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donor complex



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Transition metal/photocatalyst-free synthesis of geminal diamines *via* a sandwich-like photoactive donor–acceptor–donor complex†

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The geminal diamine is an important molecular scaffold widely found in natural products, bioactive compounds, and pharmaceuticals. Nonetheless, the construction of this motif suffers from high temperature, excessive oxidants, and the utilization of transition metals. Herein, we present a transition metal/photocatalyst-free strategy for the synthesis of geminal diamines *via* photoinduced amidation of C(sp³)–H bonds. This reaction features high atom economy, broad substrate applicability, and good functional group tolerance. An unusual sandwich-like ternary donor–acceptor–donor complex resulting from π – π stacking and base action is proposed to be the key photosensitive species.

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Green foundation

1. Different from the traditional photoredox or EDA system, an unusual sandwich-like photosensitive ternary DAD complex is proposed to be the key species resulting from π – π stacking, electrostatic interaction, and base action. This method will provide a convenient and competitive approach for geminal diamine synthesis and provide new inspiration for green reaction construction.
2. Previously, the construction of geminal diamines suffered from high temperatures, excessive oxidants, the utilization of transition metals, and unstable starting materials. Fully avoiding these issues, we herein present a novel transition metal/photocatalyst-free strategy for this valuable synthesis.
3. We think our work is green and atom-economic enough with only a low-cost inorganic base needed and a molecule of methanol being emitted.

Introduction

Geminal diamines, as important molecular scaffolds, are widely found in natural products, bioactive compounds, and pharmaceuticals that are usually of enormous application value.¹ In the past few decades, the synthesis of such compounds has usually been achieved by thermal-driven synthesis and transition metal catalysis (Scheme 1a).² For example, Fu and coworkers reported a copper-catalyzed geminal diamine synthesis utilizing amide as a substrate and TBHP as an oxidant;^{2b} with a similar strategy, Zhao and coworkers took advantage of the nucleophilicity of the lone-pair electrons on

the N atom in benzonitrile to replace the amide as the N source.^{2d} Although these methods provide feasible access to geminal diamine compounds, several problems such as high temperature and excessive oxidant addition still exist, limiting further application of this strategy to some extent.

In the recent decade, photocatalysis has emerged as an environmentally friendly, sustainable, and unique methodology for the construction of various compounds.³ In photocatalytic systems, the reactions are always initiated by single electron transfer (SET) processes induced by photoexcitation of photosensitizers or photosensitive species, generating a range of active radical intermediates and promoting the progression of diverse reactions.⁴ As a significant part of this field, electron donor–acceptor (EDA) photochemistry, which generally involves an *in situ* photosensitive complex consisting of an electron donor and an acceptor, has experienced growth as a selective and durable radical generation approach *via* intra-complex SET, eliminating the requirement for transition metals or dyes.⁵ Tertiary amines are a kind of important active unit and electron donor, and their α -C–H functionalization has received extensive attention (Scheme 1b).⁶ In 2011, Macmillan *et al.* successfully arylated the tertiary amine α -C

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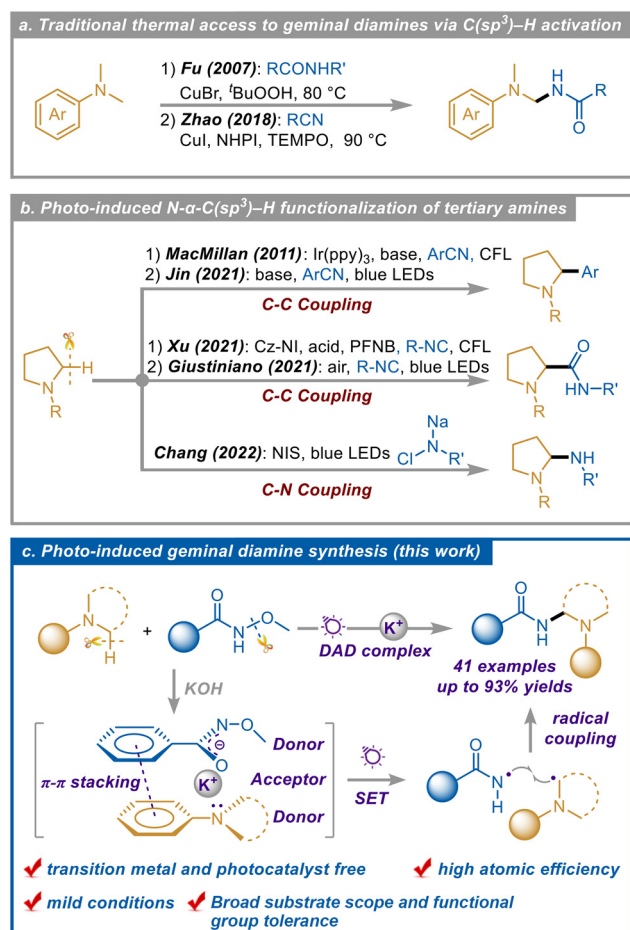
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Scheme 1 Research progress on the synthesis of geminal diamines involving tertiary amines.

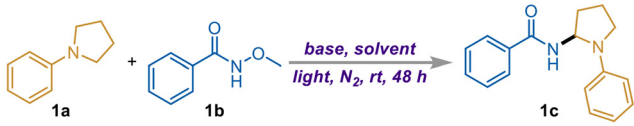
(sp³)-H bonds using Ir as a catalyst and benzonitrile compounds as substrates.⁷ Later, the synthesis of compounds with similar structures was achieved by Jin *et al.* through an EDA process.⁸ In 2021, amidation of the tertiary amine α-C(sp³)-H bond was conducted by the Ugi-type reaction of tertiary amine and isonitrile which was achieved by Xu⁹ through the traditional photocatalytic process and by Giustiniano^{6f} through the EDA process. According to the above reaction systems, the EDA reaction pathway exhibits some advantages including simple conditions, operation convenience, and direct substrate activation. However, the essential matching between the electron donor and the acceptor for forming a stable photosensitive EDA complex always limits the rapid development of this chemistry. Moreover, most of these works focus on the construction of C-C bonds, which is not practical for the synthesis of geminal diamines. Impressively in 2022, the controllable amination of the tertiary amine α-C(sp³)-H bonds was achieved by the Chang group *via* a cyclic imine salt intermediate *in situ*.¹⁰ The system underwent a series of polar addition, elimination, photoinduced homolysis, hydrogen atom transfer, and halogen atom transfer processes, using somewhat

unstable *N*-chloro-*N*-sodio-carbamates as amination reagents. Accordingly, considerable space and demand still exist for the facile and mild access to valuable geminal diamines with abundant-sourced and stable materials.

Based on previous works¹¹ and our previous findings,¹² *N*-alkoxy benzamides can be applied as redox-neutral and atom-efficient amidation reagents for C(sp³)-H bonds *via* metal nitrene intermediates. However, additional photocatalysts or transition metal catalysts were essential in these systems. Employing an EDA pathway instead of these catalytic systems has not been reported due to the inadequate electron-deficient characteristics for *N*-alkoxy benzamides as an electron acceptor. In our design, a strong base may transform the *N*-alkoxy benzamide into an anion that can act as an electron donor instead, and this anion, the corresponding alkali metal cation, and another donor are proposed to form a tertiary photoactive complex for novel photo-transformation. Herein, we developed a photocatalyst/transition metal-free and efficient strategy to achieve photoinduced tertiary amine α-C(sp³)-H activation and C-N coupling based on the radicals generated from the photoexcited intra-SET process of a sandwich-like electron donor-acceptor-donor (DAD) ternary photoactive complex, and geminal diamines were successfully constructed *via* radical coupling (Scheme 1c). The protocol exhibited mild and green conditions, high atom utilization, wide substrate range, and good functional group tolerance.

Results and discussion

According to our previously established system,^{12a} we started the investigation for the model reaction of *N*-phenylpyrrolidine (**1a**) and *N*-methoxybenzamide (**1b**) with *fac*-Ir(ppy)₃ and CuCl as catalysts, Cs₂CO₃ as the base and MeCN as the solvent under irradiation with 405 nm LEDs (Table 1, entry 1). Satisfyingly, the desired geminal diamine product **1c** was successfully obtained in a 27% yield. To our surprise, removing either or both catalysts did not markedly affect the yield of **1c**, indicating the possible formation of a photosensitive species that was similar to the EDA complex in this reaction system (entries 2–4). Various bases including KO^tBu, KOH, LiOH, NaOH, K₃PO₄, and DIPEA were tested then (entries 4–11), suggesting that strong bases with potassium ions significantly boosted the production of **1c** with KOH appearing to be the best choice (entry 6). Further increasing the equivalents of KOH provided an enhanced yield of 76% (entry 7). Different types of solvents were also examined, showing acetonitrile to still be the best one (entries 12–15). We were pleased to find that as the illumination wavelength of the LEDs changed (entries 16–18), the yield of **1c** finally reached its highest point of 92% at 395 nm (entry 17). Additionally, variations in leaving groups exhibited no positive effects (Table S1,† entries 19–21), and only *N*-ethoxybenzamide delivered the desired product in a comparable yield when the reaction time was long enough. Control experiments showed that the reaction gave a decreased yield when it was exposed to water or air (entries 22 and 23),

Table 1 Optimization of the reaction conditions^a


Entry	Base	Solvent	Light	Yield ^b (%)
1 ^{c,d}	Cs ₂ CO ₃	MeCN	405 nm	22
2 ^{c,e}	Cs ₂ CO ₃	MeCN	405 nm	17
3 ^{c,f}	Cs ₂ CO ₃	MeCN	405 nm	24
4 ^c	Cs ₂ CO ₃	MeCN	405 nm	26
5 ^c	KO ^t Bu	MeCN	405 nm	45
6 ^c	KOH	MeCN	405 nm	50
7	KOH	MeCN	405 nm	76
8 ^c	LiOH	MeCN	405 nm	40
9 ^c	NaOH	MeCN	405 nm	38
10 ^c	K ₃ PO ₄	MeCN	405 nm	6
11 ^c	DIPEA	MeCN	405 nm	14
12	KOH	DCE	405 nm	Trace
13	KOH	Acetone	405 nm	15
14	KOH	MeOH	405 nm	Trace
15	KOH	DMSO	405 nm	42
16	KOH	MeCN	365 nm	68
17	KOH	MeCN	395 nm	92
18	KOH	MeCN	455 nm	N.D.

^a Reaction conditions: **1a** (0.1 mmol), **1b** (3 equiv.), base (2 equiv.), and solvent (2 mL) under N₂ and irradiation from 30 W LEDs for 48 h.

^b Isolated yield. ^c 1 equiv. of the base was added. ^d 0.2 mol% of *fac*-Ir(ppy)₃ and 20 mol% of CuCl was added. ^e 0.2 mol% of *fac*-Ir(ppy)₃ was added. ^f 20 mol% of CuCl was added.

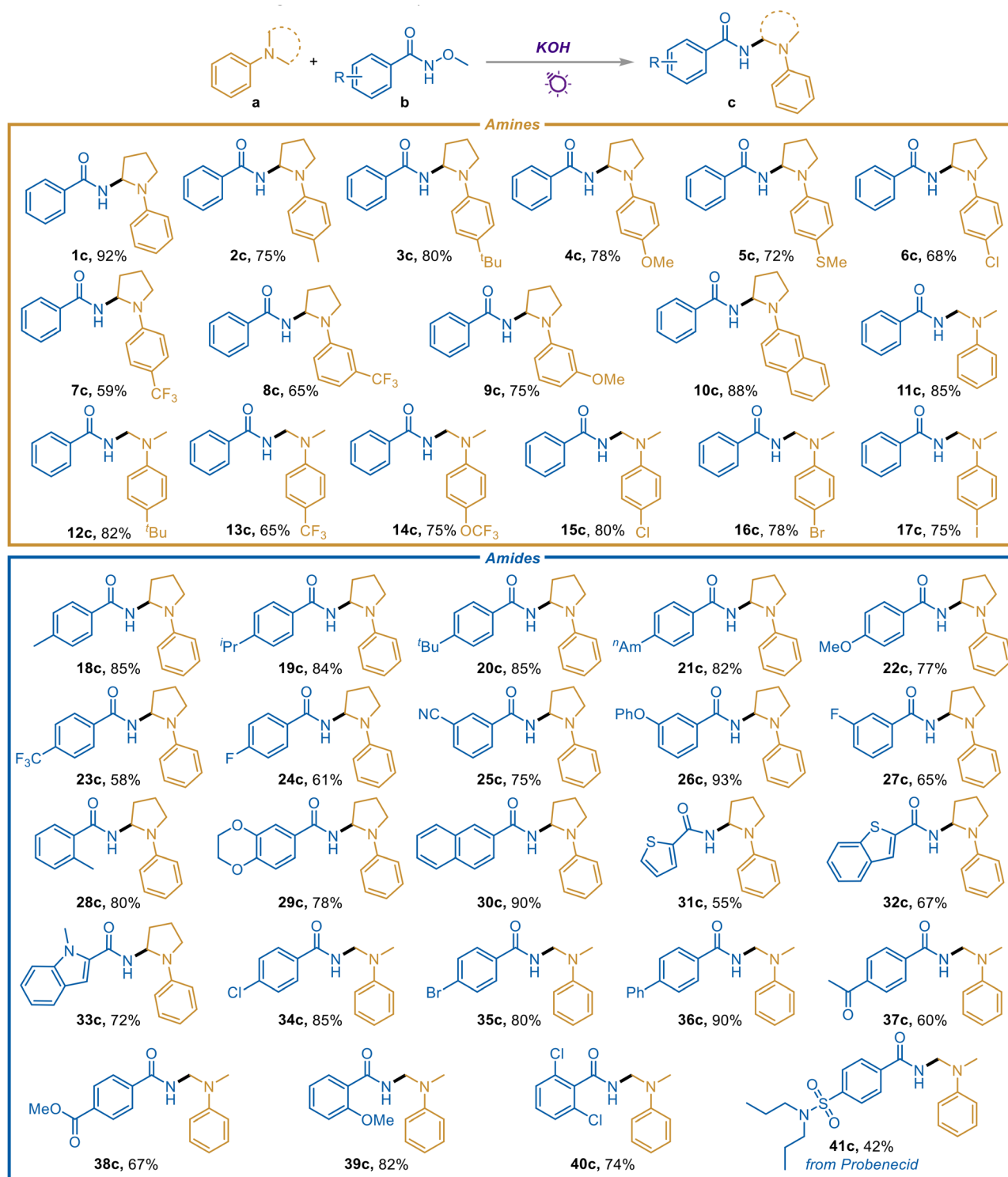
and the reaction would not occur without light as an energy source (entry 24).

With the optimized reaction conditions in hand, the scope of tertiary amines was investigated first (Scheme 2). To our delight, kinds of *N*-aryl pyrrolidines with electron-donating groups including methyl (**2c**), *tert*-butyl (**3c**), methoxyl (**4c** and **9c**), and methylthio (**5c**) were all suitable substrates, delivering the corresponding *gem*-diamines in good yields. Compounds containing trifluoromethyl are beneficial for drug discovery and the development of new materials. Significantly, trifluoromethyl-substituted *N*-aryl pyrrolidines at *para*- and *meta*-positions also provided the corresponding products smoothly (**7c** and **8c**). When naphthyl pyrrolidine was employed as a substrate, **10c** was obtained in an excellent yield, possibly due to the enlarged conjugation system and the promoted light absorption capacity. Furthermore, we were pleased to find that dimethyl arylamines with various functional groups were also effective candidates (**11c–17c**), and the reaction efficiency was generally higher than that of *N*-aryl pyrrolidines. As vital synthons, halogen-substituted *N*-aryl pyrrolidines and dimethyl arylamines were all demonstrated to be compatible substrates, offering a good chance of further derivatization (**6c** and **15c–17c**).

Subsequently, diverse amides were examined to extend the application scope (Scheme 2). It was gratifying to observe that a variety of electron-donating group substituted aromatic amides including alkyl (**18c–21c** and **28c**) and ether (**22c**, **26c**,

29c, and **39c**) modified ones can furnish the corresponding *gem*-diamines in significant yields. The substituted position showed no obvious influence (**18c** and **28c**, **24c** and **27c**). Besides, heterocyclic compounds are often considered to be toxic to metal catalysts, but in our transition metal-free system, the heteroaryl amides reacted smoothly and offered the hetero-aromatic-containing geminal diamines effectively (**31c–33c**). Notably, halogen-substituted amides (**24c**, **27c**, **34c**, **35c**, and **40c**) were readily converted into the corresponding *gem*-diamines efficiently, rendering a wide platform for further derivatization. Even as an electron donor, the amide substrates are still gratifyingly tolerant to various electron-withdrawing groups including trifluoromethyl (**23c**), cyano (**25c**), acetyl (**37c**), and ester (**38c**), and the desired *gem*-diamines were obtained in good yields. An amide derived from Probenecid, which is primarily used in treating gout and hyperuricemia,¹³ was also tested, and the drug motif was successfully introduced to the α -amido tertiary amine structure (**41c**), facilitating the development of this method in further drug discovery.

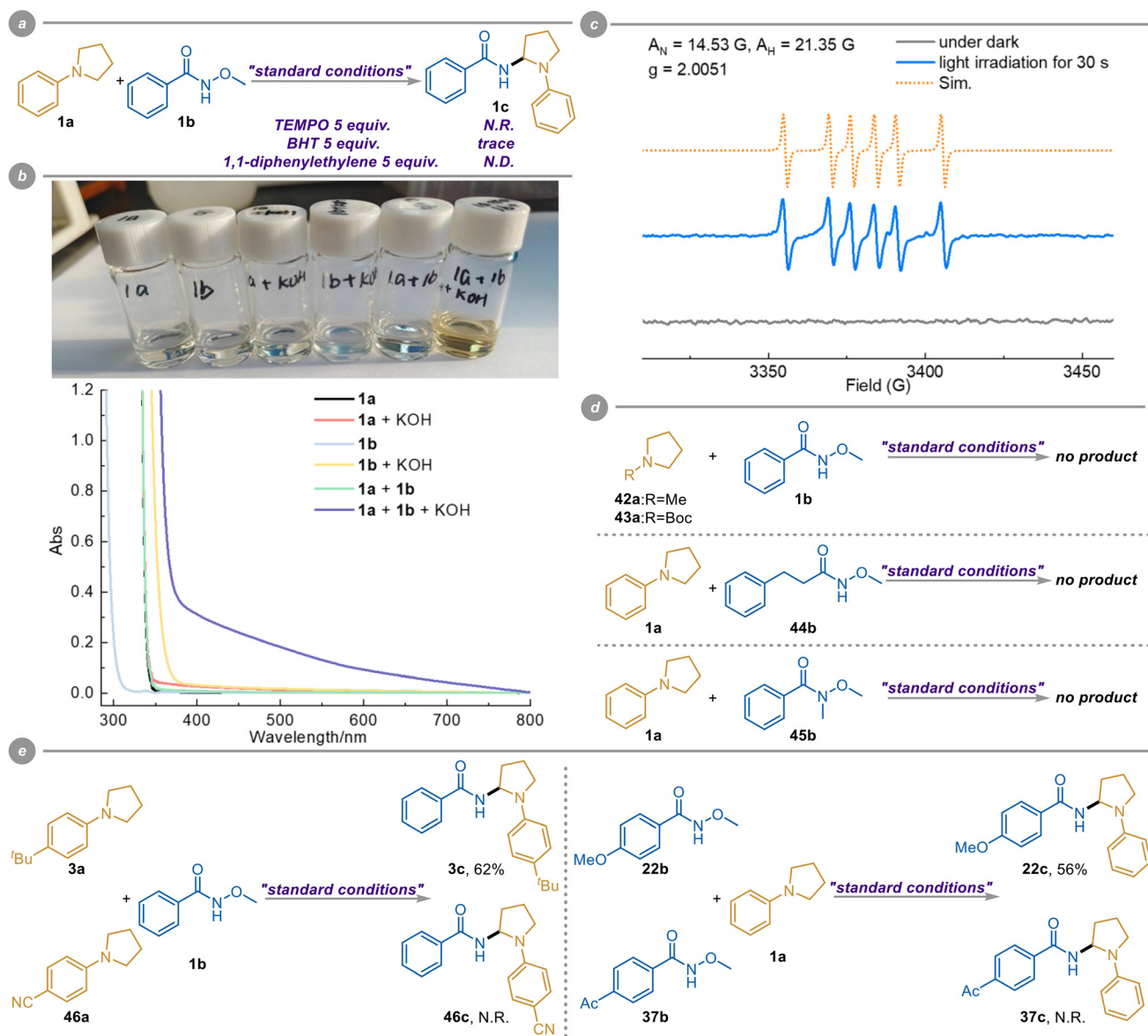
To explore the reaction mechanism of this catalyst-free system, several mechanistic experiments were conducted. When stoichiometric radical quenchers including 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), 2,6-di-*tert*-butyl-4-methylphenol (BHT), and 1,1-diphenyl-ethylene were respectively added to the reaction system, the yields of **3a** were slashed dramatically, and the corresponding radical adducts were observed in High-Resolution Mass Spectrometry (HRMS) analyses, indicating that the reaction underwent a radical pathway (Scheme 3a, for details see the ESI†). To further investigate the photosensitive species inside the simple system, UV-visible absorption spectroscopy was performed on different combinations of the components. As displayed in Scheme 3b (for details see the ESI†), no obvious absorption was observed in the visible range for either **1a** or **1b**, or a simple mixture of **1a** and **1b**. The addition of KOH would slightly enhance the absorption of **1a** or **1b**, but the outcomes were still weak in the range over 390 nm. Exhilaratingly, a ternary mixture of **1a**, **1b**, and KOH emerged with strong absorption at values over 380 nm, indicating that a ternary complex of **1a**, **1b**, and K⁺ with the ability to absorb light successfully formed *in situ*. A distinct color change could also be observed in the real photograph. In addition, electron spin-resonance (ESR) experiments were carried out to further distinguish the radical category (Scheme 1c, for details see the ESI†). The ESR spectrum of a mixture of *N,N*-dimethyl-aniline (**11a**) and *N*-methoxybenzamide (**1b**) in MeCN with 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) as a radical spin trap under dark conditions showed no signal of a trapped radical. After irradiation for 30 s, an obvious sextet signal ($g = 2.0051$, $A_N = 14.53$ mT, $A_H = 21.35$ mT) was observed, indicating the appearance of a carbon-centered radical¹⁴ (Scheme 3d). Furthermore, the key factors for the formation process of the ternary photosensitive complex were studied by substrate control experiments (Scheme 3d & e). When aliphatic tertiary amine 1-methyl pyrrolidine (**42a**), secondary amide *tert*-butyl pyrrolidine-1-carboxylate (**43a**), or aliphatic amide *N*-methoxy-3-phenylpropanamide



Scheme 2 Substrate scope. Reaction conditions: amines (**a**, 0.2 mmol, 1 equiv.), amides (**b**, 3 equiv.), KOH (2 equiv.), MeCN (2 mL) under N₂ and irradiation from 30 W 395 nm LEDs for 48 h.

(**44b**) was respectively employed as the substrate instead, no desired product was observed, implying that the π - π stacking interaction between the aromatic rings of the two substrates

was vital for the formation of the photosensitive species. A tertiary amide *N*-methoxy-*N*-methylbenzamide (**45b**) without a reactive hydrogen was also tried and no product was provided,

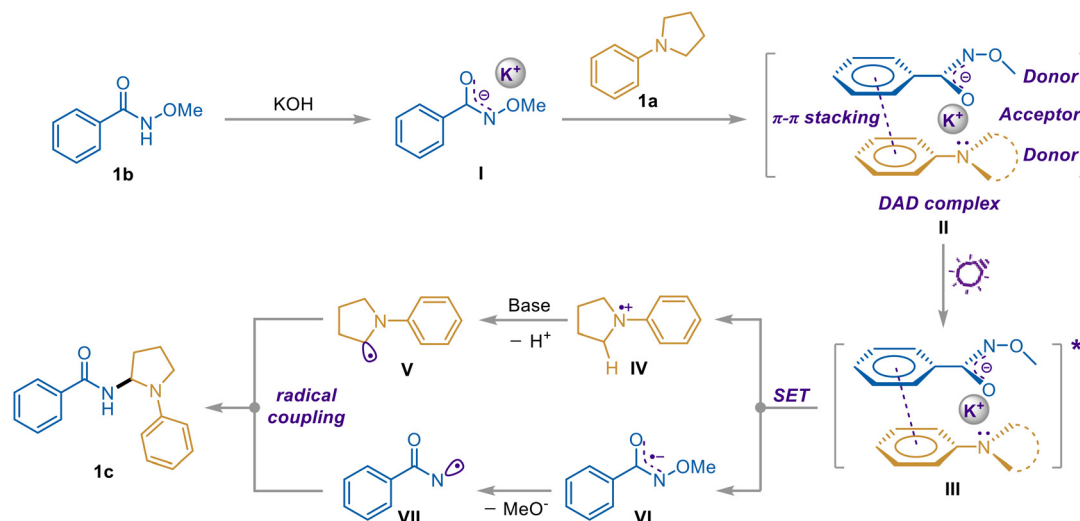


Scheme 3 Mechanistic studies. (a) Control experiments with TEMPO, BHT, and 1,1-diphenylethylene. (b) UV-vis absorption spectrum. (c) Electron spin-resonance (ESR) spectrum. (d) Control experiments with different types of substrates. (e) Competition experiments.

demonstrating the importance of the *in situ* deprotonation of **1b** with KOH for the formation of the photosensitive complex. Moreover, the competition reaction of **3a** with **46a** and **22b** with **37b** showed that the assembling of the DAD complex favored aromatics with a denser electron density. These results further demonstrated that both substrate **a** and **b** acted as electron donors in the *in situ* formed complex.

Based on the above results and our research experience,^{12a} a plausible reaction mechanism for the present transition metal/photocatalyst-free synthesis of geminal diamines is proposed in Scheme 4. Initially, KOH deprotonates **1b** (pK_a 8.88)¹⁵ to form the amide anion **I**, transforming **1b** from a relatively electron-deficient amide structure to an electron-rich conju-

gated anionic structure. Consequently, the electron-donor anion **I**, the electron-acceptor cation K^+ , and another electron-donor tertiary amine **1a** can form a sandwich-like ternary photosensitive DAD complex *in situ* via π - π stacking and electrostatic interaction. The photoactive complex **II** flips to its excited state **III** under light irradiation, followed by an intra-SET process to generate the tertiary amine radical cation **IV** and the amide radical anion **VI**. With the assistance of base, the N - α -carbon radical **V** is delivered by eliminating the N - α -proton of **IV** (confirmed by EPR). Meanwhile, removing the methoxide anion as a leaving group from **VI** provides the nitrogen radical **VII**. Finally, a dual-radical coupling reaction between **V** and **VII** results in the desired *gem*-diamine **1c**.



Scheme 4 Proposed reaction pathway.

Conclusions

Overall, we herein develop a transition metal/photocatalyst-free method for the synthesis of valuable geminal diamines under extremely mild and simple conditions with high atom economy and good functional group compatibility. Different from the traditional EDA system, an unusual sandwich-like photosensitive ternary DAD complex is proposed to be the key species resulting from π - π stacking, electrostatic interaction, and base action. We believe that this method will provide an alternative and competitive approach for geminal diamine synthesis and also give some new inspiration for the activation and construction of special structures without photosensitizers.

Author contributions

Y.J. supervised the project. Y.J., M.L., S.-X.L., and L.Y. guided the project. Y.J., Z.X., Z.C., and S.L. conceived and designed the study. All authors performed and analyzed the experiments. Z.X., Z.C., S.L., and Y.J. wrote and revised the paper.

Data availability

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

Conflicts of interest

There are no conflicts to declare.

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References

- (a) Y. Nishimura, W. Wang, S. Kondo, T. Aoyagi and H. Umezawa, *J. Am. Chem. Soc.*, 1988, **110**, 7249–7250; (b) H. Mitsunuma, M. Shibasaki, M. Kanai and S. Matsunaga, *Angew. Chem., Int. Ed.*, 2012, **51**, 5217–5221.
- (a) V. V. Zhdankin, M. McSherry, B. Mismash, J. T. Bolz, J. K. Woodward, R. M. Arbit and S. Erickson, *Tetrahedron Lett.*, 1997, **38**, 21–24; (b) Y. Zhang, H. Fu, Y. Jiang and Y. Zhao, *Org. Lett.*, 2007, **9**, 3813–3816; (c) X. Liu, Y. Zhang, L. Wang, H. Fu, Y. Jiang and Y. Zhao, *J. Org. Chem.*, 2008, **73**, 6207–6212; (d) B. Lin, S. Shi, Y. Cui, Y. Liu, G. Tang and Y. Zhao, *Org. Chem. Front.*, 2018, **5**, 2860–2863; (e) S. K. Singh, N. Chandna and N. Jain, *Org. Lett.*, 2017, **19**, 1322–1325; (f) Q. Xia and W. Chen, *J. Org. Chem.*, 2012, **77**, 9366–9373; (g) T. Song, Y. Luo, K. Wang, B. Wang, Q. Yuan and W. Zhang, *ACS Catal.*, 2023, **13**, 4409–4420.
- (a) C. R. Stephenson, T. P. Yoon and D. W. MacMillan, *Visible light photocatalysis in organic chemistry*, John Wiley & Sons, 2018; (b) K. L. Skubi, T. R. Blum and T. P. Yoon, *Chem. Rev.*, 2016, **116**, 10035–10074; (c) N. A. Romero and D. A. Nicewicz, *Chem. Rev.*, 2016, **116**, 10075–10166; (d) J. Xuan and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 6828–6838; (e) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322–5363; (f) H.-T. Ji, K.-L. Wang, W.-T. Ouyang, Q.-X. Luo, H.-X. Li and W.-M. He, *Green Chem.*, 2023, **25**, 7983–7987; (g) J. Liu,

- L. Guo, Z. Chen, Y. Guo, W. Zhang, X. Peng, Z. Wang and Y.-F. Zeng, *Chem. Commun.*, 2024, **60**, 3413–3416.
- 4 (a) I. Ghosh, T. Ghosh, J. I. Bardagi and B. König, *Science*, 2014, **346**, 725–728; (b) M. H. Shaw, J. Twilton and D. W. C. MacMillan, *J. Org. Chem.*, 2016, **81**, 6898–6926; (c) L. Marzo, S. K. Pagire, O. Reiser and B. König, *Angew. Chem., Int. Ed.*, 2018, **57**, 10034–10072; (d) P. Xiang, K. Sun, S. Wang, X. Chen, L. Qu and B. Yu, *Chin. Chem. Lett.*, 2022, **33**, 5074–5079; (e) S. Dutta, J. E. Erchinger, F. Strieth-Kalthoff, R. Kleinmans and F. Glorius, *Chem. Soc. Rev.*, 2024, **53**, 1068–1089.
 - 5 (a) C. G. S. Lima, T. de M. Lima, M. Duarte, I. D. Jurberg and M. W. Paixão, *ACS Catal.*, 2016, **6**, 1389–1407; (b) J. Wu, L. He, A. Noble and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2018, **140**, 10700–10704; (c) M.-C. Fu, R. Shang, B. Zhao, B. Wang and Y. Fu, *Science*, 2019, **363**, 1429–1434; (d) D. Leifert and A. Studer, *Angew. Chem., Int. Ed.*, 2020, **59**, 74–108; (e) G. E. M. Crisenza, D. Mazzarella and P. Melchiorre, *J. Am. Chem. Soc.*, 2020, **142**, 5461–5476; (f) A. K. Wortman and C. R. J. Stephenson, *Chem*, 2023, **9**, 2390–2415; (g) M. Sharique, B. Matsuo, A. Granados, S. Kim, M. Arshad, H. Oh, V. E. Wu, M. Huang, A. Csakai, L. A. Marcaurelle and G. A. Molander, *Chem. Sci.*, 2023, **14**, 14193–14199; (h) L. van Dalsen, R. E. Brown, J. A. Rossi-Ashton and D. J. Procter, *Angew. Chem., Int. Ed.*, 2023, **62**, e202303104; (i) S. M. Treacy, D. R. Vaz, S. Noman, C. Tard and T. Rovis, *Chem. Sci.*, 2023, **14**, 1569–1574; (j) G. Guo, X. Li, J. Ma, Y. Shi, J. Lv and D. Yang, *Chin. Chem. Lett.*, 2024, **35**, 110024; (k) M.-H. Zhou, J. Jiang and W.-M. He, *Chin. Chem. Lett.*, 2025, **36**, 110446; (l) J. D. Lasso, D. J. Castillo-Pazos, J. M. Salgado, C. Ruchlin, L. Lefebvre, D. Farajat, D. F. Perepichka and C.-J. Li, *J. Am. Chem. Soc.*, 2024, **146**, 2583–2592; (m) T. Yan, J. Yang, K. Yan, Z. Wang, B. Li and J. Wen, *Angew. Chem., Int. Ed.*, 2024, **63**, e202405186; (n) X.-L. Huang, D.-L. Zhang, Q. Li, Z.-B. Xie, Z.-G. Le and Z.-Q. Zhu, *Org. Lett.*, 2024, **26**, 3727–3732.
 - 6 (a) Y. Zhang, H. Peng, M. Zhang, Y. Cheng and C. Zhu, *Chem. Commun.*, 2011, **47**, 2354–2356; (b) F. Alonso, A. Arroyo, I. Martín-García and Y. Moglie, *Adv. Synth. Catal.*, 2015, **357**, 3549–3561; (c) L. Niu, S. Wang, J. Liu, H. Yi, X.-A. Liang, T. Liu and A. Lei, *Chem. Commun.*, 2018, **54**, 1659–1662; (d) B. T. Matsuo, J. T. M. Correia and M. W. Paixão, *Org. Lett.*, 2020, **22**, 7891–7896; (e) C. Russo, J. Amato, G. C. Tron and M. Giustiniano, *J. Org. Chem.*, 2021, **86**, 18117–18127; (f) C. Russo, G. Graziani, R. Cannalire, G. C. Tron and M. Giustiniano, *Green Chem.*, 2022, **24**, 3993–4003; (g) X. Li, H. Zhao, L. Meng, J. Dong, C. Yang, Z. Wei, X. Wang, J. Xu and B. Fan, *J. Org. Chem.*, 2023, **88**, 5300–5310.
 - 7 A. McNally, C. K. Prier and D. W. C. MacMillan, *Science*, 2011, **334**, 1114–1117.
 - 8 C. Xu, F.-Q. Shen, G. Feng and J. Jin, *Org. Lett.*, 2021, **23**, 3913–3918.
 - 9 M.-J. Yi, H.-X. Zhang, T.-F. Xiao, J.-H. Zhang, Z.-T. Feng, L.-P. Wei, G.-Q. Xu and P.-F. Xu, *ACS Catal.*, 2021, **11**, 3466–3472.
 - 10 W. Lee, D. Kim, S. Seo and S. Chang, *Angew. Chem., Int. Ed.*, 2022, **61**, e202202971.
 - 11 (a) Z. Zhang, Y. Deng, M. Hou, X. Lai, M. Guan, F. Zhang, R. Qi and G. Qiu, *Chem. Commun.*, 2022, **58**, 13644–13647; (b) S. Xie, S. Tang, M. Hou, W. Xie, M. Guan, T. Bai, L. He and G. Qiu, *Org. Lett.*, 2024, **26**, 11134–11139.
 - 12 (a) J. Lei, M. Li, Q. Zhang, S. Liu, H. Li, L. Shi, W.-F. Jiang, C. Duan and Y. Jin, *Org. Lett.*, 2023, **25**, 2300–2305; (b) Z. Gan, J. Chen, H. Wang, Z. Xue, Z. Chen, Y. Zhang, L. Wang, H. Zi, S. Liu, L. Shi and Y. Jin, *Org. Lett.*, 2024, **26**, 7751–7756; (c) R. Cui, Q. Liao, Y. Zhao, L. Wang, Y. Zhang, S. Liu, Z. Gan, Y. Chen, Y. Shi, L. Shi, M. Li and Y. Jin, *Org. Lett.*, 2024, **26**, 8222–8227; (d) Y. Zhang, D. Fu, Z. Chen, R. Cui, W. He, H. Wang, J. Chen, Y. Chen, S.-J. Li, Y. Lan, C. Duan and Y. Jin, *Nat. Commun.*, 2024, **15**, 8619.
 - 13 S. E. McKinney, H. M. Peck, J. M. Boche, B. B. Byham, G. S. Schuchardt and K. H. Beyer, *J. Pharmacol. Exp. Ther.*, 1951, **102**, 208–214.
 - 14 G. R. Buettner, *Free Radical Biol. Med.*, 1987, **3**, 259–303.
 - 15 J. E. Bartmess, in *PATAI'S Chemistry of Functional Groups*, 2010, DOI: [10.1002/9780470682531.pat0506](https://doi.org/10.1002/9780470682531.pat0506).