



Cite this: *Chem. Sci.*, 2026, 17, 2193

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 16th October 2025
Accepted 24th November 2025

DOI: 10.1039/d5sc08002a

rsc.li/chemical-science

Acyl-oxyallenes as α,β -unsaturated ketone surrogates for Giese radical addition

Jiarong Jin,^a Xin Li,^a Yicheng Luo,^a Jianfu Chen,^{*c} Wenjun Tang^{†ab} and Kang Du^{*a}

Oxyallenes are valuable building blocks in organic synthesis, most commonly exploited as π -allyl metal precursors in transition-metal-catalyzed allylation reactions. In contrast, their engagement in radical processes remains largely unexplored. Herein, we disclose a Giese-type radical addition protocol in which acyl-substituted oxyallenes function as *in situ* precursors to α,β -unsaturated ketones, enabling efficient coupling with 2-azaallyl radicals. This metal-free method delivers a wide range of γ -amino ketones in high yields with broad functional group tolerance, mild conditions, and scalability to gram quantities. Mechanistic studies, including radical trapping and isotopic labeling, support a pathway involving radical addition of the 2-azaallyl radical to transient enone intermediates. These findings establish a new reactivity mode of oxyallenes in radical chemistry and provide an efficient route to synthetically and pharmaceutically valuable amino ketones.

Introduction

Oxyallenes represent a versatile class of C3 synthons in modern organic synthesis.¹ The presence of an alkoxy group on the allene core induces polarization across the π -system, thereby enabling distinct reactivity profiles at different carbon centers. Under metalation conditions, deprotonation at the C1 position furnishes lithiated alkoxyallenes that react with a wide array of electrophiles.^{1a-f} Conversely, the C2 carbon is susceptible to direct electrophilic attack^{2a-c} or acid-mediated activation—either by Lewis acids^{1g,h,2d} or Brønsted acids^{2e,f}—leading to the formation of reactive oxonium intermediates. These intermediates subsequently undergo nucleophilic additions at the C1 or C3 positions, as illustrated in Fig. 1A. In transition-metal-catalyzed allylation chemistry, oxyallenes readily undergo hydro-metalation with a transient M–H species to furnish π -allyl metal intermediates with diverse reactivity profiles. Advances in this area include Pd- and Rh-catalyzed allylic substitution with pronucleophiles,³ and hydrofunctionalization reactions catalyzed by Ir, Ru, and Cu with carbonyls/imines (Fig. 1B).⁴ Despite their broad utility in polar reactions and transition metal catalysis, radical-based transformations remain conspicuously

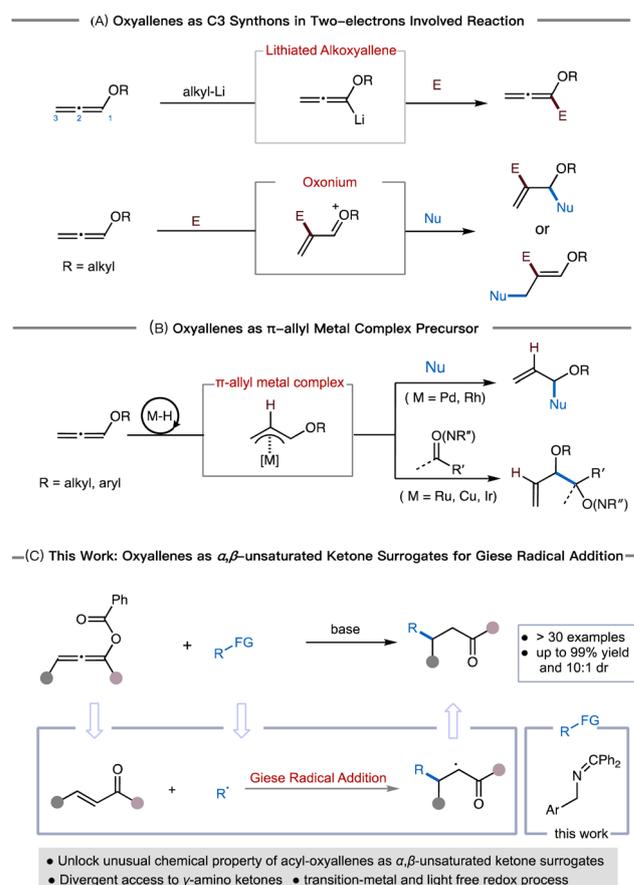


Fig. 1 Introduction.

^aSchool of Chemistry and Materials Science, Hangzhou Institute for Advanced Study, University of Chinese Academy of Sciences, Hangzhou 310024, Chin. E-mail: kangdu@ucas.ac.cn

^bState Key Laboratory of Bio-Organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Ling Ling Rd, Shanghai 200032, China. E-mail: tangwenjun@sioac.ac.cn

^cState Key Laboratory of Green Chemical Engineering and Industrial Catalysis, Key Laboratory for Advanced Materials, Centre for Computational Chemistry and Research Institute of Industrial Catalysis, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China. E-mail: jfchen@ecust.edu.cn



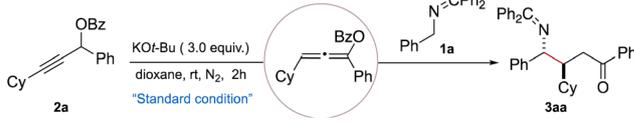
underexplored.⁵ Herein, we demonstrate the first use of acyl-substituted oxyallenes as α,β -unsaturated ketone surrogates in Giese-type radical addition reactions. This method allows for the gradual liberation of the enone from acyl-oxyallene while maintaining a relatively lower concentration of enone. This approach offers potential advantages in modulating the molecular weight and distribution of polymers in radical polymerization. Additionally, it could influence both the reactivity and selectivity in the Giese radical addition.

As postulated in Fig. 1C, *O*-acyl oxyallenes can presumably be accessed analogously to alkoxyallenes *via* base-promoted isomerization of propargylic esters (*e.g.*, *MOt*-Bu). Unlike relatively stable alkoxyallene, this *O*-acyl oxyallene intermediate could further undergo a cascade sequence involving transesterification and protonation at the C2 position, ultimately generating an α,β -unsaturated ketone that serves as a Giese-type radical acceptor. We selected 2-azaallyl radicals to engage in Giese radical addition with the *in situ* generated α,β -unsaturated ketones, furnishing γ -amino ketones—structural analogues of γ -aminobutyric acid (GABA), the principal inhibitory neurotransmitter in the central nervous system and a core scaffold in numerous pharmaceuticals.^{6,7} Foundational work⁸ by Walsh and co-workers demonstrated that 2-azaallyl radicals can be formed from *N*-benzyl ketimines under basic conditions *via* a single-electron transfer (SET) process between the corresponding 2-azaallyl anion and an electron acceptor (*e.g.*, *N*-benzyl ketimine). Motivated by our continued interest in α -C–H functionalization of aliphatic amines,⁹ we sought to develop a Giese-type radical addition between acyl-oxyallenes and *N*-benzyl ketimines under basic conditions.

Results and discussion

Following these considerations, we selected *N*-benzyl ketimine **1a** (2.0 equiv.) and 3-cyclohexyl-1-phenylprop-2-yn-1-yl benzoate **2a** (1.0 equiv.) as model substrates to evaluate the feasibility of the proposed transformation. Under the optimized conditions, the reaction was carried out in 1,4-dioxane at room temperature for 2 hours using *KOt*-Bu (3.0 equiv.) as the base, affording the desired γ -amino ketone (**3aa**) in 89% yield (83% isolated) with a 10 : 1 diastereomeric ratio (dr). The effect of various reaction parameters was systematically investigated (Table 1; see the SI for additional data). Modification of the base loading, either increasing or decreasing the amount of *KOt*-Bu, led to diminished yields (entries 2 and 3). The use of alternative alkoxide bases such as *NaOt*-Bu and *LiOt*-Bu also resulted in reduced efficiency (entries 4 and 5). Notably, replacing *KOt*-Bu with sterically hindered bases such as *MHMDS* (M = Li, Na, K)—commonly used in 2-azaallyl anion-enabled radical processes⁸ completely suppressed the reaction (entries 6–8), likely due to steric hindrance impeding the isomerization of the propargylic ester to the corresponding enone intermediate. Further examination of the ester leaving group revealed that propargylic alcohol derivatives bearing alternative activating groups, such as acetyl (Ac) or *tert*-butylcarbonyl (Boc), provided lower yields (entries 9 and 10). Solvent screening showed that replacing dioxane with toluene or *n*-hexane significantly decreased the product yield (entries 11 and 12). A reduction in reaction

Table 1 Reaction optimization



Entry ^a	Deviation from standard conditions	Yield ^b (%)
1	None	89 (83)
2	2.0 equiv. <i>KOt</i> -Bu	66
3	4.0 equiv. <i>KOt</i> -Bu	76
4	<i>NaOt</i> -Bu vs. <i>KOt</i> -Bu	20
5	<i>LiOt</i> -Bu vs. <i>KOt</i> -Bu	0
6	<i>LiHMDS</i> vs. <i>KOt</i> -Bu	0
7	<i>NaHMDS</i> vs. <i>KOt</i> -Bu	0
8	<i>KHMDS</i> vs. <i>KOt</i> -Bu	0
9	Ac vs. Bz	60
10	Boc vs. Bz	52
11	PhMe vs. dioxane	30
12	<i>n</i> -Hexane vs. dioxane	40
13	0 °C vs. rt	50

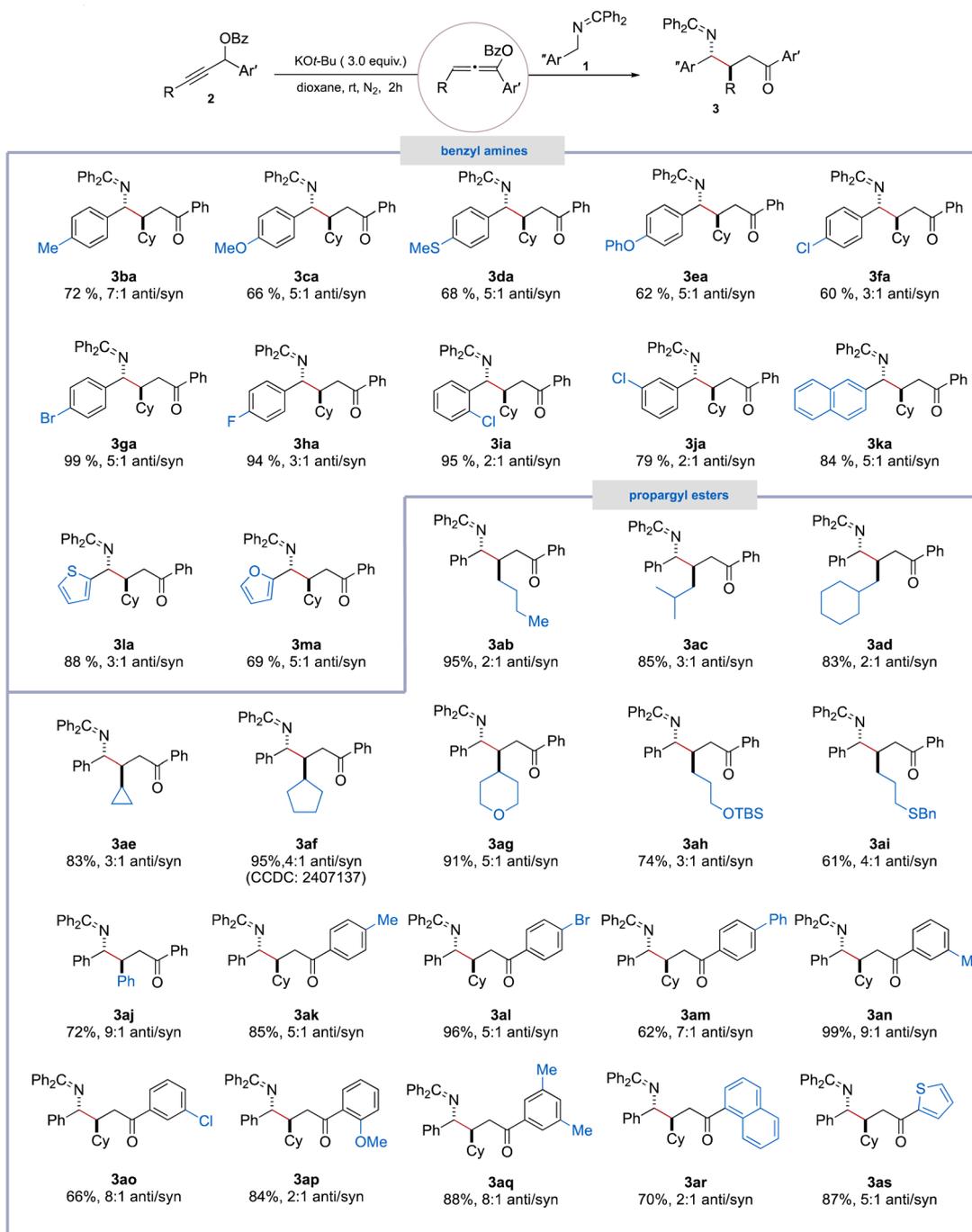
^a Unless otherwise specified, the reactions were performed at rt in dioxane (1 mL) under nitrogen for 2 h with **1a** (0.1 mmol), propargylic ester **2a** (0.2 mmol) and *KOt*-Bu (0.3 mmol, 3.0 equiv.). ^b Yield was determined by ¹H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene as the internal standard; number in the parentheses refers to isolated yield; the diastereoselectivities (dr, *anti*/*syn* ratios) were determined by ¹H NMR of the crude reaction mixture, dr = 10 : 1.

temperature from room temperature to 0 °C also led to a decrease in yield (entry 13). Based on these studies, the optimal conditions were established using *KOt*-Bu (3.0 equiv.) in dioxane at room temperature for 2 hours (entry 1).

With the optimized conditions in hand, we next explored the substrate scope of the Giese-type addition reaction (Table 2). A wide array of *N*-benzyl ketimine derivatives (**1b–1h**) bearing electronically varied substituents, including –Me, –OMe, –SMe, –OPh, –Cl, –Br, and –F at the *para*-positions of the aromatic ring, were well tolerated, affording the corresponding γ -amino ketones (**3ba–3ha**) in moderate to excellent yields (60–99%) and with a moderate dr (3 : 1 to 7 : 1). Ketimines bearing a chloro substituent at *ortho*- or *meta*-positions on the aromatic ring also proved to be suitable substrates, yielding products **3ia** and **3ja** in 95% and 79% yields respectively, albeit with a lower dr. Moreover, aromatic systems incorporating naphthyl and heteroaryl moieties, such as thiophene and furan, were also compatible with the reaction conditions, furnishing products **3ka–3ma** efficiently.

We next turned our attention to evaluating the scope of propargylic ester substrates. A broad range of alkyl-substituted propargylic esters bearing linear, α -branched, β -branched, and γ -branched unfunctionalized alkyl groups on the terminal alkyne carbon, including *n*-butyl (**2b**), isobutyl (**2c**), cyclohexylmethyl (**2d**), cyclopropyl (**2e**), and cyclopentyl (**2f**) groups, underwent smooth reactions with *N*-benzyl ketimine (**1a**), affording the corresponding γ -amino ketones (**3ab–3af**) in high to excellent yields (83–95%), with the dr ranging from 2 : 1 to 4 : 1.¹⁰ In addition, substituents on the terminal alkyne carbon with diverse



Table 2 Substrate scope^a

^a Unless otherwise specified, the reactions were performed at rt in dioxane under nitrogen for 2 h with **1** (0.2 mmol), propargyl ester **2** (0.4 mmol) and KOt-Bu (0.6 mmol); the relative configurations were determined or assigned by analogy on the basis of the X-ray structure of **3af**; the diastereoselectivities (*anti/syn* ratios) were determined by ¹H NMR of the crude reaction mixture.

functional groups, including tetrahydro-2*H*-pyran (**2g**), OTBS (**2h**), thioether (**2i**), and phenyl (**2j**), were found to be compatible with these reaction conditions. Moreover, aryl-substituted propargyl esters bearing electron-donating (–Me and –OMe) or electron-withdrawing groups (–Br, –Cl, and –Ph) on the aromatic ring at *para*-, or *meta*- or *ortho*-positions were found to be well

tolerated to furnish the corresponding γ -amino ketones (**3ak**–**3ap**) in moderate to excellent yields (62–99%) with the dr varied from 2:1 to 9:1. Additionally, substrates featuring more complex aryl groups, such as 3,5-dimethylphenyl, naphthalenyl, and thiophenyl at the C1-position, also proved to be effective, delivering the corresponding products **3aq**–**3as** in good yields.



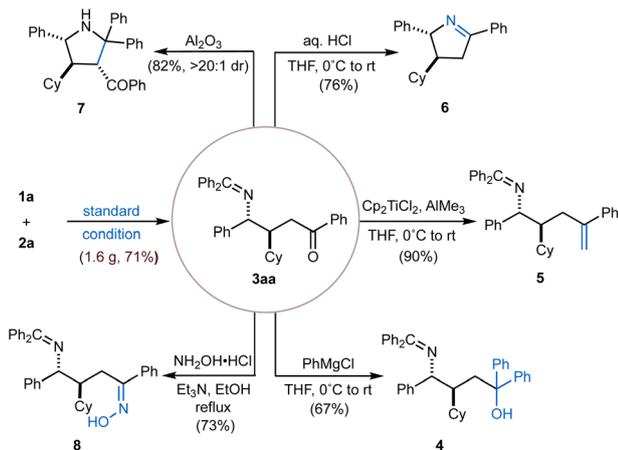


Fig. 2 Synthetic applications.

To demonstrate the synthetic utility of this methodology, we performed a gram-scale reaction, which successfully afforded the desired product **3aa** in 71% yield. The versatility of this γ -amino ketone scaffold was further highlighted through a series of downstream functionalizations of the C=O double bond (Fig. 2). For example, selective nucleophilic addition of PhMgCl furnished the corresponding tertiary alcohol (**4**) in 67% yield. Alternatively, olefination by employing Tebbe reagent (Cp_2TiCl_2 and AlMe_3) afforded alkene product **5** in 90% yield. Condensation with hydroxylamine hydrochloride delivered oxime **8** in 73% yield. In addition, a cascade sequence involving imine hydrolysis followed by intramolecular condensation under acidic aqueous conditions (aq. HCl), led to the formation of cyclic imine (**6**) in 76% yield. Finally, intramolecular cyclization of **3aa** via a Mannich-type reaction under basic conditions (basic Al_2O_3) yielded the multi-substituted pyrrolidine (**7**) in 82% yield with >20 : 1 dr.

To gain insight into the Giese radical addition, we conducted a series of mechanistic experiments (Fig. 3). First, the addition of radical scavengers such as 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO) or butylated hydroxytoluene (BHT) under standard conditions completely suppressed the formation of the desired γ -amino ketone. Instead, in the presence of TEMPO, a distinct byproduct **9** was isolated in 25% yield, indicating the interception of a 2-azaallyl radical intermediate. Next, the reaction of *N*-benzyl ketimine (**1n**), bearing an *ortho*-allyl substituent on the aromatic ring, with propargyl ester **2a** under standard conditions yielded a cyclized product **10** in 40% yield, and no addition product **3na** was observed (Fig. 3A). The above observations are consistent with a radical-mediated mechanism, wherein the 2-azaallyl radical could participate in bond forming events at both carbons adjacent to the nitrogen.

It was expected that treatment of propargylic benzoate **2a** under standard conditions in the absence of ketimine **1a** would afford the expected benzoyl-oxallene or the corresponding enone; however, neither of these intermediates were successfully isolated, only byproduct **13** (8% yield). We reason that both the intermediates are too reactive to be isolated under basic conditions. Benzoyl-oxallene, under basic conditions (*e.g.* KOt-Bu), subsequently transformed to enone, which could be

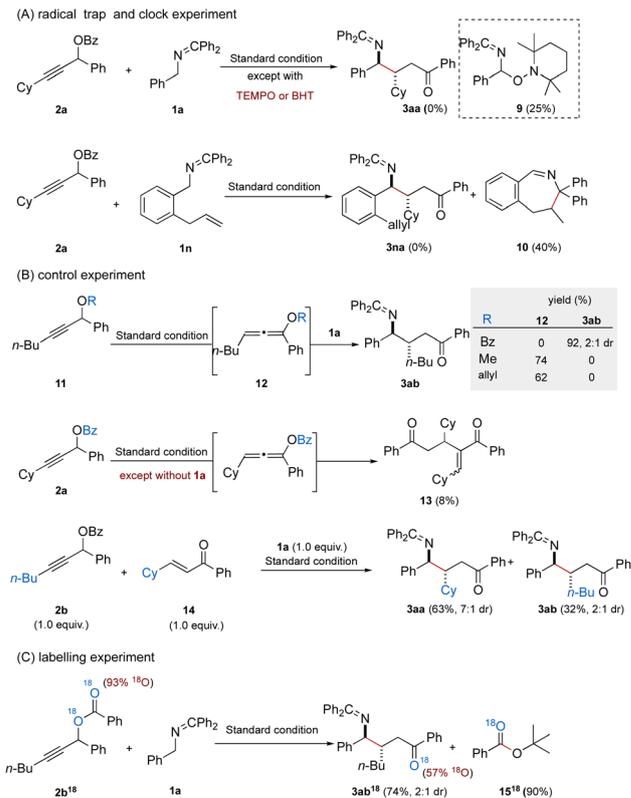


Fig. 3 Mechanistic studies.

consumed by participating in other reaction pathways such as dimerization.¹¹ To illustrate *O*-acyl oxallenes as precursors to enones, we performed a series of control experiments (Fig. 3B). When propargylic ether substituted with methyl or allyl groups reacted with *N*-benzyl ketimine **1a** under the standard reaction conditions, the corresponding alkoxyallenes were isolated in moderate yields (74% and 62%) and no formation of the desired product **3ab** was observed, likely due to the inert reactivity of these alkoxyallenes, which appear unable to undergo further transformation into the reactive enone intermediate. Next, a competitive experiment was conducted by employing both propargylic benzoate **2b** and enone (**14**) in the presence of **1a** under standard conditions. The desired products **3aa** and **3ab** were obtained in 63% and 32% yield, respectively, thereby supporting the hypothesis that enones serve as the radical acceptors for 2-azaallyl radicals. Finally, an ^{18}O -labelling experiment was performed to elucidate the formation pathway of the enone (Fig. 3C). When ^{18}O -enriched propargylic benzoate **2b¹⁸** (93% ^{18}O) was treated with **1a** under standard conditions, the resulting product **3ab¹⁸** incorporated 57% ^{18}O , and *tert*-butyl benzoate (**15¹⁸**) was isolated in 90% yield. These findings are consistent with a nucleophilic benzoyl transfer mechanism.

Based on the above experimental observations and the pioneering studies on 2-azaallyl radicals by the Walsh group, we propose a plausible mechanism for this transformation (Fig. 4). The reaction is initiated by the base-mediated isomerization of propargylic benzoate to benzoyl-oxallene, which undergoes a sequence of benzoyl group transfer and protonation steps at the



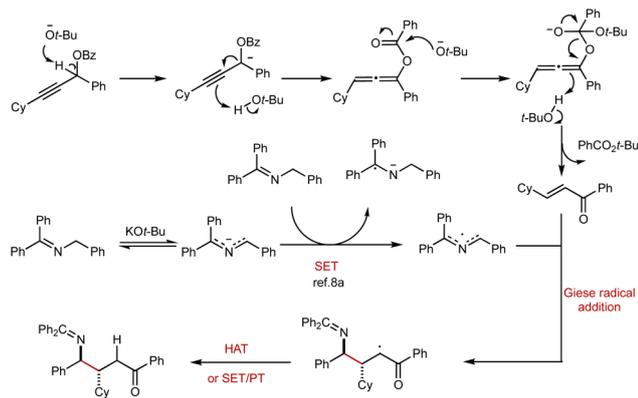


Fig. 4 Plausible mechanism.

C2 position of oxallene, ultimately furnishing the enone *in situ*. Concurrently, deprotonation of the *N*-benzyl ketimine by KO*t*-Bu generates a 2-azaallyl anion, which serves as a super-electron donor. A single-electron transfer (SET) from this anion to another molecule of *N*-benzyl ketimine produces a 2-azaallyl radical along with a ketimine radical anion.^{8a} The resulting 2-azaallyl radical then undergoes a Giese-type radical addition to the *in situ* generated enone, forming a new C–C bond and yielding a α -carbonyl radical intermediate. This α -carbonyl radical could react with *N*-benzyl ketimine *via* hydrogen atom transfer (HAT) to produce the final product. Alternatively, the SET/PT pathway (SET with either the 2-azaallyl anion or the ketimine radical anion, followed by protonation transfer) is also feasible.

Conclusions

In summary, we have revealed that acyl-oxallenes serve as effective α,β -unsaturated ketone precursors in Giese-type radical additions with 2-azaallyl radicals, culminating in the synthesis of a series of γ -amino ketones. This protocol exhibits remarkable yield, broad substrate scope, and notable functional group tolerance. Moreover, the downstream diversification of the γ -amino ketone products highlights the synthetic utility and pharmaceutical relevance of this methodology. Mechanistic investigations support a radical pathway featuring C–C bond-formation *via* 2-azaallyl radical addition to transient enone intermediates. These findings expand the synthetic utility of oxallenes, and efforts to further explore their potential as α,β -unsaturated ketone surrogates are ongoing.

Author contributions

J. J., X. L., Y. L., J. C., W. T., and K. D. contributed to the chemical experiments, J. J., X. L., and Y. L. performed all chemical reactions reported, and K. D. and W. T. wrote the manuscript with contributions from all authors.

Conflicts of interest

There are no conflicts to declare.

Data availability

CCDC 2407137 contains the supplementary crystallographic data for this paper.¹⁰

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: reaction optimizations, experimental procedures, characterization and X-ray data. See DOI: <https://doi.org/10.1039/d5sc08002a>.

Acknowledgements

We are grateful for the financial support from the National Natural Science Foundation of China (22101234 and 82188101), the National Key R&D Program of China (2022YFA1503702 and 2021YFF0701601), startup funding and the Research Funds of Hangzhou Institute for Advanced Study, UCAS (2024HIAS-Y015 and 2024HIAS-P003).

Notes and references

- For selected reviews on alkoxyallenes, see: (a) R. Zimmer, *Synthesis*, 1993, 165; (b) H.-U. Reissig, S. Hormuth, W. Schade, M. O. Amombo, T. Watanabe, R. Pulz, A. Hausherr and R. Zimmer, *J. Heterocycl. Chem.*, 2000, **37**, 597; (c) N. Krause and A. S. K. Hashmi, *Modern Allene Chemistry*, Wiley-VCH, Weinheim, 2004, p. 425; (d) M. Brasholz, H.-U. Reissig and R. Zimmer, *Acc. Chem. Res.*, 2009, **42**, 45; (e) R. Zimmer and H.-U. Reissig, *Chem. Soc. Rev.*, 2014, **43**, 2888; (f) M. A. Tius, *Chem. Soc. Rev.*, 2014, **43**, 2979; (g) E. Manoni and M. Bandini, *Eur. J. Org. Chem.*, 2016, 3135; (h) H.-U. Reissig and R. Zimmer, *Synthesis*, 2017, **49**, 3291; (i) V. M. Schmiedel and H.-U. Reissig, *Curr. Org. Chem.*, 2019, **23**, 2976.
- (a) S. Li, J. Lv and S. Luo, *Org. Chem. Front.*, 2018, **5**, 1787; (b) T. Zhang, D. Ji and J. Sun, *Org. Biomol. Chem.*, 2023, **21**, 3340; (c) C. Peng, Q. Guo, G.-X. Xu, L. Huo, W. Wu, T.-Y. Chen, X. Hong and P. Hu, *J. Am. Chem. Soc.*, 2024, **146**, 14422; (d) D.-M. Cui, Z.-L. Zheng and C. Zhang, *J. Org. Chem.*, 2009, **74**, 1426; (e) H. Zhou, Z. Wei, J. Zhang, H. Yang, C. Xia and G. Jiang, *Angew. Chem., Int. Ed.*, 2017, **56**, 1077; (f) J. Zhang, L. Zhu, K. Shen, H. Yang, X.-C. Hang and G. Jiang, *Chem. Sci.*, 2019, **10**, 1070.
- For selected recent reviews, see: (a) P. Koschker and B. Breit, *Acc. Chem. Res.*, 2016, **49**, 1524; (b) G. Li, X. Huo, X. Jiang and W. Zhang, *Chem. Soc. Rev.*, 2020, **49**, 2060; (c) R. Blicke, M. Taillefer and F. Monnier, *Chem. Rev.*, 2020, **120**, 13545; (d) H. Wang, Q. Zhang and W. Zi, *Acc. Chem. Res.*, 2024, **57**, 468.
- For selected recent reviews, see: (a) M. Xiang, D. E. Pfaffinger and M. J. Krische, *Chem.–Eur. J.*, 2021, **27**, 13107, for selected recent examples, see: ; (b) M. Xiang, D. E. Pfaffinger, E. Ortiz, G. A. Brito and M. J. Krische, *J. Am. Chem. Soc.*, 2021, **143**, 8849; (c) N. Navaneetha, S. Maurya, P. Behera, S. B. Jadhav, L. R. Magham, J. B. Nanubolu, L. Roy and R. Chegondi, *Chem. Sci.*, 2024, **15**, 20379; (d) S. Maurya, N. Navaneetha,



- P. Behera, J. B. Nanubolu, L. Roy and R. Chegondi, *Angew. Chem., Int. Ed.*, 2025, **64**, e202420106.
- 5 For an early example of radical polymerization of alkoxyallenes, see: T. Yokozawa, M. Tanaka and T. Endo, *Chem. Lett.*, 1987, 1831.
- 6 For selected examples of γ -amino acid and derivative synthesis through radical reactions, see: (a) Y. Miyake, K. Nakajima and Y. Nishibayashi, *J. Am. Chem. Soc.*, 2012, **134**, 3338; (b) L. Chu, C. Ohta, Z. Zuo and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 10886; (c) L. Ruiz Espelt, I. S. McPherson, E. M. Wiensch and T. P. Yoon, *J. Am. Chem. Soc.*, 2015, **137**, 2452; (d) A. Millet, Q. Lefebvre and M. Rueping, *Chem.-Eur. J.*, 2016, **22**, 13464; (e) J. J. Murphy, D. Bastida, S. Paria, M. Fagnoni and P. Melchiorre, *Nature*, 2016, **532**, 218; (f) J. Ma, J. Lin, L. Zhao, K. Harms, M. Marsch, X. Xie and E. Meggers, *Angew. Chem., Int. Ed.*, 2018, **57**, 11193; (g) X. Shen, Y. Li, Z. Wen, S. Cao, X. Hou and L. Gong, *Chem. Sci.*, 2018, **9**, 4562; (h) J. B. McManus, N. P. R. Onuska and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2018, **140**, 9056; (i) A. Trowbridge, D. Reich and M. J. Gaunt, *Nature*, 2018, **561**, 522; (j) J. Ye, I. Kalvet, F. Schoenebeck and T. Rovis, *Nat. Chem.*, 2018, **10**, 1037; (k) R. A. Aycok, C. J. Pratt and N. T Jui, *ACS Catal.*, 2018, **8**, 9115; (l) M. A. Ashley, C. Yamauchi, J. C. K. Chu, S. Otsuka, H. Yorimitsu and T. Rovis, *Angew. Chem., Int. Ed.*, 2019, **58**, 4002; (m) Y. Aramaki, N. Imaizumi, M. Hotta, J. Kumagai and T. Ooi, *Chem. Sci.*, 2020, **11**, 4305; (n) L. Leng, Y. Fu, P. Liu and J. M. Ready, *J. Am. Chem. Soc.*, 2020, **142**, 11972; (o) S. K. Pagire, N. Kumagai and M. Shibasaki, *Chem. Sci.*, 2020, **11**, 5168; (p) E. Le Saux, D. Ma, P. Bonilla, C. M. Holden, D. Lustosa and P. Melchiorre, *Angew. Chem., Int. Ed.*, 2021, **60**, 5357; (q) A. S. K. Lahdenperä, P. D. Bacoş and R. J. Phipps, *J. Am. Chem. Soc.*, 2022, **144**, 22451; (r) L.-C. Wang, Y. Yuan, Y. Zhang and X.-F. Wu, *Nat. Commun.*, 2023, **14**, 7439; (s) Y. Qin, R. Cauwenbergh, S. Pradhan, R. Maiti, P. Franck and S. Das, *Nat. Commun.*, 2023, **14**, 7604; (t) Y. Luo, Y. Zhou, F. Xiao, X. He, Z. Zhong, Q.-L. Zhou, W. Cao, X. Liu and X. Feng, *ACS Catal.*, 2024, **14**, 12031.
- 7 (a) D. L. Martin and R. W. Olse, *GABA in the Nervous System: The View at Fifty Years*, Lippincott Williams & Wilkins, 2000; (b) D.-H. Ngo and T. S. Vo, *Molecules*, 2019, **24**, 2678.
- 8 For selected examples, see: (a) M. Li, O. Gutierrez, S. Berritt, A. Pascual-Escudero, A. Yeşilçimen, X. Yang, J. Adrio, G. Huang, E. Nakamaru-Ogiso, M. C. Kozłowski and P. J. Walsh, *Nat. Chem.*, 2017, **9**, 997; (b) M. Li, S. Berritt, L. Matuszewski, G. Deng, A. Pascual-Escudero, G. B. Panetti, M. Poznik, X. Yang, J. J. Chruma and P. J. Walsh, *J. Am. Chem. Soc.*, 2017, **139**, 16327; (c) R. A. Shelp and P. J. Walsh, *Angew. Chem., Int. Ed.*, 2018, **57**, 15857; (d) G. Deng, M. Li, K. Yu, C. Liu, Z. Liu, S. Duan, W. Chen, X. Yang, H. Zhang and P. J. Walsh, *Angew. Chem., Int. Ed.*, 2019, **58**, 2826; (e) Z. Liu, M. Li, G. Deng, W. Wei, P. Feng, Q. Zi, T. Li, H. Zhang, X. Yang and P. J. Walsh, *Chem. Sci.*, 2020, **11**, 7619; (f) G. Deng, S. Duan, J. Wang, Z. Chen, T. Liu, W. Chen, H. Zhang, X. Yang and P. J. Walsh, *Nat. Commun.*, 2021, **12**, 3860; (g) D. Zou, L. Gan, F. Yang, H. Wang, Y. Pu, J. Li and P. J. Walsh, *Nat. Commun.*, 2021, **12**, 7060; (h) S. Duan, Y. Zi, L. Wang, J. Cong, W. Chen, M. Li, H. Zhang, X. Yang and P. J. Walsh, *Chem. Sci.*, 2022, **13**, 3740; (i) Y. Jiang, D. Liu, M. E. Rotella, G. Deng, Z. Liu, W. Chen, H. Zhang, M. C. Kozłowski, P. J. Walsh and X. Yang, *J. Am. Chem. Soc.*, 2023, **145**, 16045; (j) W.-J. Yue and R. Martin, *Angew. Chem., Int. Ed.*, 2023, **62**, e202310304; (k) Y. Jiang, D. Liu, L. Zhang, C. Qin, H. Li, H. Yang, P. J. Walsh and X. Yang, *Chem. Sci.*, 2024, **15**, 2205.
- 9 Z. Wang, S. Guo, Z. Shen, R. Wei, R. Jiang, G. Liu, Q. Zhou, K. Du and W. Tang, *Chem Catal.*, 2025, **5**, 101331.
- 10 CCDC 2407137: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/ccdc.csd.cc21stlt](https://doi.org/10.5517/ccdc.csd.cc21stlt).
- 11 F.-Y. Zhang and E. J. Corey, *Org. Lett.*, 2006, **6**, 3397.

