



Cite this: DOI: 10.1039/d5gc02973b

Received 12th June 2025,

Accepted 31st July 2025

DOI: 10.1039/d5gc02973b

rsc.li/greenchem

Photoinduced carbonylative multicomponent reaction of anilines and arylaldehydes

Mao-Lin Yang^a and Xiao-Feng Wu^{ib} *^{a,b}

While the carbonyl alkylation amination of alkyl aldehydes has been established as a powerful strategy for accessing tertiary amines, analogous transformations involving aryl aldehydes remain underexplored. Herein, we introduce a photoinduced carbonylative amination strategy with arylaldehydes, enabling the efficient synthesis of valuable α -aminoketones. This

transformation features a four-component reaction wherein carbon monoxide acts as a carbonyl source and aniline serves as the amine moiety. The method proceeds under mild, photo-induced conditions and provides a streamlined, atom-economical approach to structurally diverse α -aminoketones through a one-pot one-step protocol.

Green foundation

1. A general photo-induced four-component carbonylation reaction without metal catalyst.
2. High selectivity photocatalytic multi-radical-coupling for the direct synthesis of α -aminoketones with broad substrate scope.
3. Lower CO pressure for the further research.

Introduction

Carbonyl functionalization of aldehydes remains a central and enduring theme in synthetic chemistry.^{1–3} However, conjugative stabilization by the aromatic ring renders arylaldehydes less electrophilic and significantly less reactive toward nucleophilic functionalization, underscoring the need for efficient strategies to enable their carbonyl functionalization. While its single functionalization has been well established—such as reductive amination,^{1,4} cyanation,⁵ and aldol condensation⁶—the development of precise methods for dual functionalization remains a long-standing challenge. α -Aminoketones represent valuable synthetic targets;⁷ However, conventional approaches often involve multistep sequences and exhibit low selectivity and limited functional group tolerance, thereby restricting their utility in the streamlined synthesis of structurally diverse scaffolds.⁸ A compelling alternative involves a direct approach that installs both amino and carbonyl groups onto aldehydes

via a carbonyl carbonylative amination strategy (CCA strategy), provides an efficient and straightforward approach to access these compounds from simple precursors, potentially addressing many of the limitations. However, the identification of carbonyl sources compatible with such transformations remains a significant synthetic challenge (Fig. 1a).

Carbon monoxide (CO) has been recognized as an abundant, cost-effective, and versatile source of carbonyl group.^{9–13} Its diverse and innovative applications in synthesis have been extensively explored, and the significance of these developments was highlighted by the 2021 Nobel Prize in Chemistry.¹⁴ In an addition, multicomponent reactions (MCRs) as an efficient tool for building complex molecules, making them well-suited for synthesizing α -aminoketones through carbonylation, including imine and carbonyl addition. However, in traditional metal-catalyzed MCRs carbonylation reactions, the nitrogen lone pair preferentially coordinates with the metal, leading to amide formation and preventing access to α -aminoketones.^{15–21} Radical-based MCRs provide an alternative strategy to overcome these limitations, enabling distinct reactivity under mild conditions. Recent advances in photoinduced single-electron transfer (SET) have facilitated environmentally friendly approaches for constructing complex

^aLeibniz-Institut für Katalyse e.V., Albert-Einstein-Str. 29a, 18059 Rostock, Germany.
E-mail: xiao-feng.wu@catalysis.de

^bDalian National Laboratory for Clean Energy, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 116023 Liaoning, China



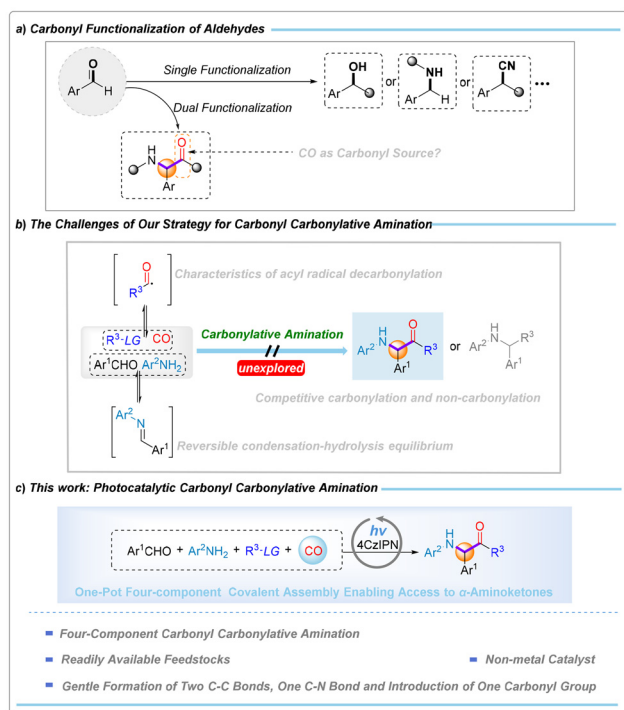


Fig. 1 Background of carbonyl carbonylative amination and our design.

molecular architectures *via* radical MCRs.^{22–29} However, these protocols are often hindered by competing side reactions, particularly in gas-trapping processes, limiting their application in carbonylation chemistry for α -aminoketone synthesis.

Thus, developing an efficient photoinduced four-component carbonyl carbonylative amination strategy (CCA strategy) for α -aminoketones synthesis is desirable. Such a transformation represents a highly appealing strategy, offering: (1) a novel four-component CCA strategy, marking a significant milestone in the development of precise and practical methods for carbonyl dual functionalization of carbonylation and amination in one pot; (2) broadening the chemical space of α -aminoketones; (3) aligning with the principles of sustainable chemistry through efficient CO conversion in multicomponent protocol with high atom economy. However, the challenges for such transformation are obvious (Fig. 1b). First, acyl radicals generated from the capture of carbon monoxide are inherently unstable due to their propensity for decarbonylation. Second, imine intermediates exist in a condensation-hydrolysis equilibrium, which can interfere with the SET step of the reaction. Most critically, the reaction is hindered by competing non-carbonylation side reactions, which complicate the selective formation of the desired α -aminoketones.

Based on these considerations and our ongoing interest in developing sustainable carbonylative transformations,^{30–35} we designed a photoinduced carbonylation catalytic system for carbonyl carbonylative amination. This photocatalytic process proceeds through a sequential SET pathway, enabling an efficient CO-inclusive four-component reaction. CO is crea-

tively employed as the carbonyl source, while aniline serves as the amine source in CCA process. This strategy achieves high-precision dual functionalization at the aldehyde carbonyl center, leading to the formation of a wide range of structurally diverse α -aminoketones in a one-pot manner. The success of this transformation provides valuable insights into carbonyl dual functionalization and supports the development of sustainable carbonylation methodologies.

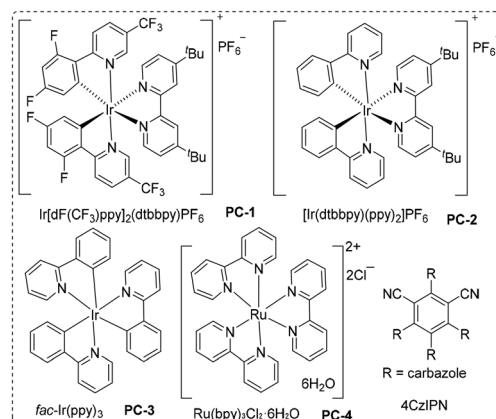
Results and discussion

To realize the above design of photocatalytic CO-inclusive four-component CCA strategy access to α -aminoketones, we initially employed benzaldehyde **1a**, aniline **2a**, and Hantzsch ester **3a** as model substrates under 400–500 nm irradiation, wherein we explored the carbonylation under 50 bar of CO, as shown in Table 1. After screening, 4CzIPN (5 mol%) was identified as a more effective photocatalyst than the alternatives (Table 1,

Table 1 Optimization of the reaction conditions

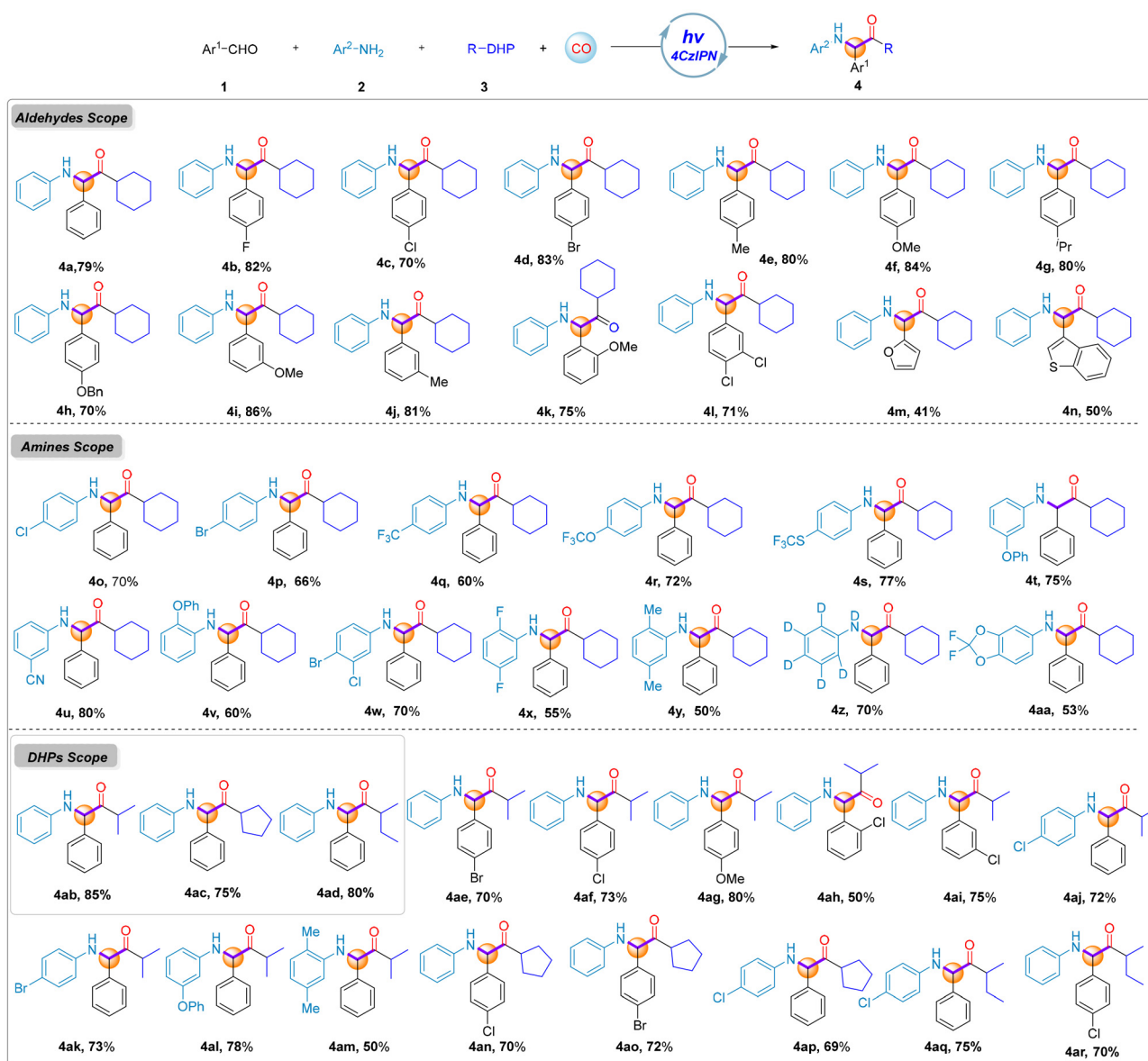
Entry	Variations as shown	Yield (%)
1 ^{c,f}	4CzIPN	84 (79)
2 ^{c,d}	4CzIPN	50
3 ^{c,e}	4CzIPN	75
4 ^{c,e}	PC-1 instead of 4CzIPN	43
5 ^{c,e}	PC-2 instead of 4CzIPN	76
6 ^{c,f}	40 °C, 4CzIPN	80
7 ^{c,f}	50 °C, 4CzIPN	68
8 ^{c,f}	THF, DCE, DMSO, MeCN as solvent, 4CzIPN	0–60
9 ^{a,f}	4CzIPN	70
10 ^{b,f}	4CzIPN	79
11 ^{c,f}	15 h (or 20 h, 28 h) instead of 24 h, 4CzIPN	40 (or 75, 85)
12	Without light, base, CO or 4CzIPN	—

Reaction conditions: **1a** (0.1 mmol), **2a** (0.1 mmol), **3a** (0.1 mmol^a, 0.12 mmol^b, 0.15 mmol^c), PC (1.5 mol%^d, 3 mol%^e, 5 mol%^f), CO (50 bar), CHCl₃ (1 mL), 400–500 nm, 30 °C, 24 h. Determined by GC with hexadecane as internal standard. Isolated yield is shown in parentheses.



entries 1–5), the optimal reaction temperature was found to be 30 °C (Table 1, entries 6 and 7), and the optimal reaction solvent was CHCl₃ (Table 1, entries 1 and 8). To achieve efficient CO conversion in this multi-component system, we investigated the effects of substrate ratio and reaction time. The optimal substrate ratio was found to be 1 : 1 : 1.5 (1a/2a/3a), with the ideal reaction time being 24 h (Table 1, entries 9–13). Additional control experiments underscored the essential roles of CO, light and the photocatalyst, in achieving a successful transformation (Table 1, entries 14 and 15). Finally, the optimal reaction conditions are shown in Table 1, entry 1 (1a/2a/3a = 1 : 1 : 1.5), CHCl₃ (0.1 M), CO (50 bar), 4CzIPN (5 mol%), under 400–500 nm irradiation, at 30 °C for 24 h.

Under the optimized conditions, we explored the applicability of this carbonyl carbonylative amination strategy for the synthesis of various α -aminoketones (Scheme 1). A series of substituted arylamines and arylaldehydes were tested at the first stage, and the carbonylated products α -aminoketones **4a–4n**, were obtained in moderate to good yields (41–86%). Among them, *para*-substituted benzaldehydes exhibited superior reactivity in the transformation, affording the corresponding α -aminoketone products **4b–4h** (*p*-F, Cl, Br, Me, OMe, OBn, *i*Pr) in good yields ranging from 70% to 84%. *meta*-Substituted benzaldehydes also performed well under the reaction conditions, delivering products **4i** (*m*-OMe) and **4j** (*m*-Me) in 86% and 81% yields, respectively. Even *ortho*-substituted



Scheme 1 Substrate scope. Reaction conditions: **1** (0.2 mmol), **2** (0.2 mmol), **3** (0.3 mmol), CHCl₃ (2.0 mL), CO (50 bar), 4CzIPN (5 mol%), under 400–500 nm irradiation, at 30 °C for 24 h. Isolated yield.

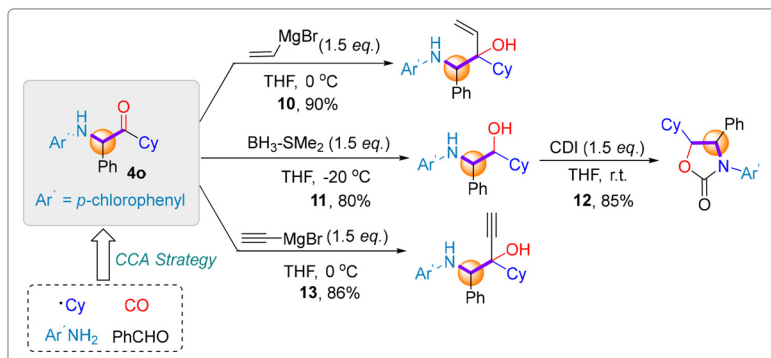


substrates, despite increased steric hindrance, underwent smooth conversion to give the desired product **4k** in 75% yield. Furthermore, the disubstituted benzaldehyde bearing substituents at the *ortho*- and *meta*- positions (3,4-dichlorobenzaldehyde) furnished the target compound **4l** in 71% yield. Notably, heteroaromatic aldehydes such as benzo[d][1,3]dioxole-5-carbaldehyde and furan-2-carbaldehyde were also compatible, providing products **4m** and **4n** in moderate yields of 41% and 50%, respectively. The substrate scope of arylamines was next investigated. *para*-Substituted anilines bearing $-\text{Cl}$, $-\text{Br}$, $-\text{CF}_3$, $-\text{OCF}_3$, and $-\text{SCF}_3$ groups were well tolerated, affording the corresponding products **4o–4s** in yields ranging from 60% to 77%. *meta*-Substituted anilines, such as those containing $-\text{OPh}$ and $-\text{CN}$ groups, also reacted smoothly to furnish products **4t** and **4u** in 75%–80% yield. Sterically hindered *ortho*-substituted aniline 2-phenoxyaniline was compatible with the reaction conditions, delivering product **4v** in 60% yield. Disubstituted anilines were also suitable substrates, providing the desired products **4w–4y** in moderate yields (50%–70%). Moreover, deuterated aniline benzen-2,3,4,5,6- d_5 -amine- d_2 gave product **4z** in 70% yield, and fluorinated heteroaryl-fused aniline 2,2-difluorobenzo[d][1,3]dioxol-5-amine underwent the transformation to afford **4aa** in 53% yield. Different substituted Hantzsch esters were also successfully employed in this transformation, affording products **4ab–4ad** in good yields (75%–85%). In addition, various combinations of benzaldehydes, anilines, and Hantzsch esters participated smoothly in the reaction, delivering the corresponding α -aminoketone products **4ae–4ar** in consistently good yields (50%–80%). These results underscore the broad substrate scope and excellent performance of this new CCA strategy for the synthesis of α -aminoketones. However, no desired product could be detected when alkyl aldehydes or alkyl amines were tested under the current system.

Further synthetic transformations of our produced products were performed subsequently (Scheme 2). Leveraging our CCA strategy, we successfully executed carbonyl functionalization reactions, including alkenylation, alcoholization, and alkynylation, leading to the efficient synthesis of 1-((4-chlorophenyl)amino)-2-cyclohexyl-1-phenylbut-3-en-2-ol **10**, 2-((4-chlorophenyl)amino)-1-cyclohexyl-2-phenylethan-1-ol **11**, and 1-((4-chlorophenyl)amino)-2-cyclohexyl-1-phenylbut-3-yn-2-ol **13** in high yields. Furthermore, building upon the CCA strategy and alcoholization, we demonstrated that cyclization-based post-modification could be effectively carried out under simple experimental conditions, affording 3-(4-chlorophenyl)-5-cyclohexyl-4-phenyloxazolidin-2-one **12** with excellent efficiency. These results not only further enriched for the way of post-functionalization of carbonyl compounds but also promote the development of further functionalization of carbonylation products, with carbon monoxide serving as a C1 source. More importantly, they underscore the synthetic utility of the proposed photocatalytic, CO-enabled four-component carbonylative amination strategy, highlighting its broad applicability and potential in complex molecule synthesis.

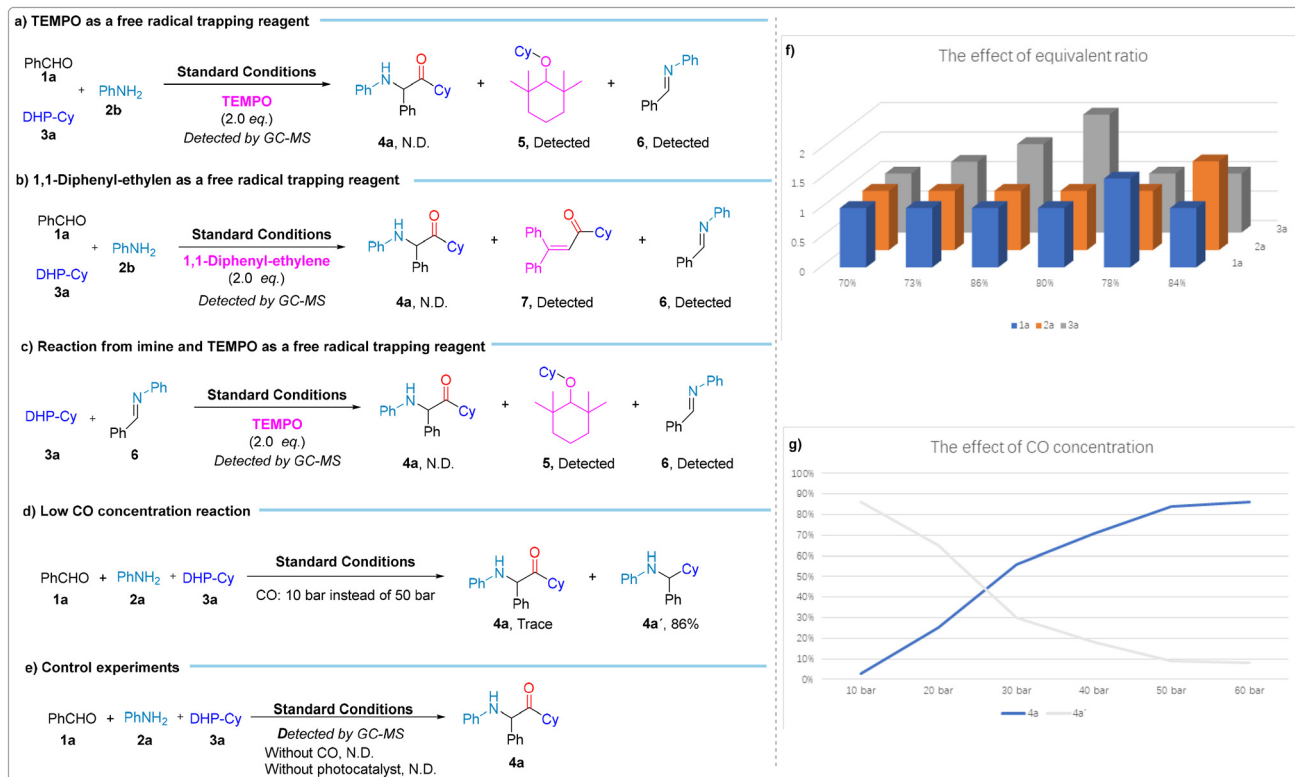
To further elucidate the mechanism of this reaction, several mechanistic experiments were performed (Schemes 3 and 4). Initially, 2,2,6,6-tetramethyl-1-piperidinoxyl (TEMPO) was employed as a free radical scavenger to probe the involvement of free radicals in the reaction pathway. Under standard reaction conditions, no product **4a** was formed (Scheme 3, eqn (a)). Instead, cyclohexyl-TEMPO **5** was detected as the main product *via* GC-MS analysis. Additionally, imine **6** was observed, providing evidence for the involvement of the cyclohexyl radical and imine in the reaction pathway. Subsequently, we performed a reaction with 1,1-diphenylethylene and analyzed the products by GC-MS (Scheme 3, eqn (b)). Contrary to expectations, product **4a** was not formed. However, the detection of 1-cyclohexyl-3,3-diphenylprop-2-en-1-one **7** and imine **6** supported the involvement of cyclohexyl radicals and imines in the reaction mechanism. Then, we initiated the reaction with imine **6**. Upon adding TEMPO to the reaction system, GC analysis revealed no formation of product **4a**, cyclohexyl-TEMPO **5** and imine **6** was detected (Scheme 3, eqn (c)).

Our results reveal that under 10 bar of CO, the predominant product is the non-carbonylated compound **4a'** (Scheme 3, eqn (d)). Control experiments were conducted to verify the necessity of the reaction conditions (Scheme 3, eqn (e)). When the reactions were carried out in the absence of light, CO, or photocatalyst, the desired product was not observed. These

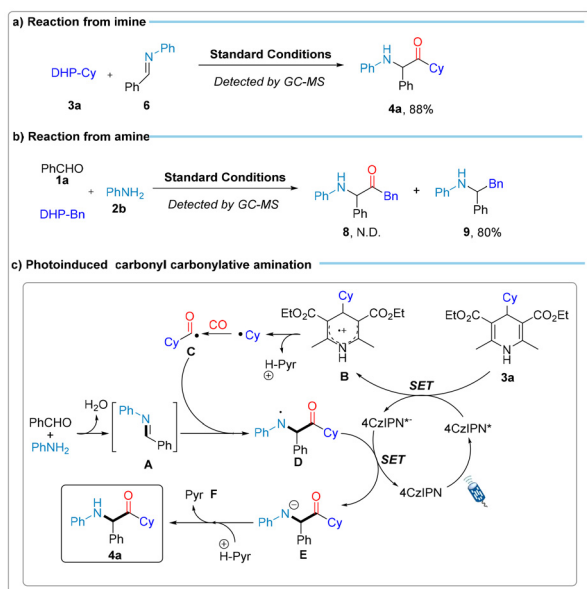


Scheme 2 Synthetic transformations.





Scheme 3 Radical capture experiments, and exploration of influencing factors of catalytic system. **1a**, **2a** and **3a**: (f) CO (50 bar), CHCl₃ (1.0 mL), 4CzIPN (5 mol%), 30 °C, 24 h, 400–500 nm. (g) Reaction conditions: **1a** (0.1 mmol), **2a** (0.1 mmol), **3a** (0.15 mmol), CO, CHCl₃ (1.0 mL), 4CzIPN (5 mol%), 30 °C, 24 h, 400–500 nm. Determined by GC with hexadecane as internal standard.



Scheme 4 Photoinduced four-component carbonyl carbonylative amination.

findings indicate that light, CO, and the photocatalyst are essential for the carbonyl carbonylative amination to proceed. Considering the multi-radical nature of the gas trapping reac-

tion, several side-coupling reactions may occur, which could hinder the efficient formation of the target compounds. To mitigate this, we examined the influence of feedstock ratio and CO concentration on the reaction, ensuring exclusion of interference from non-carbonylation by-products (Scheme 3, eqn (f)). Further optimization showed that the optimal feedstock ratio revealed that the ideal ratio of 1 : 1 : 1.5 (**1a** : **1b** : **1c**), and the ideal CO pressure is 50 bar (Scheme 3, eqn (g)). These results validate our hypothesis that the competing non-carbonylation pathway presents a major hurdle, which can be mitigated by tuning the CO concentration and the feedstock composition. To further investigate the reaction pathway, we separately examined the use of imine **6** and DHP-Bn (Scheme 4, eqn (a) and (b)). The reaction with imine **6** led to the detection of the carbonylation product **4a**. And when DHP-Bn was employed as the reactant, only the non-carbonylation product **9** was observed which implies the importance of the properties of the radical intermediate.

Based on all the experimental results and literature precedents,^{1,30–37} we propose the following possible catalytic cycle (Scheme 4, eqn (c)). Initially, the aldehydes and aniline undergo condensation to yield imine intermediate **A**. Simultaneously, under light irradiation, 4CzIPN is excited, leading to the oxidation of Hantzsch esters (**3a**) by the photo-activated species (4CzIPN*), generating intermediate **B**. This process results in the formation of cyclohexyl radical and the

release of diethyl 2,6-dimethylpyridine-3,5-dicarboxylate (H-Pyr). The cyclohexyl radical subsequently captures CO to form the acyl radical C, which undergoes radical addition to imine intermediate A, generating intermediate D. Subsequently, with the assistance of photocatalytic SET, the excited intermediate E is formed. Finally, the protonation of intermediate E with pyridinium ion (PyH⁺) furnishes the desired carbonylation product α -aminoketone 4a and the by-product pyridine F.

Conclusions

In summary, we report the development of a photoinduced CO-inclusive four-component carbonyl carbonylative amination (CCA) strategy for the synthesis of α -aminoketones from anilines and arylaldehydes, achieving high regioselectivity and moderate to good yields. This transformation introduces a novel approach to carbonyl functionalization by CO capture, enabling the regioselective dual functionalization of arylaldehydes under mild photocatalytic conditions. Additionally, the success of this carbonyl multiple post-functionalization provides valuable insights into the application potential of CCA strategy and fostering the sustainable development of CO conversion processes.

Author contributions

X.-F. W. conceived and directed the project. M.-L. Y. performed all the experiments, prepared the manuscript and the SI.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the SI.

General comments, general procedure, analytic data, and NMR spectra. See DOI: <https://doi.org/10.1039/d5gc02973b>.

Acknowledgements

We appreciate the financial support provided by National Key R&D Program of China (2023YFA1507500), the Chinese Scholarship Council. We also thank the analytical department of Leibniz-Institute for Catalysis for their excellent analytical service here. We appreciate the general support from Professor Armin Börner in Leibniz-Institute for Catalysis.

References

- 1 R. Kumar, N. J. Flodén, W. G. Whitehurst and M. J. Gaunt, *Nature*, 2020, **581**, 415–420.
- 2 L. Zhang and D. A. Nagib, *Nat. Chem.*, 2024, **16**, 107–113.
- 3 S. Sebastian, Monik, A. K. Khatana, E. Yadav and M. K. Gupta, *Org. Biomol. Chem.*, 2021, **19**, 3055–3074.
- 4 T. Irrgang and R. Kempe, *Chem. Rev.*, 2020, **120**, 9583–9674.
- 5 N. Kurono and T. Ohkuma, *ACS Catal.*, 2016, **6**, 989–1023.
- 6 A. Tampieri, K. Föttinger, N. Barabers and F. Medina, *Appl. Catal., B*, 2022, **319**, 121889.
- 7 L. A. T. Allen, R.-C. Raclea, P. Natho and P. J. Parsons, *Org. Biomol. Chem.*, 2021, **19**, 498.
- 8 S. Barranco, F. Cuccu, M. Uras and A. Frongia, *Chem. – Eur. J.*, 2024, **30**, e202400355.
- 9 X.-F. Wu, H. Neumann and M. Beller, *Chem. Soc. Rev.*, 2011, **40**, 4986–5009.
- 10 Y.-H. Li, Y.-Y. Hu and X.-F. Wu, *Chem. Soc. Rev.*, 2018, **47**, 172–194.
- 11 J.-B. Peng, H.-Q. Geng and X.-F. Wu, *Chem*, 2019, **5**, 526–552.
- 12 J.-B. Peng, F.-P. Wu and X.-F. Wu, *Chem. Rev.*, 2019, **119**, 2090–2127.
- 13 M. Yang, Y. Liu, X. Qi, Y. Zhao and X. Wu, *Green Synth. Catal.*, 2024, **5**, 211–269.
- 14 <https://www.nobelprize.org/prizes/chemistry/2021/summary/>.
- 15 H. Alper, *Tetrahedron Lett.*, 1988, **29**, 5113–5116.
- 16 Y. Zhang, J. Ji, X. Zhang, S. Lin, Q. Pan and L. Jia, *Org. Lett.*, 2014, **16**, 2130–2133.
- 17 L. Liu and H. Sun, *Angew. Chem., Int. Ed.*, 2014, **53**, 9865–9869.
- 18 R. D. Dghaym, R. Dhawan and B. A. Arndtsen, *Angew. Chem.*, 2001, **113**, 3328–3330.
- 19 B. A. Arndtsen, *Chem. – Eur. J.*, 2009, **15**, 302–313.
- 20 Z. Zhang, Y. Liu, L. Ling, Y. Li, Y. Dong, M. Gong, X. Zhao, Y. Zhang and J. Wang, *J. Am. Chem. Soc.*, 2011, **133**, 4330–4341.
- 21 F.-P. Wu and X.-F. Wu, *Angew. Chem., Int. Ed.*, 2021, **60**, 695–700.
- 22 L. Lu, R. Shi and A. Lei, *Trends Chem.*, 2022, **4**, 179–190.
- 23 N. Holmberg-Douglas and D. A. Nicewicz, *Chem. Rev.*, 2022, **122**, 1925–2016.
- 24 T. Shen and T. H. Lambert, *Science*, 2021, **371**, 620–626.
- 25 T. Shen, Y.-L. Li, K.-Y. Ye and T. H. Lambert, *Nature*, 2023, **614**, 275–280.
- 26 B. Lu, M. Xu, X. Qi, M. Jiang, W.-J. Xiao and J.-R. Chen, *J. Am. Chem. Soc.*, 2022, **144**, 14923–14935.
- 27 B. Lu, Y. Cheng, L.-Y. Chen, J.-R. Chen and W.-J. Xiao, *ACS Catal.*, 2019, **9**, 8159–8164.
- 28 B. Lu, Z. Zhang, M. Jiang, D. Liang, Z.-W. He, F.-S. Bao, W.-J. Xiao and J.-R. Chen, *Angew. Chem., Int. Ed.*, 2023, **62**, e202309460.
- 29 B. Lu, F.-S. Bao, Z.-W. He, W.-J. Xiao and J.-R. Chen, *Chin. J. Chem.*, 2024, **42**, 990–996.



- 30 G. M. Torres, Y. Liu and B. A. Arndtsen, *Science*, 2020, **368**, 318–323.
- 31 Y. Wang, H. Yang, Y. Zheng, M. Hu, J. Zhu, Z.-P. Bao, Y. Zhao and X.-F. Wu, *Nat. Catal.*, 2024, **7**, 1065–1075.
- 32 H. Yang, Y. Wang, L.-C. Wang and X.-F. Wu, *Chem. Sci.*, 2024, **15**, 14304–14309.
- 33 J. Zhang, L.-C. Wang, Y. Wang and X.-F. Wu, *Green Chem.*, 2024, **26**, 11686–11694.
- 34 M. Yang, Y. Liu, P. Yang, Y. Zhao and X.-F. Wu, *Sci. China: Chem.*, 2025, **68**, 2485–2490.
- 35 M.-L. Yang and X.-F. Wu, *Green Chem.*, 2025, **27**, 5257–5264.
- 36 Q. Li, L.-C. Wang and X.-F. Wu, *Green Chem.*, 2025, **27**, 8492–8497.
- 37 Z. Yao, J. Yang, Z. Luo, H. Wang, X. Zhang, J. Ye, L. Xu and Q. Shi, *Green Chem.*, 2022, **24**, 7968–7973.

