

Heterocycles

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## **Construction of Bridged Benzazepines via Photo-Induced Dearomatization**

Ting-Ting Song, Yong-Kang Mei, Yan Liu, Xiao-Yu Wang, Shi-Yu Guo, Ding-Wei Ji, Boshun Wan, Weiming Yuan,\* and Qing-An Chen\*

Abstract: Bridged benzazepine scaffolds, possessing unique structural and physicochemical activities, are widespread in various natural products and drugs. The construction of these skeletons often requires elaborate synthetic effort with low efficiency. Herein, we develop a simple and divergent approach for constructing various bridged benzazepines by a photocatalytic intermolecular dearomatization of naphthalene derivatives with readily available  $\alpha$ -amino acids. The bridged motif is created via a cascade sequence involving photocatalytic 1,4-hydroaminoalkylation, alkene isomerization and cyclization. Interestingly, the diastereoselectivity can be regulated through different reaction modes in the cyclization step. Moreover, aminohydroxylation and its further bromination have also been demonstrated to access highly functionalized bridged benzazepines. Preliminary mechanistic studies have been performed to get insights into the mechanism. This method provides a divergent synthetic approach for construction of highly functionalized bridged benzazepines, which have been otherwise difficult to access.

### Introduction

Bridged benzazepine scaffolds bearing hybrid 2D/3D fused rings are prevalent units among many natural products and bioactive compounds and have drawn increasing interest in medicinal chemistry (Scheme 1a). For example, the natural

[\*] T.-T. Song, Y.-K. Mei, Y. Liu, X.-Y. Wang, S.-Y. Guo, D.-W. Ji, B. Wan, Q.-A. Chen Dalian Institute of Chemical Physics, Chinese Academy of Sciences

457 Zhongshan Road, Dalian 116023 (China) E-mail: qachen@dicp.ac.cn

Y.-K. Mei, Y. Liu, X.-Y. Wang, Q.-A. Chen University of Chinese Academy of Sciences Beijing 100049 (China)

W. Yuan

Key Laboratory of Material Chemistry for Energy Conversion and Storage, Ministry of Education, Hubei Key Laboratory of Bioinorganic Chemistry and Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology Wuhan 430074 (China) E-mail: yuanwm@hust.edu.cn

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product alkaloid aphanorphine has attracted considerable attention due to its potential pharmacological activity.<sup>[1]</sup> The alkaloid ribasine with bridged benzazepine skeleton has been verified to exhibit antitumor activity.<sup>[2]</sup> Additionally, varenicline, based on a bridged benzazepine scaffold, has been marketed to treat smoking addiction.<sup>[3]</sup> However, the preparation of these intriguing ring systems often requires elaborate synthetic effort from pre-functionalized substrates with low step economy. Thus, developing a novel and divergent method for the construction of bridged benzazepines is highly desirable.

In recent years, photoinduced dearomatization<sup>[4]</sup> has drawn much attention as it enables rapid access to threedimensional molecules from simple aromatic compounds under mild conditions.<sup>[5]</sup> Despite significant process achieved in this subfield, in most cases, highly reactive electron-rich (hetero)aryl substrates such as indoles, phenols, and pyrroles were employed and the reactions mainly delivered spiro- or fused-ring products.<sup>[6]</sup> In contrast, dearomatizations of less reactive electron-deficient arenes are underdeveloped. In the limited examples, Birch-type reduction constitutes a major dearomatization platform for electron-poor arenes. Therefore, further exploring divergent transformations beyond Birch reduction<sup>[7]</sup> to afford more structurally complex and diverse molecules is highly desirable. Moreover, compared with intramolecular dearomatization reactions,<sup>[8]</sup> the intermolecular variants are more flexible to increase the functional diversity of target dearomative products, and do not require additional steps to prepare complex substrates. However, due to the issues of site- and stereoselectivities control coupled with unfavorable entropy decrease, the intermolecular dearomatization functionalization is still of great challenge.

Curran and other groups have made good contributions in photo-induced intermolecular dearomatization of electron-deficient arenes to afford 1,4-cyclohexadiene scaffolds via radical 1,4-hydrofunctionalization with different radical precursors.<sup>[8e,9]</sup> You and co-workers demonstrated an elegant example of photoinduced 1,2-hydroalkylative dearomatization/cyclization sequence to afford lactam-fused 1,2-dihydronaphthalenes from  $\beta$ -ester-substituted naphthalenes.<sup>[10]</sup> Inspired by these pioneering works and based on our ongoing interests in divergent olefin transformation<sup>[11]</sup> and photocatalytic aminoalkylation,<sup>[12]</sup> we herein report a photocatalytic intermolecular 1,4-hydroaminoalkylation of  $\alpha$ -substituted naphthalene derivatives, coupled with alkene isomerization/cyclization sequence to construct bridged benzazepine scaffolds (Scheme 1c). Various native and





*Scheme 1.* Bridged polycycles and their construction via photo-induced dearomatization.

easily accessible  $\alpha$ -amino acids are used as both alkylation and amination reagents. Of particular note, a divergent diastereoselective synthesis of bridged benzazepines could be furnished by tuning base-promoted or photo-induced intramolecular aza-cyclization. To the best of our knowledge, this reaction represents a rare example of constructing bridged-ring system via photoinduced single-electron transfer approach, despite several intriguing cases via the energy transfer pathway have been reported.<sup>[13]</sup>

### **Results and Discussion**

The initial trial involved the reaction of methyl 1-naphthoate **1a** with *N*-phenyl glycine **2a** in the presence of the photocatalyst 4CzIPN under irradiation with blue LEDs at room temperature (Table 1a). Then  $Cs_2CO_3$  was subsequently added to further promote the isomerization and Michael addition (entry 1). To our delight, the desired bridged product **5a** was produced in 66% yield with excellent diastereoselectivity (>95:5 dr) without the remain of **3a** 

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and **4a** (entry 1). Photosensitizers  $[Ir(ppy)_2(dtbbpy)]PF_6$ (PC-1) and  $Ir(ppy)_3$  (PC-2) were less efficient or inefficient (Table S1, entries 2 and 3). Given the cost of photocatalyst, 4CzIPN was used for subsequent screening while [Ir(dF- $(CF_3)ppy_2(dtbbpy)]PF_6$  (**PC-3**) could also give **5a** with a comparable yield (Table S1, entry 4). Inorganic base NaH-CO<sub>3</sub> was also efficient at promoting the dearomative process (Table S1, entry 5). When organic base 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) was added into reaction system, 5a could not be generated (entry 2, also see Table S1 in the Supporting Information for full details). Replaced THF with MeOH led to low yield (entry 3). The control experiments confirmed the necessity of both photocatalyst and visible light irradiation (entries 4 and 5) and indicated that Na<sub>2</sub>CO<sub>3</sub> is essential to the dearomative process (entry 6). By contrast, a catalytic amount of DBU (0.5 eq.) promoted a thorough isomerization to produce 4a in 69% yield (Table S1, entry 13). Almost no isomerization occurred in the absence of extra base (Table S1, entry 14).

Subsequent efforts were focused on the optimization for the formation of bridged product by using photocatalyst at



#### Table 1: Optimization studies of divergent synthesis of bridged benzazepines.<sup>a</sup>



a) Optimization of one-pot reaction conditions <sup>a</sup>							
	4-	$1a + 2a \rightarrow PC, Na_2CO_3, hv$					
	Ta	+ 2a	then (	Cs <sub>2</sub> CO <sub>3</sub>	ъа		
	Entry	Condi	tions	Yield of <b>5a</b> <sup>b</sup>	dr of <b>5a</b> <sup>b</sup>		
	1	Conditi	ons A	66%	> 95:5		
	2	DBU instead	of Na <sub>2</sub> CO <sub>3</sub>	0	0		
	3	MeOH inste	ad of THF	31%	> 95:5		
	4	Without	4CzIPN	0			
	5	Withou	t light	0			
	6	Without I	Na <sub>2</sub> CO <sub>3</sub>	14%	> 95:5		

<sup>a</sup>Reaction conditions A: Entry 1: **1a** (0.10 mmol), **2a** (0.20 mmol), Na<sub>2</sub>CO<sub>3</sub> (0.40 eq.) and 4CzIPN (4 mol%) were added twice every 24 h, 48 h in total, Cs<sub>2</sub>CO<sub>3</sub> (4.0 eq.). Entries 2-5: Cs<sub>2</sub>CO<sub>3</sub> (2.0 eq.).

c) Optimization of cyclized aminohydroxylation reaction <sup>a</sup>						
1a	+ 2a	PC, base, //		<sup>/2</sup> → 7a		
		then DBU				
Entry	Entry Conditio		Yield of <b>7a</b> <sup>b</sup>	dr of <b>7a</b> <sup>b</sup>		
1	Withou	ut P(OEt) <sub>3</sub>	33%	88:12		
2	<ul> <li>2 Conditions C</li> <li>3 MeCN instead of MeOH</li> <li>4 DCM instead of MeOH</li> <li>5 Without TFA</li> </ul>		90%	85:15		
3			57%	85:15		
4			72%	86:14		
5			0			
6 N <sub>2</sub> atn		nosphere	0			
<sup>a</sup> Reaction conditions C: 4a was isolated by adding DBU (0.5 eq.). 4a (0 mmol), TFA (2.0 eq.), P(OEt) <sub>3</sub> (2.0 eq.), MeOH (0.2 M), RT, air, 12 h.						
<sup>b</sup> Yields and the ratio of diastereomers were determined by GC-FID.						

room temperature (Table 1b). Surprisingly, an inversion of the major diastereomer was obtained during this hydroamination process when treating **4a** with 4CzIPN, delivering reversed diastereomer **5a'** in 93% yield with moderate diastereoselectivity (81:19 dr, entry 1). [Ir(ppy)<sub>2</sub>-(dtbbpy)]PF<sub>6</sub> (**PC-1**) also proved highly efficient at promoting the hydroamination process (entry 2). While Ir(ppy)<sub>3</sub> (**PC-2**) exhibited slightly reduced catalytic activity (entry 3). MeOH was identified as the optimal reaction solvent compared with THF, MeCN and DCM (entry 4, also see Table S2 in the Supporting Information for full details).

19	+ 2a	PC, base, hv	PC, hv	59'	
Ta		24	then DBU		Ja
Entry	Conditions		Yield of <b>5a'</b> <sup>b</sup>	dr of <b>5a'</b> <sup>b</sup>	
1	Conditions B			93%	81:19
2	PC-1 instead of 4CzIPN			92%	81:19
3	lr(	ppy) <sub>3</sub> i	nstead of 4CzIPN	59%	83:17
4	THF instead of MeOH			73%	74:26
5	Without 4CzIPN			30%	79:21
6	In the dark			0	

b) Optimization of hydroamination for reverse diastereoselectivity<sup>a</sup>

<sup>a</sup>Reaction conditions B: **4a** was isolated by adding DBU (0.5 eq.). **4a** (0.10 mmol), 4CzIPN (2 mol%), MeOH (1 mL), blue LEDs, RT, 24 h. **PC-1**: [Ir(ppy)<sub>2</sub>(dtbbpy)]PF<sub>6</sub>.

d)	d) Optimization of cascade aminohydroxylation/bromination <sup>a</sup>						
	1a	+	2a	PC, base, <i>hv</i> then DBU	-	Acid, <mark>O</mark> 2 [Br <sup>-</sup> ]	→ 8a
	Entry		Conditions			Yield of <b>8a</b> <sup>b</sup>	dr of <b>8a</b> <sup>b</sup>
	1		Conditions D			61%	> 95:5
	2	Me	MeCN instead of DCM			48%	94:6
	3	т	THF instead of DCM			38%	93:7
	4	Т	TfOH instead of TFA			28%	87:13
	5	LiBr (2	iBr (2.0 eq.) instead of CuBr <sub>2</sub>			25%	76:24
	6	NaBr (2.0 eq.) instead of CuBr <sub>2</sub>				trace	n.d.
<sup>a</sup> Reaction conditions D: <b>4a</b> was isolated by adding DBU (0.5 eq.). <b>4a</b> (0.10 mmol), TFA (2.0 eq.), CuBr <sub>2</sub> (1.0 eq.), DCM (0.2 M), RT, air, 12 h.							

Additionally, lower yield was obtained in the absence of photosensitizer (entry 5). And no desired product was observed without the irradiation of blue LEDs (entry 6).

After realizing photocatalytic intramolecular hydroamination, we further explored the possibility of aminohydroxylation of **4a** with green  $O_2$  as hydroxyl source. This alkene difunctionalization reaction can further increase the functional diversity of target molecules and provides additional synthetic platform for further elaboration as hydroxyl group is a versatile intermediate. Initial investigations were first performed using isolated product **4a** (Table 1c). Under air, the intramolecular aminohydroxylated product 7a was obtained with 33% yield at room temperature (entry 1). Adding  $P(OEt)_3$  as oxygen extracting reagent improved the yield of **7a** to 90% (entry 2). MeCN and DCM gave slightly lower yields compared with MeOH as solvent (entries 2-4). The control experiments showed that the absence of TFA or O<sub>2</sub> resulted in complete inactivity of this transformation (entries 5 and 6). Unexpectedly, when CuBr<sub>2</sub> was added to the reaction system above, which is often used as a combined oxidant with O<sub>2</sub> in coupling reactions, cascade aminohydroxylation/bromination occurred in one pot to deliver bromination product 8a (Table 1d). The evaluation of solvent indicated that DCM could serve as a more efficient solvent than MeCN or THF (entries 1-3). In comparison, when TFA was replaced by TfOH, only 28% yield of 8a was achieved (entry 4). Other bromine sources such as LiBr or NaBr showed lower reactivity or inactivity (entries 5 and 6).

Subsequently, the one-pot protocol was used to test the generality on aromatic substrates and amino acids (Scheme 2A). Aromatic substrates with diverse ester moieties all performed well under the optimized conditions to provide bridged products 5a-5g in 31-65% yields with excellent diastereoselectivity (>95:5 dr). The structure of 5a has been further confirmed by single crystal X-ray crystallography (CCDC: 2234822).<sup>[14]</sup> A variety of 6-alkoxy-substituted naphthyl esters proved effective substrates for the dearomative reaction, producing diverse substituted benzazepines as products. A wide range of alkoxy substituents, including those containing alkyl (1h), alkoxy (1i), benzyl (1j) and ester (1k) moieties, were well tolerated, providing bridged products (5h-5k) in moderate yields with high diastereoselectivity (>95:5 dr). To our delight, 51 bearing aryl substituent could also be obtained in comparable yield (53%). Moreover, the bromine-containing product at the C5 position (5m) could also be afforded.

Next, substitutions at the N-aryl glycines were evaluated (Scheme 2B). While most of the substituted N-aryl glycines did afford bridged products (5n and 5p-5u) in a one-pot protocol, the difficulty of separation resulted in significantly diminished yields. Thus we opted for a two-step protocol involving isolation of the mixture of 3 and 4 in such cases (5n and 5p–5u). The *para*-substituted *N*-aryl glycines bearing various electron-withdrawing groups performed well, affording the products (5n-5q) in 41–60% yields with excellent diastereoselectivity (>95:5 dr). The structure of 50 has been further confirmed by single crystal X-ray crystallography (CCDC: 2242097).<sup>[14]</sup> And the bridged product (5r) with the electron-donating substituent (4-Pr) could also be obtained in a reasonable yield. Then, metasubstituted and naphthyl N-aryl glycines (5s-5u) were further investigated and could also be tolerated in this protocol. The structure of 5t has been further confirmed by single crystal X-ray crystallography (CCDC: 2242098).<sup>[14]</sup> Probably due to steric hindrance, no desired product (5v or 5w) was observed for the substrates with an o-Me or o-Br group.

Next, we examined the scope for the hydroamination of isolated product 4 for the construction of bridged benzaze-

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pines with reverse diastereoselectivity (Scheme 3a). Substrates bearing a variety of ester moieties were found to provide the desired adducts in good yields (5a'-5d' and 5f'). Furthermore, methoxyl substituted bridged product 5h'could also be accessed. The presence of a chlorine atom at the C4 position of the *N*-phenyl ring in 40 promoted the formation of 5o' in 90 % yield. And *para*-Br and *para*-OCF<sub>3</sub> could also be tolerated (5p' and 5q'). The *ortho*-substituted anilino groups (-Me and -Br) showed good reactivities and excellent diastereoselectivities (>95:5 dr, 5w' and 5x') during the hydroamination under the catalysis of [Ir(dF-(Me)ppy)<sub>2</sub>(dtbbpy)]PF<sub>6</sub>.

Subsequently, the cyclized aminohydroxylation reactions from the corresponding isomerization products were investigated under optimized conditions (Scheme 3b). Initial study with 4a was carried out to provide corresponding hydroxylated product 7a in 85% isolated yield. A variety of substituents including OMe, OAc and 4-OMeC<sub>6</sub>H<sub>4</sub> were well-tolerated, delivering hydroxylated bridged products (7b-7d) in reasonable yields with moderate diastereoselectivities. X-ray structure of 7b is presented to confirm the configuration of the product (CCDC: 2284104).<sup>[14]</sup> And the para- and meta-substituted N-aryl glycines bearing various electron-withdrawing groups (-OCF<sub>3</sub>, -Cl and -F) performed well, affording the products (7e-7g) in 46-70% yields. Substrate scopes of cascade aminohydroxylation/bromination were also examined (Scheme 3c). The model substrate 4a gave product 8a in 55% yield with excellent diastereoselectivity (>95:5 dr). The structure of 8a was confirmed by single crystal X-ray crystallography (CCDC: 2284105).<sup>[14]</sup> Notably, alkoxy- and Cl-substituted arenes were applicable in this protocol, affording the terminal products in 34-68 % yields (8b-8e). The ortho- and meta-substituted N-aryl glycines were feasible substrates and the products 8f and 8g could be obtained in moderate yields with high diastereoselectivity.

To gain insight into the reaction mechanism, a series of experiments were conducted (Scheme 4). First, light on/off experiments were carried out and showed that the reaction was interrupted in the absence of light (Scheme 4a). The quantum yield of the standard reaction forming 3a and 4a is 0.31 (Scheme 4a). These results implied that the necessity of visible light and an extended radical chain process is impracticable. Moreover, the Stern-Volmer luminescence quenching experiments were performed using naphthyl ester 1a and N-phenyl glycine 2a, respectively. The results demonstrated that the luminescence emission of photocatalyst 4CzIPN\* was quenched more efficiently by 2a than by **1a**. It implies that a reductive quenching mechanism is probably enrolled photocatalytic quenching cycle (Scheme 4b). In addition, the dearomative process was suppressed when adding radical inhibitor TEMPO or BHT. And the observation of BHT-adducts by ESI-HRMS suggests that  $\alpha$ amino radical intermediate is likely involved in the reaction (Scheme 4c).

To understand the nature of the two pathways for the construction of bridged motif, various control experiments were conducted (Scheme 4d). No reaction occurred in absence of light even with the addition of the photocatalyst







Reaction condition: 1 (0.30 mmol), 2 (0.60 mmol), Na<sub>2</sub>CO<sub>3</sub> (0.40 eq.) and 4CzIPN (4 mol%) in THF (2 mL) was irradiated by 24 W blue LEDs at room temperature for 24 h, additional 2 (0.60 mmol), Na<sub>2</sub>CO<sub>3</sub> (0.40 eq.), and 4CzIPN (4 mol%) were added after 24 h, 48 h in total. Then Cs<sub>2</sub>CO<sub>3</sub> (4.0 eq.) and ROH (1 mL) were added and stirred at room temperature for 24 h. Isolated yields were given. <sup>a</sup>Step 2: 60 °C. <sup>b</sup>The mixture of 3 and 4 in step 1 was isolated by column chromatography in order to remove *N*-methyl aromatic amines. And Cs<sub>2</sub>CO<sub>3</sub> (0.50 eq.) and MeOH (1 mL) were added in step 2.

Scheme 2. Substrate scope for one pot construction of bridged benzazepines.

(entries 1 and 2). In comparison, direct excitation of 4a promoted Michael addition to provide 5a and 5a' in 30% overall yield with 20:80 dr (entry 3). Besides, the combina-

tion of light and photocatalyst proved highly efficient at promoting the hydroamination process to deliver 5a and 5a' in excellent yield (93%, 19:81 dr, entry 4). A strong

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Isolated yield was given and dr was determined by <sup>1</sup>H NMR analysis of crude compounds. <sup>a</sup>[Ir(dF(Me)ppy)<sub>2</sub>(dtbbpy)]PF<sub>6</sub> (2 mol%) was used instead of 4CzIPN.

Scheme 3. Substrate scope for divergent transformations.



**Research Articles** 





Scheme 4. Mechanistic studies.

inorganic base (Cs<sub>2</sub>CO<sub>3</sub>) could facilitate Michael addition, providing **5a** and **5a**' in excellent yield and diastereoselectivity (99%, >95:5 dr) compared with NaHCO<sub>3</sub> (entries 5 and 6). A transesterification occurred when using EtOH as solvent instead of MeOH to produce **5b** and **5b**' in 63% yield (95:5 dr) (entry 7). Furthermore, corresponding light on/off experiments and quantum yield (0.50) of the standard reaction forming **5a** and **5a**' were also carried out (Scheme 4e), which confirms the importance of light and the impossibility of the radical chain process. Due to the poor solubility of 4CzIPN in methanol, photosensitizer  $[Ir(ppy)_2-(dtbbpy)]PF_6$  (**PC-1**) with the same catalytic activity was used in Stern – Volmer luminescence quenching experiments (Scheme 4f). The results showed that **4a** efficiently quenches the excited state of catalyst **PC-1**, which reveals the electron transfer event involved in this catalytic cycle.

Moreover, interconversion experiments between 5a and 5a' were performed to figure out which one is thermodynamic product. The experimental results showed that 5a could not be converted to 5a' under either alkaline

condition or photocatalytic condition (Scheme 4g, eq. 1). When using 5a' as substrate, high yield (95%) of product 5a was obtained with the aid of base (Scheme 4g, eq. 2). However, no transformation occurred under photo condi-



Scheme 5. Proposed mechanism and synthetic utilizations.

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tion (Scheme 4g, eq. 2). These results indicate that **5a** is a thermodynamically stable product.

Taking the above results together, a plausible mechanism is proposed as outlined (Scheme 5, top left). The photoexcited species PC\* first undergoes a single-electron reduction by 2 to deliver  $PC^{-}$  and N-aryl glycine radical cation A. A subsequent deprotonation and decarboxylation give  $\alpha$ -amino radical **B**. Giese addition of  $\alpha$ -amino radical **B** to naphthalene 1 to forges a new C-C bond with concomitant formation of benzyl radical intermediate C. A second single electron transfer (SET) reduction of radical C by the reductive  $PC^{{\scriptscriptstyle\bullet-}}$  affords carbon anion D and simultaneously regenerates the photocatalyst. Then, protonation of intermediate D yields 1,4-dihydronaphthalene 3. With the aid of extra base, isomerization of double bond occurs to get more stable product 4. Then 4 could undergo two respective pathways (either Michael addition or light-promoted hydroamination) to give desired bridged products 5 and 5'.

In more details (Scheme 5a, top right),<sup>[15]</sup> isomerization product **4** undergoes single-electron oxidation by photoexcited species PC\* to form corresponding aminium radical intermediate **E**. A subsequent intramolecular radical addition provides carbon-centered radical species **F** along with C–N bond formation. The targeted reversed diastereomer **5'** and regular diastereomer **5** could be obtained by successive SET reduction and proton transfer processes. On the other hand, product **5** could also be obtained from **4** via traditional Michael addition in the presence of extra base.

For the proposed mechanism of intramolecular aminohydroxylation (Scheme 5a), compound 4 is firstly oxidized by  $O_2$  to produce  $O_2^{\bullet-}$  and corresponding aminium radical intermediate E. And a subsequent intramolecular radical addition converts E to carbon-centered radical species H. Then intermediate **H** captures  $O_2^{\bullet-}$  to afford an anion **I**, which can obtain a proton to generate the peroxide J. Finally, intermediate **J** undergoes a reduction by  $P(OEt)_3^{[16]}$ to deliver the desired aminohydroxylation product 7. Interestingly, when CuBr<sub>2</sub> was added to the above reaction system, further bromination at para-position of aromatic rings of N-aryl anilines proceeded under oxidative condition. At the same time, probably due to the coordination of CuBr<sub>2</sub>, the cascade aminohydroxylation/bromination products exhibited excellent diastereoselectivity. And a single electron transfer of 7 to  $Cu^{2+}$  generates a radical cation L, which is immediately captured by the nucleophile (Br-) to give a radical intermediate M.<sup>[17]</sup> Then, another electron transfer to  $Cu^{2+}$  deliver the cationic species N. A final H<sup>+</sup> elimination produces the bromination product 8.

To further demonstrate the synthetic potential, scale-up reactions and further modification have been performed. As shown in Scheme 5b, functionalized bridged benzazepines **5a** (1.05 g), **5o** (1.12 g) and **5p** (1.19 g) have been isolated in a gram scale with 60%, 57% and 53% yields, respectively. Basic hydrolytic conditions afforded unprotected carboxylic acids (**9a** and **9o**) in good yields with maintaining excellent diastereoselectivities (>95:5 dr). And alcohol product **10a** was obtained in 89% yield by the reduction of **5a** with LiAlH<sub>4</sub>. Further esterification could give the corresponding product **11a** in 82% yield. In addition, Mitsunobu reaction

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of **10a** was carried out to deliver bridged bisamino product **12a** in 80% yield with retention of the stereoscopic configuration. Furthermore, epiandrosterone derivative **13a** with complex pharmaceutically relevant structure could also be afforded in high yield. An oxidative coupling of **5a** in MeCN/H<sub>2</sub>O promoted by cerium(IV) ammonium nitrate (CAN) occurred to deliver benzidine **14a** in moderate yield.<sup>[18]</sup> Under Pd catalysis, the cross-coupling reaction of **5p** with MeOH gave product **15** bearing a good deprotection *p*-methoxyphenyl (PMP) group.<sup>[19]</sup> Under oxidative condition, the PMP group on the nitrogen could be cleaved efficiently to form a secondary amine. Although its fluorescence is too weak to be purified directly, a subsequently protection by tosyl chloride afforded the desired amide **16** in 68% yield (two steps).

### Conclusion

In conclusion, we have developed a mild and divergent synthetic protocol to convert simple aromatic substrates into value-added and structurally complex bridged benzazepines via a photocatalytic dearomatization. Various native  $\alpha$ -amino acids are used as both alkylation and amination reagents. Mechanistic studies elucidated that the reaction proceeds through a cascade sequence involving photoredox-catalyzed 1,4-hydroaminoalkylation, base-promoted alkene isomerization, and stereodivergent intramolecular hydroamination. The switchable diastereoselectivity could be furnished by the manipulation of basepromoted or photoinduced intramolecular hydroamination. In addition, the functional modifications of the bridged ring skeletons were achieved by one-pot cascade aminohydroxylation/bromination processes. Furthermore, synthetic applications indicated that these products can serve as versatile handle for construction of various bridged benzazepines.

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### Conflict of Interest

The authors declare no conflict of interest.

### **Data Availability Statement**

The data that support the findings of this study are available in the supplementary material of this article. **Keywords:** Amino Acids • Dearomatization • Heterocylces • Photocatalysis • Synthetic Methods

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