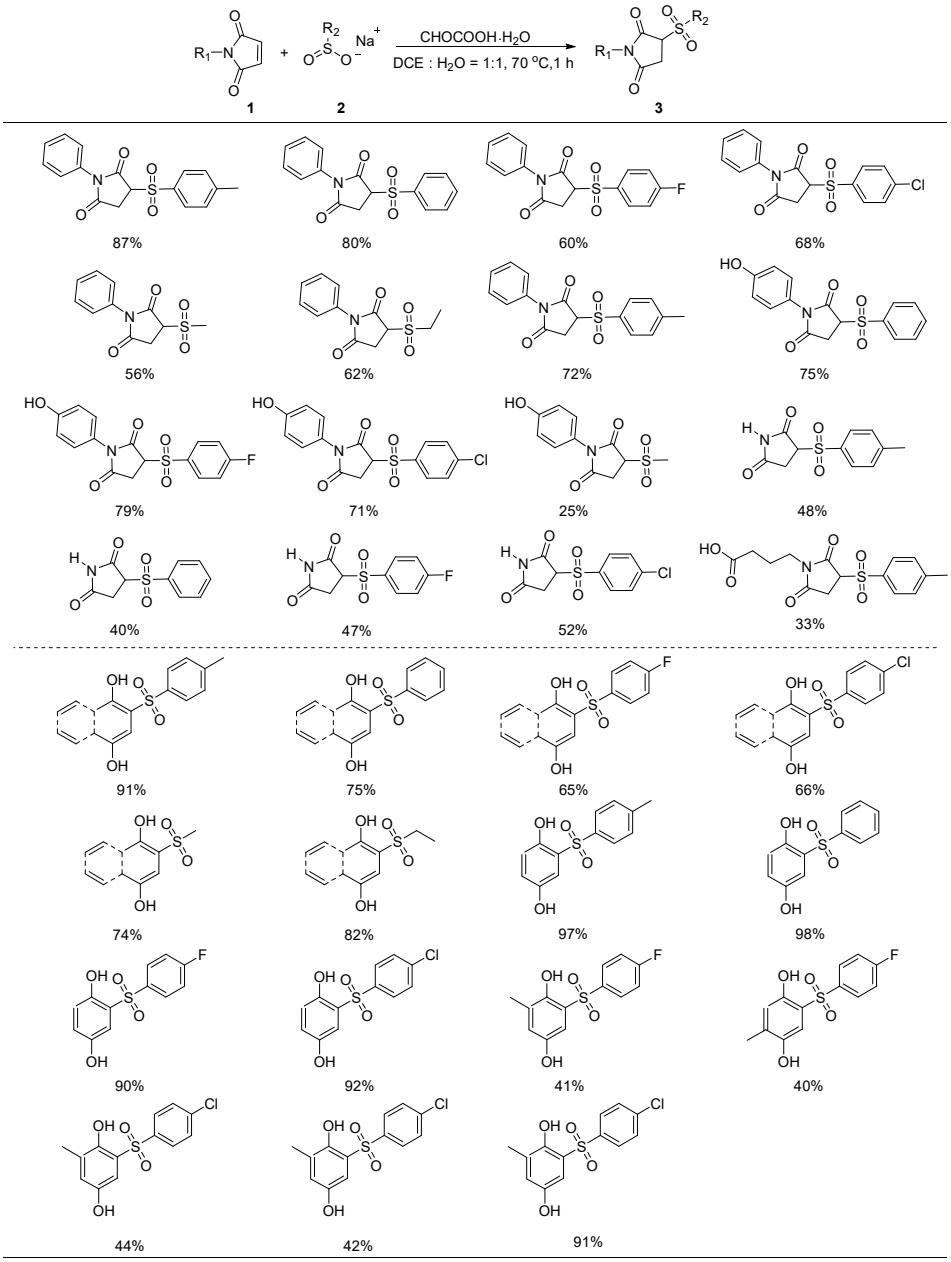
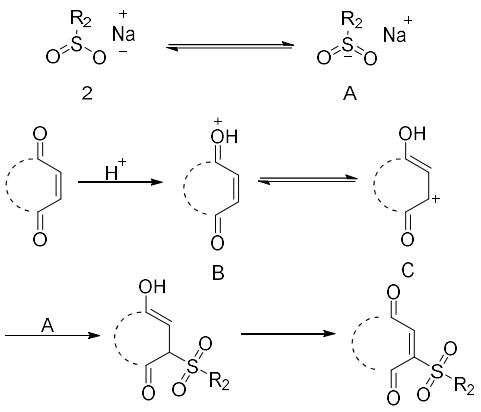


Figure 35. α-sulfonylation of maleimides.



Scheme 33. Plausible reaction mechanism.

In 2025, Zhu's group reported a novel post-synthetic modification strategy for pillararenes [43]. Using glyoxylic acid monohydrate as the promoter, the reductive addition of sodium sulfinates to pillararene-quinone was realized, affording a series of hydroquinone-type 4-O-sulfonylated pillararene derivatives (15 examples in total) (Figure 36). This method establishes a new route for highly selective 4-O-sulfonylation of pillararene-quinone. Unlike the common aromatic C–H sulfonylation between quinones and aryl sodium sulfinates under acidic conditions, this transformation features mild reaction conditions, high selectivity, and simple operation. The reaction exhibits good substrate scope. Aryl sodium sulfinates bearing electron-donating groups, electron-withdrawing groups, as well as ortho-/meta-substituents, mostly give satisfactory yields, whereas heterocyclic and alkyl sodium sulfinates show relatively limited applicability. In addition, the obtained products can undergo diverse functional-group transformations, thereby facilitating the introduction of various functional moieties. Mechanistic studies reveal a plausible pathway for this reductive addition reaction. This strategy not only provides a new route for post-synthetic modification of pillararenes, but also holds promise for the functionalization of other pillararene and calixarene homologues. (Scheme 34).

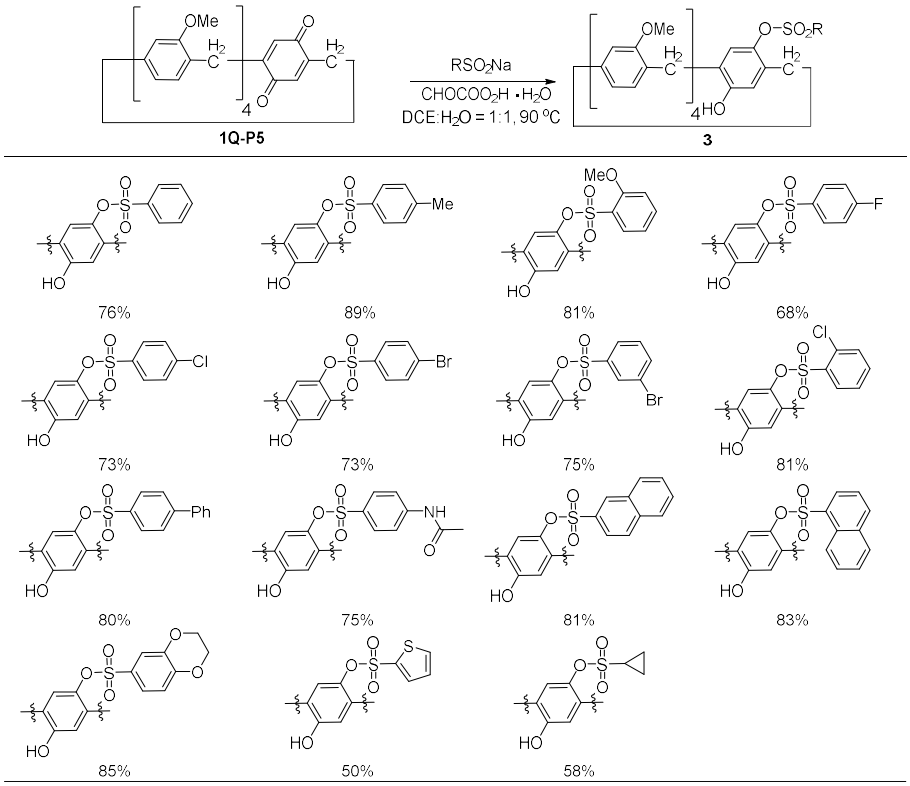
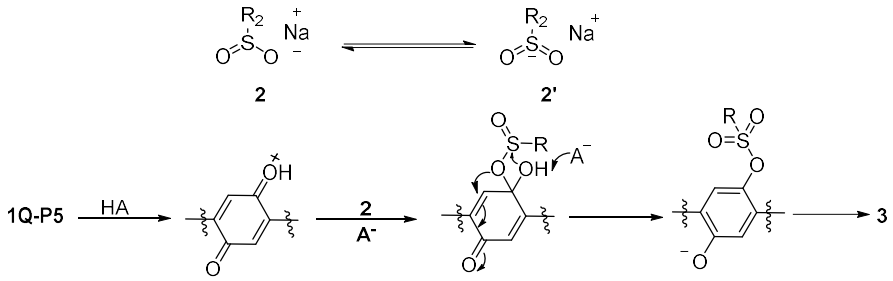


Figure 36. Reductive addition to pillararene-quinone.



Scheme 34. Plausible reaction mechanism.

5. Conclusions and Outlook

Glyoxylic acid, as a cheap, readily available, and low-toxicity α-keto acid, has seen significant progress in organic synthesis in recent years. As a C1 synthon, glyoxylic acid has successfully achieved formylation, deuterated formylation, sulfonylmethylation, and methylenation of various substrates such as aryl/alkenylboronic acids, aryl halides, indoles, enamines, and *N*-heterocycles via decarboxylative pathways, avoiding the need for high-pressure syngas, toxic metal catalysts, or harsh conditions in traditional methods. In particular, photoredox, electrochemical, and persulfate-mediated metal-free strategies provide new tools for the mild and green construction of aldehydes, formamides, and methylene-bridged heterocycles. As a C2 synthon, glyoxylic acid can construct α-arylglycine scaffolds in Petasis-type three-component reactions, introduce polar fragments for surfactant design in Morita-Baylis-Hillman reactions, and furnish pharmaceutically relevant core structures such as 4-arylquinolines and 6-substituted menadiones in cyclization reactions.

Despite the many excellent works, the chemistry of glyoxylic acid still faces some challenges and opportunities: (1) In asymmetric catalytic transformations, how to effectively suppress the fast racemic background reaction remains difficult, requiring more efficient catalysts and chiral ligands. (2) When glyoxylic acid acts as a C1 synthon, the decarboxylation process often requires stoichiometric oxidants or strongly oxidizing conditions; developing systems with catalytic amounts of oxidants and air/oxygen as the terminal oxidant is more in line with sustainable development requirements. (3) Currently, the types of C2 synthon reactions involving glyoxylic acid are relatively few; exploring more novel cyclization, ring-expansion, or rearrangement reactions will enrich its application scenarios. It is expected that the chemistry of glyoxylic acid will move toward more efficient, highly selective, and environmentally friendly directions in the future, and play a greater role in late-stage drug modification, total synthesis of natural products, and functional materials preparation.

Acknowledgments

We express our thanks for funding support from the Outstanding Youth Program of the XPCC (2024DB005), Autonomous Region Tianchi Young Doctor of Excellence (CZ003132, CZ002746), and Young Topnotch Program Project (BJZK202408).

Author Contributions

Data Curation, W.W., J.Y., J.G. and T.P.; Writing—Original Draft Preparation, W.W. and P.L.; Writing—Review & Editing, L.X. and P.L.; Supervision, L.X. and P.L.; Project Administration, P.L. and J.H.; Funding Acquisition, P.L., J.H. and C.L.

Ethics Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

No new data were generated or analysed in support of this review. All data cited in this work are available from the original publications listed in the references.

Funding

This work was supported by the Outstanding Youth Program of the XPCC (2024DB005), Autonomous Region Tianchi Young Doctor of Excellence (CZ003132, CZ002746), and Young Topnotch Program Project (BJZK202408).

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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