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Preparation of (*Z*)-α,β-Disubstituted Enamides via Palladium-Catalyzed Addition of Boronic Acids to Ynamides

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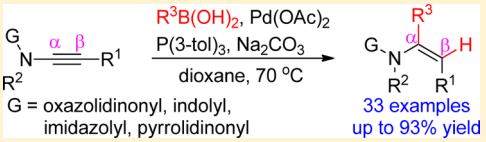
Supporting Information

ABSTRACT: A Pd-catalyzed, highly regio- and stereoselective addition of boronic acids to ynamides has been realized. This protocol generates (*Z*)-α,β-disubstituted enamides in high yields with excellent regio- and stereoselectivity under the mild reaction conditions, thereby providing a good complementary method for the diverse synthesis of multifunctional enamides. A wide collection of functional groups are found to be tolerated. It represents a straightforward and useful means to assemble stereodefined enamides from readily available starting materials.

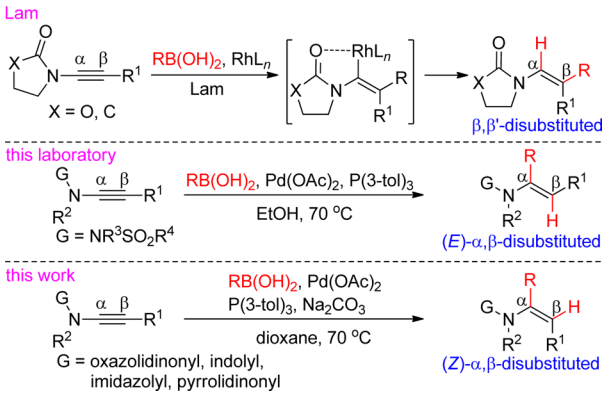


INTRODUCTION

Enamides are versatile building blocks that can be utilized in the heterocycle construction, asymmetric hydrogenation, and synthesis of bioactive molecules, such as salicylihalamides, lobatamides, oximidines, and others.[1] Accordingly, a myriad of efforts have been devoted to the generation of this framework. Despite the impressive advances in this field, it is still highly desirable to develop simple as well as effective methods for the regio- and stereoselective preparation of enamides, particularly the thermodynamically unfavorable *Z*-isomers. Recently, the functionalization of ynamides, mainly featured by hydrometalation, carbometalation, or heterometalation processes, has emerged as an appealing strategy to construct enamides.[2−6]

In particular, by taking advantage of the coordination interaction between oxygen and rhodium atoms, Lam and coworkers successfully achieved an elegant Rh-catalyzed addition of boronic acids to ynamides that produced β,β′-disubstituted enamides in good to excellent regioselectivity (rr ≥ 6:1) (Scheme 1).[7,8] Recent studies in our laboratory have focused on the transformation of ynamides,[9,10] and as an example, we have accomplished a Pd-catalyzed *trans*-addition of boronic acids to *N*-sulfonyl ynamides, giving (*E*)-α,β-disubstituted enamides regio- and stereoselectively under the mild conditions.[10] In contrast, the coupling of boronic acids with ynamides affording stereodefined (*Z*)-α,β-disubstituted enamides is still unrevealed. In this report, a Pd-catalyzed stereospecific addition of boronic acids[10−12] to ynamides leading to (*Z*)-α,β-disubstituted enamides has been achieved. Clearly, it can offer a good complementary method to previous interest[7,10] in the assembly of multisubstituted enamides with high scaffold diversity.

Scheme 1. Summary of Addition of Boronic Acids to Ynamides



RESULTS AND DISCCUSION

Initial studies to optimize the reaction conditions were performed with ynamide **1a** and $PhB(OH)_2$ (**2a**) as the test substrates. Pleasantly, when the reaction was conducted with 5 mol % of $Pd(OAc)_2$, 10 mol % of PPh_3, and 1.5 equiv of Na_2CO_3 in dioxane under a nitrogen atmosphere at 70 °C for 4 h, **3aa** was isolated in 80% yield (Table 1, entry 1). Other bases, including Cs_2CO_3, K_3PO_4, KF, and CsF, resulted in low yield or poor regioselectivity (Table 1, entries 3−6). In addition, switching dioxane to other solvents, such as THF, DMF, and toluene, just led to the inferior results (Table 1, entries 8−10). Then, we examined the ligand for this reaction. Generally, variation of ligands did not affect the regioselectivity of addition; however, it did have a significant impact on the reaction efficiency (Table 1, entries 11−17), and specifically, the utilization of $P(3\text{-tol})_3$ as the ligand afforded the highest efficiency, giving **3aa** in 90% yield with excellent regio- and stereoselectivity. Of note, the reaction could be carried out under an atmosphere of air, nevertheless with somewhat lower yield (Table 1, entry 18). As such, the best reaction conditions found for Pd-catalyzed addition of boronic acids to ynamides consisted of 5 mol % of $Pd(OAc)_2$, 10 mol % of $P(3\text{-tol})_3$, 1.5 equiv of boronic acids, and 1.5 equiv of Na_2CO_3 in dioxane at 70 °C for 4 h.

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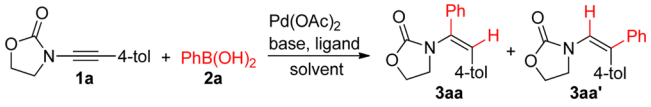
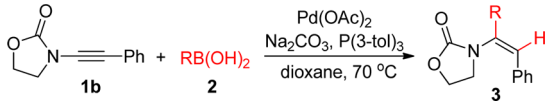
Table 1. Optimization of the Reaction Conditions[a]



entry	base	ligand	solvent	3aa/3aa′[b]	yield (%)[c]
1	Na_2CO_3	PPh_3	dioxane	>20:1	80
2	K_2CO_3	PPh_3	dioxane	>20:1	69
3	Cs_2CO_3	PPh_3	dioxane	>20:1	18
4	K_3PO_4	PPh_3	dioxane	>20:1	34
5	KF	PPh_3	dioxane	>20:1	32
6	CsF	PPh_3	dioxane	2:1	71
7		PPh_3	dioxane	1.5:1	63
8[d]	Na_2CO_3	PPh_3	THF	6:1	87
9[d]	Na_2CO_3	PPh_3	DMF	>20:1	25
10[d]	Na_2CO_3	PPh_3	toluene	>20:1	65
11	Na_2CO_3	$P(2\text{-tol})_3$	dioxane	>20:1	86
12	Na_2CO_3	$P(3\text{-tol})_3$	dioxane	>20:1	90
13	Na_2CO_3	$P(4\text{-tol})_3$	dioxane	>20:1	85
14	Na_2CO_3	$P(2\text{-furyl})_3$	dioxane	>20:1	87
15	Na_2CO_3	$P(4\text{-OMeC}_6H_4)_3$	dioxane	>20:1	78
16	Na_2CO_3	PCy_3	dioxane	>20:1	62
17	Na_2CO_3	dppb	dioxane	>20:1	31
18[e]	Na_2CO_3	$P(3\text{-tol})_3$	dioxane	>20:1	76

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.45 mmol), $Pd(OAc)_2$ (5 mol %), ligand (10 mol %), base (1.5 equiv), and solvent (1.5 mL) at 70 °C for 4 h. [b]Determined by GC. [c]Isolated yield. [d]6 h. [e]Under air atmosphere.

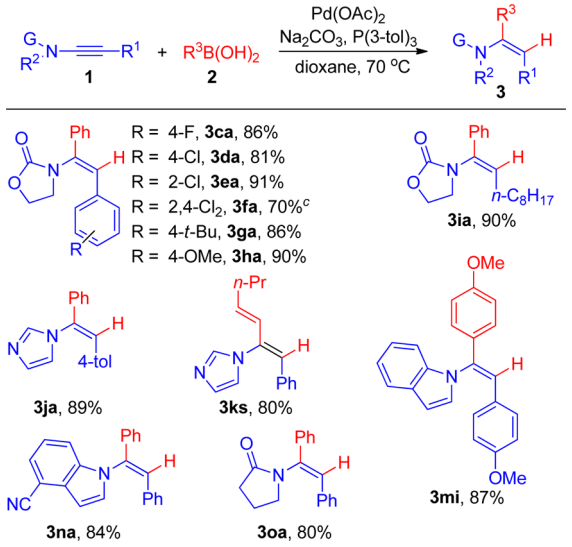
Table 2. Scope of Boronic Acids[a]



entry	R (**2**)	yield (%)[b]
1	Ph (**2a**)	89 (**3ba**)
2	4-F-C_6H_4 (**2b**)	93 (**3bb**)
3	2,4-F_2-C_6H_3 (**2c**)	91 (**3bc**)
4	3-NO_2-C_6H_4 (**2d**)	72 (**3bd**)
5	4-Ac-C_6H_4 (**2e**)	76 (**3be**)
6	4-CN-C_6H_4 (**2f**)	70 (**3bf**)
7	4-CHO-C_6H_4 (**2g**)	65 (**3bg**)
8	4-Cl-C_6H_4 (**2h**)	76 (**3bh**)
9	4-Me-C_6H_4 (**2i**)	86 (**3bi**)
10	3-Me-C_6H_4 (**2j**)	83 (**3bj**)
11	2-Me-C_6H_4 (**2k**)	90 (**3bk**)
12	4-MeO-C_6H_4 (**2l**)	92 (**3bl**)
13	3,4-$(OMe)_2$-C_6H_3 (**2m**)	83 (**3bm**)
14	3,4-methylenedioxyphenyl (**2n**)	87 (**3bn**)
15	2-naphthyl (**2o**)	91 (**3bo**)
16	2-furyl (**2p**)	78 (**3bp**)
17	2-thienyl (**2q**)	76 (**3bq**)
18	(*E*)-styryl (**2r**)	84 (**3br**)
19	(*E*)-1-pentenyl (**2s**)	86 (**3bs**)
20	PhC≡CBF_3K (**2t**)	72 (**3bt**)

[a]Reaction conditions: **1b** (0.3 mmol), **2** (0.45 mmol), $Pd(OAc)_2$ (5 mol %), $P(3\text{-tol})_3$ (10 mol %), Na_2CO_3 (1.5 equiv), and dioxane (1.5 mL) at 70 °C. [b]Isolated yield.

Table 3. Scope of Substrates 1[a,b,c]



[a]Reaction conditions: **1** (0.3 mmol), **2** (0.45 mmol), $Pd(OAc)_2$ (5 mol %), $P(3\text{-tol})_3$ (10 mol %), Na_2CO_3 (1.5 equiv), and dioxane (1.5 mL) at 70 °C for 4–7 h. [b]Isolated yield. [c]rr > 10:1, determined by GC.

After the optimized reaction conditions had been established, the scope of this reaction was investigated using a panel of organoboron reagents (Table 2). Various boronic acids bearing either electron-donating or electron-withdrawing groups in the aryl ring of **2** turned out to be the effective reacting partners, delivering the desired (*Z*)-*α*,*β*-disubstituted enamides **3ba**–**bn** in good to excellent yields with perfect control of regio- and stereoselectivity (Table 2, entries 1–14). Notably, the steric hindrance of **2** seemed to have no detrimental effect on the reaction yield, as demonstrated by the transformation of 4-, 3-, and 2-tolylboronic acids **2i**–**k** (Table 2, entries 9–11). Further, the reaction was applicable to heteroarylboronic acids. For example, the coupling of 2-furylboronic acid (**2p**) and 2-thienylboronic acid (**2q**) proceeded efficiently to form the corresponding products in satisfactory yields (Table 2, entries 16 and 17). In addition to aryl boronic acids, alkenyl boronic acids **2r** and **2s** were also competent substrates, leading to **3br** and **3bs** in 84% and 86% yield, respectively (Table 2, entries 18 and 19). Lastly, the reaction of potassium phenylethynyltrifluoroborate (**2t**) took place smoothly to deliver **3bt** in outstanding regio- and stereoselectivity (Table 2, entry 20). In contrast, $MeB(OH)_2$ (**2u**) was not applicable to this reaction owing to the formation of some complicated byproducts. The single-crystal X-ray diffraction analysis of enamide **3bm** confirmed the regio- and stereochemistry of this Pd-catalyzed addition reaction (see the Supporting Information).

On the other hand, this transformation covers a broad range of ynamides (Table 3). Oxazolidinone-substituted ynamides, including electron-poor and electron-rich ones **1c**–**1h**, all furnished the desired hydrophenylation products in high yields (Table 3, **3ca**–**3ha**). Alkyl ynamide **1i** also underwent the facile coupling to form **3ia** in excellent yield and regioselectivity (Table 3, **3ia**). Remarkably, besides ynamides, ynamines, imidazole-substituted substrates **1j** and **1k**, for example, could also be utilized as the coupling partners without incident (Table 3, **3ja** and **3ks**). Additionally, ynamine **1m**, an indole-derived substrate, was successfully transformed into (*Z*)-*α*,*β*-disubstituted enamine **3mi**[13] in 87% isolated yield (Table 3, **3mi**). Likewise, 1-(phenylethynyl)pyrrolidin-2-one (**1o**) reacted efficiently with **2a** to give **3oa**[14] in high yield, and no erosion of regioselectivity was observed (Table 3, **3oa**).[15]

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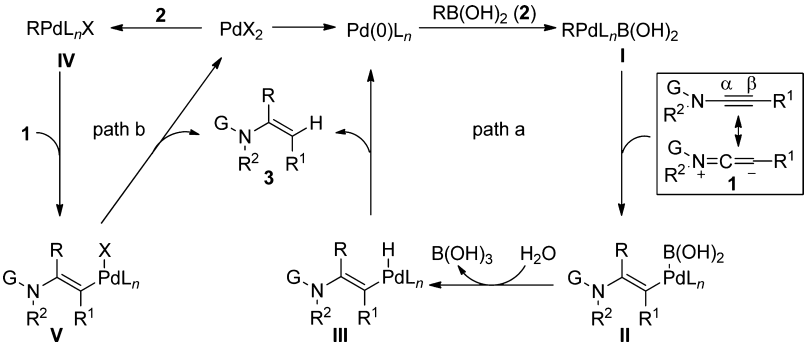
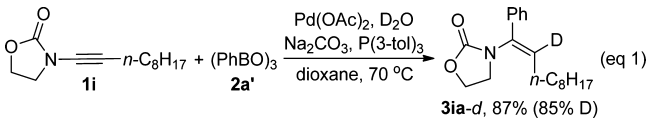
Scheme 2. Possible Mechanism

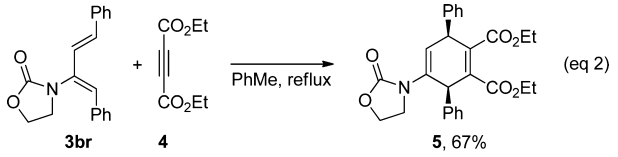


Meanwhile, ynamide **1i** was treated with 0.5 equiv of $(PhBO)_3$[16] and 5 equiv of D_2O under the standard reaction conditions, which resulted in the formation of **3ia**-*d* in 87% yield with 85% deuterium incorporation (eq 1). According to the



above results and previous reports,[10,11] a possible mechanism is proposed in Scheme 2 for this Pd-catalyzed regio- and stereoselective addition of boronic acids to ynamides and related compounds. A palladium intermediate **I**, generated by the oxidative addition of Pd(0) with **2**,[11d,17] undergoes the carbopalladation of **1** to form the species **II** regio- and stereoselectively. Then, the hydrolysis of the Pd−B bond of **II** and subsequent reductive elimination produces **3** and closes the catalytic cycle (Scheme 2, path a). However, another possibility cannot be ruled out at the current stage, which may involve the following steps: (1) generation of **IV** via transmetalation of Pd(II) complexes with boronic acids; (2) carbopalladation of **1** with **IV**, yielding an alkenyl palladium species **V**; and (3) protonolysis of the alkenyl C−Pd bond[18] of **V**, finally delivering **3** with reproduction of the Pd(II) catalyst (Scheme 2, path b).

To demonstrate the synthetic utility of this transformation, 1,3-dienamide **3br** was treated with 1.2 equiv of diethyl acetylenedicarboxylate (**4**) in toluene at reflux for 16 h; as a result, it produced the 1,4-cyclohexadiene derivative **5** in 67% yield upon isolation (eq 2).[19]



CONCLUSION

In summary, a highly regio- and stereoselective addition of boronic acids to ynamides has been accomplished with the readily available $Pd(OAc)_2/P(3\text{-tol})_3$ catalytic system. The reaction produces (*Z*)-*α*,*β*-disubstituted enamides and related compounds in high yields with excellent regio- and stereoselectivity under mild reaction conditions, thereby providing a good complementary method for the diverse synthesis of highly substituted enamides. A broad spectrum of functional groups, such as F, Cl, NO_2, Ac, CHO, CN, OMe, furyl, thienyl, alkenyl, and alkynyl substituents, are well tolerated. Overall, we believe that this protocol offers a simple, direct, and highly useful means to access (*Z*)-*α*,*β*-disubstituted enamides from the readily accessible starting materials.

EXPERIMENTAL SECTION

General. Melting points were measured by a melting point instrument and were uncorrected. Unless otherwise noted, purchased chemicals were used directly from commercial suppliers without further purification. ^{1}H, ^{13}C, and ^{19}F NMR spectra were measured on 400 or 600 MHz NMR spectrometers using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard. Chemical shifts were given in *δ* relative to TMS, and the coupling constants were given in Hz. High-resolution mass spectra (HRMS) analyses were carried out using a TOF MS instrument with an ESI source. Column chromatography was performed with silica gel (300−400 mesh) using petroleum ether/EtOAc as the eluent.

General Procedure for Pd-Catalyzed Addition of Boronic Acids to Ynamides. To a mixture of $P(3\text{-tol})_3$ (9.1 mg, 0.03 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), Na_2CO_3 (47.7 mg, 0.45 mmol), and **2a** (54.9 mg, 0.45 mmol) in 1.5 mL of 1,4-dioxane was added **1a** (60.3 mg, 0.3 mmol) under a N_2 atmosphere. After stirring at 70 °C for 4 h, the reaction mixture was quenched with 5 mL of water, extracted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 2:1) gave 75 mg of **3aa** as a white solid, 90% yield, mp 112−114 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) *δ* 2.40 (s, 3 H), 3.72 (t, *J* = 7.9 Hz, 2 H), 4.47 (t, *J* = 8.6 Hz, 2 H), 6.87 (s, 1 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.35−7.39 (m, 3 H), 7.41−7.44 (m, 2 H), 7.49−7.50 (m, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) *δ* 21.2, 45.2, 62.5, 125.7, 126.9, 128.2, 128.6, 128.7, 129.4, 132.3, 133.6, 136.4, 138.1, 156.3; MS (EI, *m*/*z*): 280 (23), 279 (M^+, 100), 234 (21), 220 (42), 192 (92); HRMS (ESI) calcd for $C_{18}H_{17}NO_2$ (M^+) 279.1259, found 279.1266.

Compound ***3ba***.[20] 71 mg, 89% yield, white solid, mp 103−105 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) *δ* 3.67 (t, *J* = 7.9 Hz, 2 H), 4.43 (t, *J* = 8.1 Hz, 2 H), 6.87 (s, 1 H), 7.29−7.33 (m, 1 H), 7.36−7.44 (m, 7 H), 7.46−7.49 (m, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) *δ* 45.2, 62.4, 125.7, 125.7, 126.8, 128.0, 128.1, 128.6, 128.7, 134.4, 135.1, 136.2, 156.2.

Compound ***3bb***. 79 mg, 93% yield, white solid, mp 129−131 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) *δ* 3.66 (t, *J* = 7.9 Hz, 2 H), 4.43 (t, *J* = 8.2 Hz, 2 H), 6.79 (s, 1 H), 7.05−7.12 (m, 2 H), 7.30−7.31 (m, 1 H), 7.37−7.46 (m, 6 H); ^{13}C NMR ($CDCl_3$, 150 MHz) *δ* 45.2, 62.5, 115.7 (d, *J* = 21.9 Hz), 126.5, 127.7 (d, *J* = 8.3 Hz), 128.1, 128.2, 128.7, 132.6 (d, *J* = 3.2 Hz), 133.6, 135.0, 156.2, 162.9 (d, *J* = 248.8 Hz); ^{19}F NMR ($CDCl_3$, 565 MHz): *δ* −112.5; MS (EI, *m*/*z*): 284 (15), 283 (M^+, 82), 238 (19), 224 (34), 196 (100); HRMS (ESI) calcd for $C_{17}H_{14}FNO_2$ (M^+) 283.1009, found 283.1016.

Compound ***3bc***. 82 mg, 91% yield, white solid, mp 137−139 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) *δ* 3.63 (t, *J* = 7.9 Hz, 2 H), 4.36 (t, *J* = 7.9 Hz, 2 H), 6.57 (s, 1 H), 6.83 (td, *J* = 2.3, 8.8 Hz, 1 H), 6.92 (td, *J* = 1.7, 8.2 Hz, 1 H), 7.29−7.32 (m, 1 H), 7.35−7.50 (m, 5 H); ^{13}C NMR ($CDCl_3$, 150 MHz) *δ* 44.8, 62.7, 104.2 (t, *J* = 26.1 Hz), 111.7 (dd, *J* = 5.6, 21.2 Hz), 121.3 (dd, *J* = 4.0, 11.9 Hz), 128.2, 128.4, 128.7, 129.1, 131.2 (dd, *J* = 4.8, 9.7 Hz), 134.7, 156.3, 160.0 (dd, *J* = 12.5, 251.0 Hz), 163.0 (dd,

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J = 12.3, 261.0 Hz); ^{19}F NMR ($CDCl_3$, 565 MHz): δ −108.9 (d, J = 8.7 Hz), −112.9 (d, J = 8.5 Hz); MS (EI, m/z): 302 (16), 301 (M^+, 93), 256 (22), 242 (59), 214 (100); HRMS (ESI) calcd for $C_{17}H_{13}F_2NO_2$ (M^+) 301.0914, found 301.0919.

Compound ***3bd***. 67 mg, 72% yield, white solid, mp 136−138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.70 (t, J = 7.9 Hz, 2 H), 4.48 (t, J = 8.2 Hz, 2 H), 6.94 (s, 1 H), 7.33−7.44 (m, 5 H), 7.53−7.61 (m, 1 H), 7.77−7.79 (m, 1 H), 8.17−8.19 (m, 1 H), 8.30−8.31 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.0, 62.8, 120.6, 123.3, 128.4, 128.7, 128.8, 128.9, 129.8, 131.6, 132.6, 134.3, 138.6, 148.6, 156.2; MS (EI, m/z): 311 (15), 310 (M^+, 100), 280 (11), 265 (11), 251 (19); HRMS (ESI) calcd for $C_{17}H_{14}N_2O_4$ (M^+) 310.0954, found 310.0965.

Compound ***3be***. 70 mg, 76% yield, white solid, mp 141−143 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.61 (s, 3 H), 3.67−3.70 (m, 2 H), 4.47 (t, J = 8.2 Hz, 2 H), 6.96 (s, 1 H), 7.32−7.34 (m, 1 H), 7.39−7.41 (m, 2 H), 7.43−7.45 (m, 2 H), 7.55 (d, J = 8.5 Hz, 2 H), 7.98 (d, J = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 26.6, 45.2, 62.6, 125.9, 128.4, 128.6, 128.8, 128.9, 129.0, 133.7, 134.7, 137.0, 141.0, 156.3, 197.3; MS (EI, m/z): 308 (11), 307 (M^+, 59), 281 (29), 248 (10), 220 (20); HRMS (ESI) calcd for $C_{19}H_{17}NO_3$ (M^+) 307.1208, found 307.1216.

Compound ***3bf***. 61 mg, 70% yield, white solid, mp 135−137 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.66 (t, J = 8.2 Hz, 2 H), 4.46 (t, J = 8.1 Hz, 2 H), 6.94 (s, 1 H), 7.34−7.35 (m, 1 H), 7.39−7.43 (m, 4 H), 7.56 (d, J = 8.3 Hz, 2 H), 7.66−7.67 (m, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.0, 62.7, 112.0, 118.5, 126.3, 128.4, 128.4, 128.9, 129.4, 129.6, 132.5, 134.3, 141.1, 156.2; MS (EI, m/z): 291 (7), 290 (M^+, 40), 281 (27), 245 (13), 231 (26); HRMS (ESI) calcd for $C_{18}H_{14}N_2O_2$ (M^+) 290.1055, found 290.1063.

Compound ***3bg***. 57 mg, 65% yield, white solid, mp 131−133 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.69 (t, J = 8.2 Hz, 2 H), 4.47 (t, J = 8.5 Hz, 2 H), 6.98 (s, 1 H), 7.33−7.34 (m, 1 H), 7.38−7.42 (m, 2 H), 7.44 (d, J = 7.2 Hz, 2 H), 7.62 (d, J = 8.2 Hz, 2 H), 7.89−7.90 (m, 2 H), 10.0 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.1, 62.6, 126.3, 128.4, 128.7, 128.8, 129.3, 130.1, 133.5, 134.5, 136.2, 142.4, 156.3, 191.4; MS (EI, m/z): 294 (12), 293 (M^+, 69), 281 (27), 248 (10), 234 (16); HRMS (ESI) calcd for $C_{18}H_{15}NO_3$ (M^+) 293.1052, found 293.1059.

Compound ***3bh***. 68 mg, 76% yield, white solid, mp 136−138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.68 (t, J = 7.8 Hz, 2 H), 4.46 (t, J = 8.3 Hz, 2 H), 6.85 (s, 1 H), 7.39−7.43 (m, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.1, 62.5, 127.0, 127.1, 128.2, 128.3, 128.7, 128.9, 133.5, 134.5, 134.8, 134.9, 156.2; MS (EI, m/z): 301 (30), 299 (M^+, 100), 254 (17), 240 (34), 212 (91); HRMS (ESI) calcd for $C_{17}H_{14}ClNO_2$ (M^+) 299.0713, found 299.0725.

Compound ***3bi***. 72 mg, 86% yield, white solid, mp 132−135 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.39 (s, 3 H), 3.67 (t, J = 7.8 Hz, 2 H), 4.43 (t, J = 8.1 Hz, 2 H), 6.83 (s, 1 H), 7.22 (d, J = 8.0 Hz, 2 H), 7.28−7.30 (m, 1 H), 7.36−7.46 (m, 6 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 21.1, 45.3, 63.4, 125.7, 125.9, 127.9, 128.1, 128.6, 129.4, 133.4, 134.4, 135.2, 138.8, 156.3; MS (EI, m/z): 280 (26), 279 (M^+, 100), 234 (33), 220 (64), 192 (73); HRMS (ESI) calcd for $C_{18}H_{17}NO_2$ (M^+) 279.1259, found 279.1263.

Compound ***3bj***. 69.5 mg, 83% yield, white solid, mp 135−137 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.42 (s, 3 H), 3.70 (t, J = 7.9 Hz, 2 H), 4.47 (t, J = 8.3 Hz, 2 H), 6.88 (s, 1 H), 7.20−7.22 (m, 1 H), 7.28−7.34 (m, 4 H), 7.39−7.47 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 45.3, 62.5, 123.0, 126.5, 126.7, 128.0, 128.2, 128.6, 128.7, 129.6, 134.6, 135.2, 136.3, 138.4, 156.3; MS (EI, m/z): 280 (18), 279 (M^+, 100), 234 (18), 220 (38), 192 (87); HRMS (ESI) calcd for $C_{18}H_{17}NO_2$ (M^+) 279.1259, found 279.1267.

Compound ***3bk***. 75 mg, 90% yield, white solid, mp 136−138 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.42 (s, 3 H), 3.60 (t, J = 8.0 Hz, 2 H), 4.38 (t, J = 8.2 Hz, 2 H), 6.43 (s, 1 H), 7.26−7.28 (m, 2 H), 7.31−7.34 (m, 2 H), 7.38−7.44 (m, 5 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 20.0, 45.0, 62.1, 126.0, 127.1, 127.6, 128.1, 128.5, 128.6, 129.6, 130.6, 134.2, 135.4, 136.2, 136.8, 154.8; MS (EI, m/z): 280 (23), 279 (M^+, 100), 234 (28), 220 (35), 206 (27); HRMS (ESI) calcd for $C_{18}H_{17}NO_2$ (M^+) 279.1259, found 279.1265.

Compound ***3bl***. 81 mg, 92% yield, white solid, mp 142−144 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.68 (t, J = 8.0 Hz, 2 H), 3.84 (s, 3 H), 4.43 (t, J = 8.3 Hz, 2 H), 6.78 (s, 1 H), 6.95 (d, J = 8.8 Hz, 2 H), 7.28−7.31 (m, 1 H), 7.37−7.43 (m, 6 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.2, 55.2, 62.4, 114.1, 124.8, 127.1, 127.7, 128.0, 128.5, 128.6, 134.0, 135.3, 156.2, 160.0; MS (EI, m/z): 296 (8), 295 (M^+, 100), 250 (9), 208 (86), 193 (28); HRMS (ESI) calcd for $C_{18}H_{17}NO_3$ (M^+) 295.1208, found 295.1217.

Compound ***3bm***. 81 mg, 83% yield, white solid, mp 142−144 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.67 (t, J = 8.1 Hz, 2 H), 3.89 (s, 3 H), 3.91 (s, 3 H), 4.42 (t, J = 8.0 Hz, 2 H), 6.77 (s, 1 H), 6.86−6.90 (m, 1 H), 7.00−7.01 (m, 2 H), 7.26−7.29 (m, 1 H), 7.35−7.37 (m, 2 H), 7.41 (d, J = 7.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.3, 55.7, 55.8, 62.3, 109.0, 111.0, 118.5, 125.1, 127.7, 127.9, 128.5, 129.0, 134.2, 135.2, 149.0, 149.6, 156.1; MS (EI, m/z): 326 (18), 325 (M^+, 100), 309 (11), 238 (39), 223 (16); HRMS (ESI) calcd for $C_{19}H_{19}NO_4$ (M^+) 325.1314, found 325.1326.

Crystal data for **3bm** ($C_{19}H_{19}NO_4$, 325.35): monoclinic, space group $P2(1)/c$, a = 12.4071(7) Å, b = 12.8438(7) Å, c = 11.3777(6) Å, U = 1632.86(15) Å^3, Z = 4, T = 296(2) K, absorption coefficient 0.093 mm^{-1}, reflections collected 25 322, independent reflections 3784 [R(int) = 0.0398], refinement by full-matrix least-squares on F^2, data/restraints/parameters 3784/0/217, goodness-of-fit on F^2 = 1.055, final R indices [$I > 2\sigma(I)$] $R1$ = 0.0439, $wR2$ = 0.1199, R indices (all data) $R1$ = 0.0631, $wR2$ = 0.1322, largest diff peak and hole 0.188 and −0.165 e·Å^{-3}. Crystallographic data for the structure **3bm** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1018715.

Compound ***3bn***. 81 mg, 87% yield, white solid, mp 157−159 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.65 (t, J = 8.0 Hz, 2 H), 4.40 (t, J = 8.3 Hz, 2 H), 5.97 (s, 2 H), 6.72 (s, 1 H), 6.81 (d, J = 8.0 Hz, 1 H), 6.92−6.97 (m, 2 H), 7.27−7.31 (m, 1 H), 7.36−7.38 (m, 4 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.2, 62.4, 101.3, 106.1, 108.3, 119.8, 125.3, 127.8, 128.0, 128.6, 130.6, 134.1, 135.1, 148.1, 148.1, 156.1; MS (EI, m/z): 310 (19), 309 (M^+, 100), 222 (87), 223 (18), 207 (11); HRMS (ESI) calcd for $C_{18}H_{15}NO_4$ (M^+) 309.1001, found 309.1009.

Compound ***3bo***. 86 mg, 91% yield, white solid, mp 164−166 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.70 (t, J = 7.9 Hz, 2 H), 4.45 (t, J = 8.4 Hz, 2 H), 7.00 (s, 1 H), 7.33−7.34 (m, 1 H), 7.42 (d, J = 7.6 Hz, 2 H), 7.48−7.52 (m, 4 H), 7.58−7.61 (m, 1 H), 7.86−7.88 (m, 3 H), 7.92 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.2, 62.5, 123.4, 125.0, 126.4, 127.2, 127.5, 128.0, 128.2, 128.3, 128.5, 128.6, 133.2, 133.3, 133.6, 134.3, 135.1, 156.3; MS (EI, m/z): 316 (17), 315 (M^+, 90), 270 (12), 256 (11), 228 (100); HRMS (ESI) calcd for $C_{21}H_{17}NO_2$ (M^+) 315.1259, found 315.1267.

Compound ***3bp***. 60 mg, 78% yield, white solid, mp 142−144 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.72 (t, J = 8.0 Hz, 2 H), 4.47 (t, J = 8.2 Hz, 2 H), 6.47 (d, J = 3.4 Hz, 1 H), 6.47−6.48 (m, 1 H), 7.08 (s, 1 H), 7.32−7.34 (m, 1 H), 7.38−7.41 (m, 2 H), 7.46−7.47 (m, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.2, 62.7, 107.8, 111.8, 125.1, 128.3, 128.4, 128.4, 128.7, 134.1, 143.1, 150.1, 156.7; MS (EI, m/z): 256 (12), 255 (M^+, 86), 207 (22), 182 (14), 168 (100); HRMS (ESI) calcd for $C_{15}H_{13}NO_3$ (M^+) 255.0895, found 255.0905.

Compound ***3bq***. 62 mg, 76% yield, white solid, mp 147−149 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.71 (t, J = 8.0 Hz, 2 H), 4.43 (t, J = 8.2 Hz, 2 H), 6.94 (s, 1 H), 7.02−7.03 (m, 1 H), 7.13 (d, J = 3.5 Hz, 1 H), 7.27−7.50 (m, 6 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.1, 62.6, 124.5, 125.7, 126.1, 127.8, 128.2, 128.2, 128.4, 128.7, 134.3, 140.9, 156.3; MS (EI, m/z): 272 (32), 271 (M^+, 84), 226 (37), 212 (52), 198 (15); HRMS (ESI) calcd for $C_{15}H_{13}NO_2S$ (M^+) 271.0667, found 271.0673.

Compound ***3br***. 73 mg, 84% yield, white solid, mp 135−137 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.67 (t, J = 7.9 Hz, 2 H), 4.47 (t, J = 7.8 Hz, 2 H), 6.63 (d, J = 15.9 Hz, 1 H), 6.73 (s, 1 H), 6.83 (d, J = 15.9 Hz, 1 H), 7.29−7.48 (m, 10 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 44.8, 62.6, 125.5, 126.7, 128.0, 128.3, 128.5, 128.7, 129.3, 131.0, 133.7, 134.4, 136.1, 156.7; MS (EI, m/z): 292 (12), 291 (M^+, 59), 246 (23), 230 (20), 218 (26); HRMS (ESI) calcd for $C_{19}H_{17}NO_2$ (M^+) 291.1259, found 291.1267.

Compound ***3bs***. 66 mg, 86% yield, white solid, mp 119−121 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.92 (t, J = 7.4 Hz, 3 H), 1.45−1.47 (m, 2 H), 2.13−2.17 (m, 2 H), 3.56 (t, J = 8.1 Hz, 2 H), 4.37 (t, J = 8.1 Hz, 2 H), 5.74−5.79 (m, 1 H), 6.05 (d, J = 15.6 Hz, 1 H), 6.47 (s, 1 H), 7.22−7.25 (m, 1 H), 7.30−7.33 (m, 4 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ

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13.6, 22.1, 34.3, 44.9, 62.5, 126.5, 127.8, 128.0, 128.1, 128.5, 132.2, 133.5, 134.6, 156.7; MS (EI, *m*/*z*): 257 (40), 256 (M^+, 26), 230 (12), 214 (83), 198 (10); HRMS (ESI) calcd for $C_{16}H_{19}NO_2$ (M^+) 257.1416, found 257.1419.

Compound ***3bt***. 62 mg, 72% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.83 (t, J = 8.1 Hz, 2 H), 4.46 (t, J = 7.7 Hz, 2 H), 6.88 (s, 1 H), 7.34−7.38 (m, 6 H), 7.43−7.51 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.2, 62.5, 85.4, 90.8, 117.5, 122.1, 128.4, 128.7, 128.7, 128.8, 128.9, 131.7, 134.2, 134.8, 156.0; MS (EI, *m*/*z*): 290 (8), 289 (M^+, 49), 288 (18), 244 (71), 230 (33); HRMS (ESI) calcd for $C_{19}H_{15}NO_2$ (M^+) 289.1103, found 289.1105.

Compound ***3ca***. 73 mg, 86% yield, white solid, mp 126−128 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.67 (t, J = 7.9 Hz, 2 H), 4.44 (t, J = 8.0 Hz, 2 H), 6.81 (s, 1 H), 7.06−7.08 (m, 2 H), 7.36−7.41 (m, 5 H), 7.45 (d, J = 7.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.2, 62.5, 115.7 (d, J = 21.6 Hz), 125.8, 128.7, 128.8, 130.0 (d, J = 8.1 Hz), 131.3 (d, J = 3.4 Hz), 134.3, 136.0, 156.2, 162.1 (d, J = 248.7 Hz); ^{19}F NMR ($CDCl_3$, 565 MHz) δ −112.5; MS (EI, *m*/*z*): 285 (11), 284 (79), 283 (M^+, 73), 238 (47), 224 (68); HRMS (ESI) calcd for $C_{17}H_{14}FNO_2$ (M^+) 283.1009, found 283.1017.

Compound ***3da***. 73 mg, 81% yield, white solid, mp 131−133 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.68 (t, J = 8.0 Hz, 2 H), 4.46 (t, J = 7.9 Hz, 2 H), 6.79 (s, 1 H), 7.33−7.36 (m, 4 H), 7.37−7.42 (m, 3 H), 7.44−7.46 (m, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.3, 62.5, 125.7, 125.9, 128.8, 128.9, 129.0, 129.4, 129.5, 133.7, 135.0, 136.0, 156.1; MS (EI, *m*/*z*): 301 (31), 299 (M^+, 100), 254 (11), 240 (34), 212 (81); HRMS (ESI) calcd for $C_{17}H_{14}ClNO_2$ (M^+) 299.0713, found 299.0717.

Compound ***3ea***. 82 mg, 91% yield, white solid, mp 136−138 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.61 (t, J = 7.9 Hz, 2 H), 4.37 (t, J = 8.2 Hz, 2 H), 6.97 (s, 1 H), 7.28−7.31 (m, 2 H), 7.41−7.46 (m, 4 H), 7.52−7.54 (m, 3 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.6, 62.5, 123.2, 126.1, 126.9, 128.7, 129.0, 129.1, 129.2, 129.5, 133.6, 133.8, 135.8, 136.6, 156.2; MS (EI, *m*/*z*): 301 (33), 299 (M^+, 96), 264 (100), 220 (59), 212 (91); HRMS (ESI) calcd for $C_{17}H_{14}ClNO_2$ (M^+) 299.0713, found 299.0725.

Compound ***3fa***. 70 mg, 70% yield, white solid, rr > 10:1, mp 149−151 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.62 (t, J = 7.8 Hz, 2 H), 4.39 (t, J = 8.2 Hz, 2 H), 6.87 (s, 1 H), 7.27−7.29 (m, 1 H), 7.43−7.46 (m, 5 H), 7.49−7.52 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.5, 62.5, 122.1, 126.2, 127.3, 128.8, 129.3, 129.4, 129.8, 132.5, 134.1, 134.3, 135.4, 137.1, 155.9; MS (EI, *m*/*z*): 335 (57), 333 (M^+, 95), 300 (27), 248 (63), 246 (100); HRMS (ESI) calcd for $C_{17}H_{13}Cl_2NO_2$ (M^+) 333.0323, found 333.0329.

Compound ***3ga***. 83 mg, 86% yield, white solid, mp 148−150 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.35 (s, 9 H), 3.71 (t, J = 8.0 Hz, 2 H), 4.47 (t, J = 8.3 Hz, 2 H), 6.85 (s, 1 H), 7.35−7.36 (m, 1 H), 7.39−7.42 (m, 6 H), 7.46−7.48 (m, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 31.1, 34.6, 45.1, 62.5, 125.6, 125.7, 126.8, 128.1, 128.5, 128.7, 132.1, 133.5, 136.4, 151.2, 156.3; MS (EI, *m*/*z*): 322 (20), 321 (M^+, 100), 306 (89), 219 (55), 207 (3); HRMS (ESI) calcd for $C_{21}H_{23}NO_2$ (M^+) 321.1729, found 321.1736.

Compound ***3ha***. 80 mg, 90% yield, white solid, mp 141−143 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.69 (t, J = 7.9 Hz, 2 H), 3.82 (s, 3 H), 4.45 (t, J = 8.2 Hz, 2 H), 6.82 (s, 1 H), 6.92 (d, J = 8.7 Hz, 2 H), 7.31−7.35 (m, 1 H), 7.37−7.41 (m, 4 H), 7.45 (d, J = 7.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 45.1, 55.1, 62.5, 114.1, 125.5, 126.6, 127.6, 128.4, 128.7, 129.7, 132.4, 136.4, 156.4, 159.3; MS (EI, *m*/*z*): 296 (28), 295 (M^+, 100), 236 (15), 208 (83), 193 (35); HRMS (ESI) calcd for $C_{18}H_{17}NO_3$ (M^+) 295.1208, found 295.1217.

Compound ***3ia***. 81 mg, 90% yield, colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.88 (t, J = 7.0 Hz, 3 H), 1.25−1.37 (m, 10 H), 1.46−1.54 (m, 2 H), 2.19−2.23 (m, 2 H), 3.64 (t, J = 8.0 Hz, 2 H), 4.46 (t, J = 8.2 Hz, 2 H), 6.00 (t, J = 7.2 Hz, 1 H), 7.31−7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.0, 22.6, 28.2, 28.8, 29.2, 29.4, 29.5, 31.8, 45.6, 62.2, 125.8, 128.1, 128.6, 130.8, 133.6, 135.7, 156.4; MS (EI, *m*/*z*): 302 (6), 301 (M^+, 25), 256 (7), 214 (33), 202 (79); HRMS (ESI) calcd for $C_{19}H_{27}NO_2$ (M^+) 301.2042, found 301.2045.

Compound ***3ia-d***. It was prepared from **1i**, 5 equiv of D_2O, and 0.5 equiv of $(PhBO)_3$ under the standard conditions, 79 mg, 87% yield, colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.25−1.37 (m, 10 H), 1.46−1.54 (m, 2 H), 2.21 (t, J = 7.3 Hz, 2 H), 3.65 (t, J = 8.0 Hz, 2 H), 4.46 (t, J = 8.2 Hz, 2 H), 6.01 (t, J = 7.2 Hz, 0.15 H), 7.28−7.36 (m, 5 H).

Compound ***3ja***. 69.5 mg, 89% yield, white solid, mp 112−114 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3 H), 6.70 (s, 1 H), 6.96 (s, 1 H), 7.06 (d, J = 8.0 Hz, 2 H), 7.13 (s, 1 H), 7.20 (d, J = 7.9 Hz, 2 H), 7.28−7.41 (m, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 119.1, 120.0, 127.6, 128.2, 128.5, 128.7, 129.5, 129.8, 134.2, 135.2, 137.6, 138.3, 140.0; MS (EI, *m*/*z*): 261 (15), 260 (M^+, 69), 259 (100), 245 (28), 232 (41); HRMS (ESI) calcd for $C_{18}H_{16}N_2$ (M^+) 260.1313, found 260.1310.

Compound ***3ks***. 57 mg, 80% yield, white solid, mp 106−108 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.89 (t, J = 7.4 Hz, 3 H), 1.36−1.42 (m, 2 H), 2.07−2.13 (m, 2 H), 5.35−5.40 (m, 1 H), 6.32 (d, J = 15.4 Hz, 1 H), 6.47 (s, 1 H), 6.63−6.68 (m, 2 H), 6.88 (s, 1 H), 7.15−2.20 (m, 2 H), 7.23 (s, 1 H), 7.39 (s, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.6, 22.1, 34.4, 119.4, 126.6, 128.1, 128.4, 128.6, 129.4, 129.7, 133.6, 133.8, 134.0, 136.8; HRMS (ESI) calcd for $C_{16}H_{19}N_2$ $(M+H)^+$ 239.1548, found 239.1526.

Compound ***3mi***.[13] 93 mg, 87% yield, colorless oil; ^{1}H NMR (CD_3COCD_3, 600 MHz) δ 3.67 (s, 3 H), 3.77 (s, 3 H), 6.61−6.66 (m, 2 H), 6.70−6.75 (m, 3 H), 6.85−6.89 (m, 2 H), 6.94−7.15 (m, 7 H), 7.65−7.69 (m, 1 H); ^{13}C NMR (CD_3COCD_3, 150 MHz) δ 55.4, 55.6, 104.3, 112.1, 114.5, 114.8, 120.9, 121.6, 122.8, 124.0, 127.7, 128.4, 129.3, 129.7, 130.8, 131.9, 134.3, 136.4, 160.0, 160.9.

Compound ***3na***. 81 mg, 84% yield, white solid, mp 132−134 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.77 (d, J = 7.6 Hz, 2 H), 6.94 (d, J = 3.2 Hz, 1 H), 7.05−7.08 (m, 1 H), 7.12−7.17 (m, 3 H), 7.19−7.20 (m, 2 H), 7.21−7.22 (m, 1 H), 7.23−7.24 (m, 2 H), 7.35−7.39 (m, 3 H), 7.47−7.48 (m, 1 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 102.7, 103.2, 116.3, 118.5, 121.8, 125.6, 125.7, 125.8, 128.2, 128.4, 128.5, 128.8, 129.1, 129.9, 131.1, 134.0, 135.0, 135.1, 137.5; MS (EI, *m*/*z*): 321 (18), 320 (M^+, 58), 319 (73), 243 (13), 178 (100); HRMS (ESI) calcd for $C_{23}H_{17}N_2$ $(M + H)^+$ 321.1392, found 321.1411.

Compound ***3oa***.[14] 63 mg, 80% yield, white solid, mp 116−118 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.14−2.19 (m, 2 H), 2.55 (t, J = 8.2 Hz, 2 H), 3.52 (t, J = 7.0 Hz, 2 H), 6.96 (s, 1 H), 7.29−7.31 (m, 1 H), 7.38−7.42 (m, 7 H), 7.46−7.57 (m, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 19.1, 31.1, 48.4, 125.6, 126.5, 127.8, 128.0, 128.4, 128.5, 128.7, 135.5, 135.7, 136.4, 175.0.

Compound ***5***. To a solution of **3br** (87 mg, 0.3 mmol) in 1 mL of toluene was added diethyl acetylenedicarboxylate (61 mg, 0.36 mmol). After stirring at reflux for 16 h, the reaction mixture was concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 1:1) gave 93 mg (67% yield) of **5** as a white solid, mp 134−136 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.99 (t, J = 7.1 Hz, 3 H), 1.04 (t, J = 7.1 Hz, 3 H), 3.08−3.12 (m, 1 H), 3.74 (q, J = 8.7 Hz, 1 H), 3.93−4.07 (m, 5 H), 4.12−4.16 (m, 1 H), 4.67 (dd, J = 4.2, 7.0 Hz, 1 H), 5.34 (d, J = 7.0 Hz, 1 H), 5.66 (dd, J = 0.8, 4.2 Hz, 1 H), 7.27−7.42 (m, 10 H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.6, 13.6, 43.3, 44.5, 46.7, 60.9, 61.0, 61.7, 117.7, 127.2, 127.5, 128.1, 128.4, 128.7, 128.9, 133.4, 133.6, 135.7, 139.2, 140.8, 155.1, 166.5, 166.7; MS (EI, *m*/*z*): 461 (M^+, 4), 460 (21), 459 (100), 414 (18), 380 (20); HRMS (ESI) calcd for $C_{27}H_{27}NO_6$ (M^+) 461.1838, found 461.1841.

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic data of products **3** and **5**, as well as the X-ray data of **3bm**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Yet, L. *Chem. Rev.* **2003**, *103*, 4283. (b) Carbery, D. R. *Org. Biomol. Chem.* **2008**, *6*, 3455. (c) Evano, G.; Gaumont, A.-C.; Alayrac, C.; Wrona, I. E.; Giguere, J. R.; Delacroix, O.; Bayle, A.; Jouvin, K.; Theunissen, C.; Gatignol, J.; Silvanus, A. C. *Tetrahedron* **2014**, *70*, 1529 and references therein.

(2) For selected reports on the synthesis of enamides via hydroaddition of ynamides, see: (a) Mulder, J. A.; Kurtz, K. C. M.; Hsung, R. P.; Coverdale, H.; Frederick, M. O.; Shen, L.; Zificsak, C. A. *Org. Lett.* **2003**, *5*, 1547. (b) Kramer, S.; Dooleweerdt, K.; Lindhardt, A. T.; Rottländer, M.; Skrydstrup, T. *Org. Lett.* **2009**, *11*, 4208. (c) Fadel, A.; Legrand, F.; Evano, G.; Rabasso, N. *Adv. Synth. Catal.* **2011**, *353*, 263. (d) Compain, G.; Jouvin, K.; Martin-Mingot, A.; Evano, G.; Marrot, J.; Thibaudeau, S. *Chem. Commun.* **2012**, *48*, 5196. (e) Smith, D. L.; Goundry, W. R. F.; Lam, H. W. *Chem. Commun.* **2012**, *48*, 1505. (f) Saito, N.; Saito, K.; Sato, H.; Sato, Y. *Adv. Synth. Catal.* **2013**, *355*, 853. (g) Sato, A. H.; Ohashi, K.; Iwasawa, T. *Tetrahedon Lett.* **2013**, *54*, 1309. (h) Maity, P.; Klos, M. R.; Kazmaier, U. *Org. Lett.* **2013**, *15*, 6246.

(3) For selected reports on the synthesis of enamides via carbometalation of ynamides, see: (a) Couty, S.; Liégault, B.; Meyer, C.; Cossy, J. *Org. Lett.* **2004**, *6*, 2511. (b) Chechik-Lankin, H.; Livshin, S.; Marek, I. *Synlett* **2005**, 2098. (c) Yasui, H.; Yorimitsu, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 373. (d) Gourdet, B.; Lam, H. W. *J. Am. Chem. Soc.* **2009**, *131*, 3802. (e) Greenaway, R. L.; Campbell, C. D.; Holton, O. T.; Russell, C. A.; Anderson, E. A. *Chem.—Eur. J.* **2011**, *17*, 14366. (f) Greenaway, R. L.; Campbell, C. D.; Chapman, H. A.; Anderson, E. A. *Adv. Synth. Catal.* **2012**, *354*, 3187. (g) Gati, W.; Couty, F.; Boubaker, T.; Rammah, M. M.; Rammah, M. B.; Evano, G. *Org. Lett.* **2013**, *15*, 3122. (h) Frischmuth, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2013**, *52*, 10084. For a review, see: (i) Minko, Y.; Pasco, M.; Chechik, H.; Marek, I. *Beilstein J. Org. Chem.* **2013**, *9*, 526.

(4) For selected reports on the synthesis of enamides via cycloaddition of ynamides, see: (a) Schotes, C.; Mezzetti, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 3072. (b) Smith, D. L.; Chidipudi, S. R.; Goundry, W. R.; Lam, H. W. *Org. Lett.* **2012**, *14*, 4934. (c) Clavier, H.; Lepronier, A.; Bengobesse-Mintsa, N.; Gatineau, D.; Pellissier, H.; Giordano, L.; Tenaglia, A.; Buono, G. *Adv. Synth. Catal.* **2013**, *355*, 403. (d) Mackay, W. D.; Fistikci, M.; Carris, R. M.; Johnson, J. S. *Org. Lett.* **2014**, *16*, 1626. (e) Dateer, R. B.; Shaibu, B. S.; Liu, R.-S. *Angew. Chem., Int. Ed.* **2012**, *51*, 113. (f) Karad, S. N.; Bhunia, S.; Liu, R.-S. *Angew. Chem., Int. Ed.* **2012**, *51*, 8722. (g) Pawar, S. K.; Vasu, D.; Liu, R.-S. *Adv. Synth. Catal.* **2014**, *356*, 2411.

(5) For other recent reports on the synthesis of enamides by functionalization of ynamides, see: (a) Rettenmeier, E.; Schuster, A. M.; Rudolph, M.; Rominger, F.; Gade, C. A.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 5880. (b) Nishimura, T.; Takiguchi, Y.; Maeda, Y.; Hayashi, T. *Adv. Synth. Catal.* **2013**, *355*, 1374. (c) Heffernan, S. J.; Beddoes, J. M.; Mahon, M. F.; Hennessy, A. J.; Carbery, D. R. *Chem. Commun.* **2013**, *49*, 2314. (d) Wang, X.-N.; Winston-McPherson, G. N.; Walton, M. C.; Zhang, Y.; Hsung, R. P.; DeKorver, K. A. *J. Org. Chem.* **2013**, *78*, 6233. (e) Brioche, J.; Meyer, C.; Cossy, J. *Org. Lett.* **2013**, *15*, 1626. (f) Walker, P. R.; Campbell, C. D.; Suleman, A.; Carr, G.; Anderson, E. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 9139. (g) Kong, Y.; Jiang, K.; Cao, J.; Fu, L.; Yu, L.; Lai, G.; Cui, Y.; Hu, Z.; Wang, G. *Org. Lett.* **2013**, *15*, 422.

(6) For selected reviews on ynamides, see: (a) DeKorver, K. A.; Li, H.; Lohse, A. G.; Hayashi, R.; Lu, Z.; Zhang, Y.; Hsung, R. P. *Chem. Rev.* **2010**, *110*, 5064. (b) Evano, G.; Coste, A.; Jouvin, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 2840.

(7) Gourdet, B.; Smith, D. L.; Lam, H. W. *Tetrahedron* **2010**, *66*, 6026.

(8) For the Rh-catalyzed addition of boronic acids to alkynes, see: (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918. (b) Lautens, M.; Yoshida, M. *Org. Lett.* **2002**, *4*, 123. (c) Panteleev, J.; Huang, R. Y.; Lui, E. K. J.; Lautens, M. *Org. Lett.* **2011**, *13*, 5314. (d) Genin, E.; Michelet, V.; Genêt, J.-P. *J. Organomet. Chem.* **2004**, *689*, 3820. (e) Zhang, W.; Liu, M.; Wu, H.; Ding, J.; Cheng, J. *Tetrahedron Lett.* **2008**, *49*, 5214. (f) Arcadi, A.; Aschi, M.; Chiarini, M.; Ferrara, G.; Marinelli, F. *Adv. Synth. Catal.* **2010**, *352*, 493. (g) Gourdet, B.; Rudkin, M. E.; Lam, H. W. *Org. Lett.* **2010**, *12*, 2554.

(9) (a) Lu, Z.; Kong, W.; Yuan, Z.; Zhao, X.; Zhu, G. *J. Org. Chem.* **2011**, *76*, 8524. (b) Lu, Z.; Cui, W.; Xia, S.; Bai, Y.; Luo, F.; Zhu, G. *J. Org. Chem.* **2012**, *77*, 9871. (c) Lu, Z.; Xu, X.; Yang, Z.; Kong, L.; Zhu, G. *Tetrahedron Lett.* **2012**, *53*, 3433.

(10) Yang, Y.; Wang, L.; Zhang, J.; Jin, Y.; Zhu, G. *Chem. Commun.* **2014**, *50*, 2347.

(11) For the Pd-catalyzed addition of boronic acids to alkynes, see: (a) Oh, C. H.; Jung, H. H.; Kim, K. S.; Kim, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 805. (b) Kim, N.; Kim, K. S.; Gupta, A. K.; Oh, C. H. *Chem. Commun.* **2004**, 618. (c) Zeng, H.; Hua, R. *J. Org. Chem.* **2008**, *73*, 558. (d) Xu, X.; Chen, J.; Gao, W.; Wu, H.; Ding, J.; Su, W. *Tetrahedron* **2010**, *66*, 2433. (e) Bai, Y.; Yin, J.; Kong, W.; Mao, M.; Zhu, G. *Chem. Commun.* **2013**, *49*, 7650.

(12) For other catalytic versions, see: (a) Shirakawa, E.; Takahashi, G.; Tsuchimoto, T.; Kawakami, Y. *Chem. Commun.* **2001**, 2688. (b) Lin, P.-S.; Jeganmohan, M.; Cheng, C.-H. *Chem.—Eur. J.* **2008**, *14*, 11296. (c) Yamamoto, Y.; Kirai, N.; Harada, Y. *Chem. Commun.* **2008**, 2010.

(13) Roche, M.; Frison, G.; Brion, J.-D.; Provot, O.; Hamze, A.; Alami, M. *J. Org. Chem.* **2013**, *78*, 8485.

(14) Gou, Q.; Deng, B.; Zhang, H.; Qin, J. *Org. Lett.* **2013**, *15*, 4604.

(15) In fact, *N*-sulfonyl ynamides are not suitable substrates for this reaction, due to the occurrence of *trans*-addition; see ref 10. Furthermore, *N*-alkynyl *tert*-butyloxycarbamates are not applicable to this reaction because of the formation of 2-oxazolones; for the related reference, see: Lu, Z.; Xu, X.; Yang, Z.; Kong, L.; Zhu, G. *Tetrahedron Lett.* **2012**, *53*, 3433.

(16) To avoid the interruption of protons, $(PhBO)_3$ was used instead of $PhB(OH)_2$ in the deuterium experiments.

(17) (a) Cho, C. S.; Motofusa, S.-I.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 883. (b) Zhou, C.; Larock, R. C. *Org. Lett.* **2005**, *7*, 259.

(18) Zhu, G.; Chen, D.; Wang, Y.; Zheng, R. *Chem. Commun.* **2012**, *48*, 5796 and references therein.

(19) For the Diels−Alder reaction of oxazolidin-2-one-substituted dienamides, see: (a) Hayashi, R.; Ma, Z.-X.; Hsung, R. P. *Org. Lett.* **2012**, *14*, 252. (b) Saito, N.; Saito, K.; Shiro, M.; Sato, Y. *Org. Lett.* **2011**, *13*, 2718. (c) Gourdet, B.; Rudkin, M. E.; Watts, C. A.; Lam, H. W. *J. Org. Chem.* **2009**, *74*, 7849 and references therein.

(20) Liu, Y.; Li, D.; Park, C.-M. *Angew. Chem., Int. Ed.* **2011**, *50*, 7333.