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Synthesis of benzazepinoisoindolinone and bridged tricyclic isoindolinone derivatives

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ABSTRACT

N-(2,2-Diethoxyethyl)isoindolin-1-ones were readily obtained via the reaction of *o*-lithiated aromatic imines with carbon monoxide under mild conditions in gram-scale, and they were double-deprotonated by two equivalents of potassium bis(trimethylsilyl)amide at the 3-position and subsequently reacted with $ArCH_2Br$ to give 3,3-dibenzyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones. Treatment of 3-benzyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones with CF_3CO_2H or $AlCl_3$ led to an intramolecular cyclization reaction to afford benzazepinoisoindolinones, while bridged tricyclic isoindolinone derivatives were successfully obtained using 3,3-dibenzyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones as the substrates. Preliminary *in vitro* tests for fungicidal activity indicate that some bridged tricyclic isoindolinones exhibit good fungicidal activities.

1. Introduction

The isoindolinone skeleton is an important structural motif which is commonly found in numerous synthetic pharmaceuticals and natural products with a wide range of biological activities (Fig. 1) [1]. Moreover, simple isoindolinone derivatives have been extensively used as building blocks for the synthesis of various important drugs and natural products [2]. As a consequence, many synthetic methods for the construction of the isoindolinone skeleton have been reported in literature [3]. Among isoindolinone derivatives, fused polycyclic isoindolinones have been attracting considerable attention in recent years because of their novel structural characteristics and extensive bioactivities [4]. A variety of synthetic approaches have also been explored to construct the fused isoindolinones with multiple functional groups, such as *N*-acyliminium cyclization [5], dearomatization of indole derivatives [6], coupling reactions [7], condensation reactions [8], photochemical reactions [9], Diels-Alder reactions [10], cascade Michael/aldol-like cyclization [11], multicomponent cascade reactions [12], and others [13]. Comparing with these rich approaches to the fused isoindolinones, the synthetic methods of the bridged polycyclic isoindolinones are few. These involve the Friedel-Crafts alkylation of phthalimide derivatives [14], the annulation reactions of thioalkynes with phthalimide-substituted donor-acceptor cyclopropanes [15], and the cascade Michael addition/cyclization of 3-carboxylate-substituted isoindolinones with ortho-hydroxychalcones [16]. In consideration of the structural diversity and the structure-activity relationship of isoindolinone derivatives, more efficient synthetic methods for the bridged polycyclic isoindolinones from simple and readily available starting materials are in great demand. Our previous investigations demonstrated that the reaction of *o*-lithiated aromatic imines with carbon monoxide, subsequently with various electrophiles under mild conditions easily gave isoindolinone derivatives [17], which inspired us to explore further application of this method for the synthesis of polycyclic isoindolinones especially the scare bridged isoindolinone derivatives. We herein report the convenient synthesis of benzazepinoisoindolinones and bridged tricyclic isoindolinones employing this strategy.

2. Results and discussion

2.1. Synthesis of N-acetal-substituted isoindolinones

The *N*-acetal-substituted isoindolinones were reported in literature [12b,18], though the starting materials were usually obtained by multistep reactions. We herein find that the *N*-acetal-substituted isoindolinones (**1a**–**1f**) are easily obtained through the

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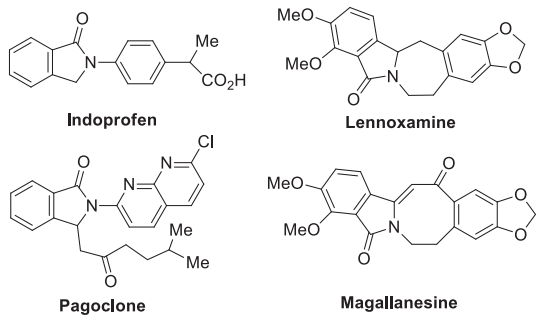


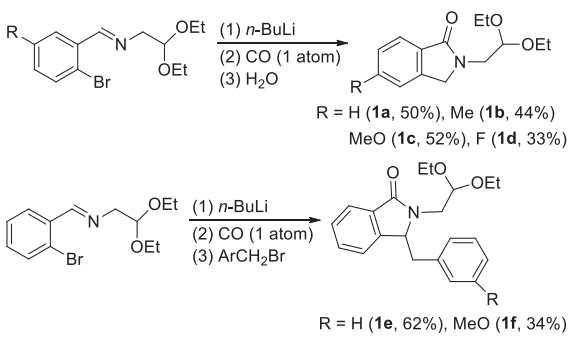
Fig. 1. Examples of pharmaceuticals (Indoprofen and Pagoclone) and natural products (Lennoxamine and Magallanesine) with the isoindolinone scaffold.

cyclization reaction of *o*-lithiated aromatic imines with carbon monoxide under mild conditions according to our previous work (Scheme 1) [17]. The deprotonation at the methylene group of isoindolinone ring by various organic strong bases has been used to synthesize various 3-monosubstituted isoindolinones [19]. We found that the double-deprotonation of the methylene group of 3-position in **1a**–**1d** was successful in one-pot. 3,3-Dibenzyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones (**2a**–**2r** and **2u**) can be conveniently obtained in moderate to excellent yields upon direct treatment of **1a**–**1d** with two equivalents of potassium bis(-trimethylsilyl)amide (KHMDS) subsequently with $ArCH_2Br$ (Scheme 2). Both electron-withdrawing fluorine and electron-donating methoxy are tolerable on the substrates (**2l**–**2r**). The ester functional groups are compatible in the preparation of 3,3-dibenzyl derivative (**2u**). In addition, unsymmetric 3,3-dibenzyl derivatives (**2s** and **2t**) can be similarly obtained through equivalent amounts of KHMDS and **1e**. Moreover, compounds

1a and **2c** were synthesized successfully in gram-scale. All these newly synthesized compounds **1** and **2** have been characterized by ^1H and ^{13}C NMR spectra as well as HRMS. The most remarkable change in ^1H NMR spectra is that the methylene protons of isoindolinone ring in **1** disappeared after reaction.

2.2. Synthesis of benzazepinoisoindolinones

Compounds **1e** and **1f** are excellent precursors for the Pomeranz–Fritsch cyclization [18]. However, treatment of **1e** with CF_3CO_2H or CH_3CO_2H/H_2SO_4 did not induce the Pomeranz–Fritsch cyclization (Scheme 3), instead it only gave the hydrolysis product **3**, which has been obtained by multistep reactions [20]. When strong Lewis acid $AlCl_3$ was introduced as the catalyst, the cyclization reaction took place to give benzazepinoisoindolinone derivative of **4a**. With **1f** as the substrate, CF_3CO_2H could smoothly induce the intramolecular cyclization to afford **4b**, which obviously



Scheme 1. Synthesis of **1a**-**1f**.

attributes to the activation of the methoxy group in **1f**. It is noteworthy that compound **4b** can be directly obtained in reasonable yield from aromatic imine, in other words, without isolation of the crude **1f**. It is known that further hydrogenation of benzazepinones with the core of **4a** and **4b** easily produces analogs of lennoxamine [18]. Thus we provide here a convenient approach to analogs of lennoxamine. The NMR spectra of **4a** and **4b** are in agreement with their structures, and the structure of **4b** has been confirmed by X-ray single crystal diffraction, which is shown in Fig. 2.

2.3. Synthesis of bridged tricyclic isoindolinone derivatives

Compounds **2** contain two benzyl groups attached to the 3-position of isoindolinone ring, so double intramolecular electrophilic aromatic substitution reactions are expected for these compounds. Indeed, bridged tricyclic isoindolinones (**5a**–**5t**) were obtained in moderate to good yields via double intramolecular cyclization reactions upon treatment of **2a**–**2t** with $AlCl_3$ (Scheme 4). The position of bromine on the benzyl group rarely affects this cyclization reaction. For example, all these ortho, meta and para-bromo substituted benzyl substrates (**2b**–**2d**) gave bridged tricyclic isoindolinones (**5b**–**5d**) in good yields. In addition, there were no other regioisomers obtained in the cyclization process even for meta-substituted benzyl substrates, such as **2c** and **2f**. Furthermore, the unsymmetric substrates **2s** and **2t** were cyclized successfully to bridged derivatives **5s** and **5t**. Halogen and methoxy are tolerable on the benzyl groups and isoindolinone ring. Compound **2u** only afforded the hydrolysis product **6** (Scheme 5), showing that the electron-withdrawing ester group is incompatible in this cyclization reaction. Taking into account that these functional groups show great potential for other organic transformations, such as the C–C coupling reactions of bromine, the amplification experiment has been done. The yield of **5c** barely reduced when **2c** was used as the substrate and the reaction was amplified to gram scale. Moreover, the demethylation of **5g** with BBr_3 is achieved (Scheme 6), which affords compound **7** in almost quantitative yield. These multifunctional compounds can probably be exploited as important intermediates in future work.

Compounds **5**–**7** were fully identified by ^1H and ^{13}C NMR spectra as well as HRMS, and the structure of **5a** was further confirmed by the X-ray crystal structure determination, which is depicted in Fig. 3.

2.4. Fungicidal activity

The preliminary *in vitro* antifungal activities of **5** and **7** were assessed at 50 μg/mL, and results are listed in Table 1. Most of bridged isoindolinone derivatives, especially compounds **5e** and **5s**, showed good fungicidal activities against *Sclerotinia sclerotiorum*, which causes serious diseases in a wide range of plants [21]. This is similar to previously reported results of 3-substituted isoindolinones [17b]. Compounds **5o**, **5q** and **5r** also showed good activities against *Rhizoctonia cerealis*. Their inhibition percentages are close to that of boscalid, a positive control drug.

In summary, a concise synthetic approach to polycyclic isoindolinones especially bridged polycyclic derivatives has been developed through *N*-acetal-substituted isoindolinones that are easily obtained from readily available starting materials under mild reaction conditions. This method is simple and efficient, and the gram-scale synthesis is achieved. Preliminary *in vitro* tests for fungicidal activity indicate that most of bridged isoindolinone derivatives exhibit good fungicidal activity against *Sclerotinia sclerotiorum*.

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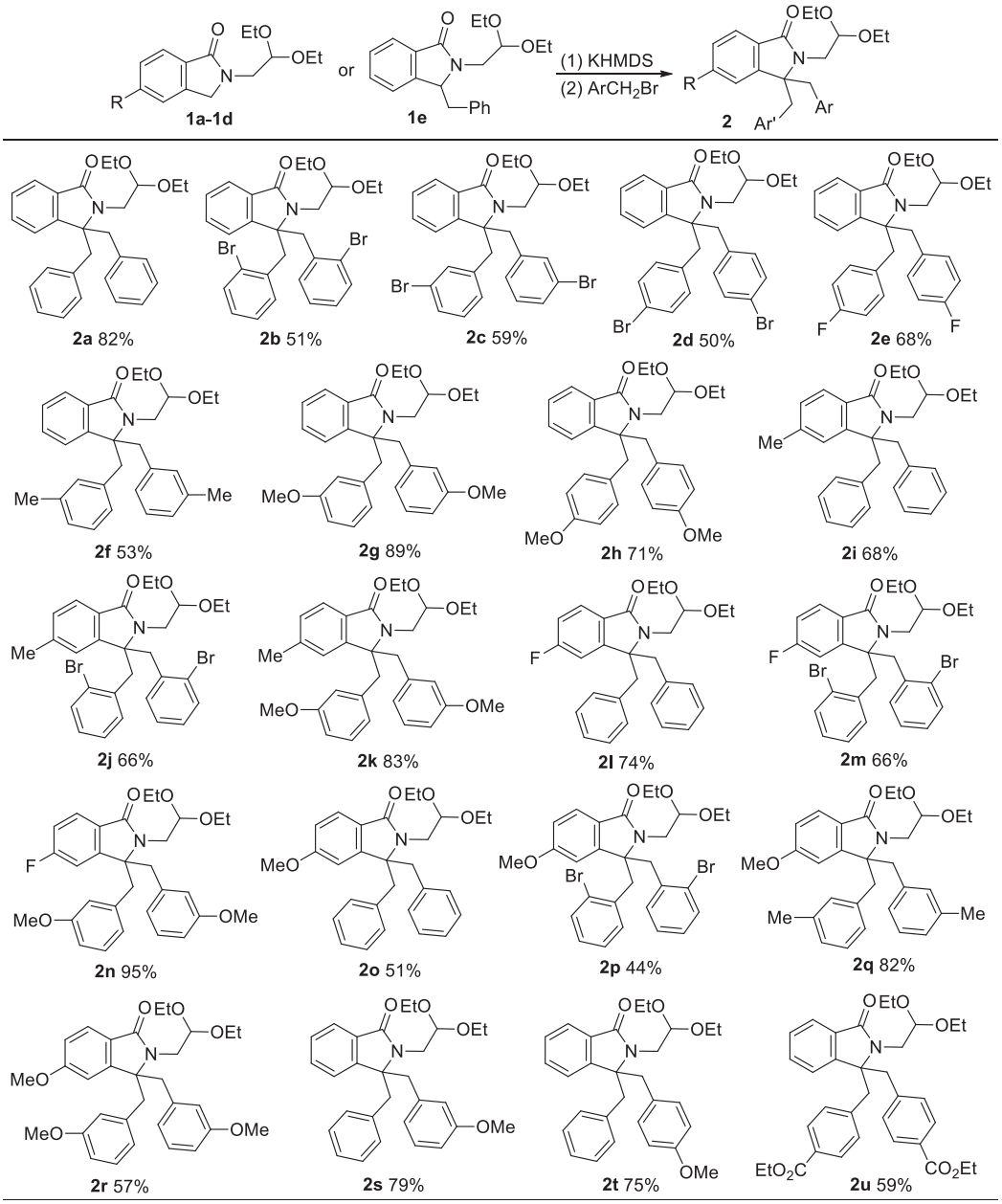
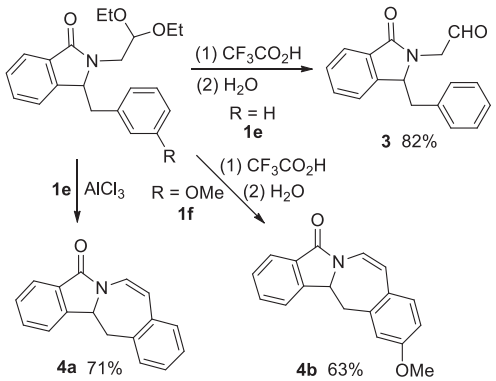


Scheme 2. Synthesis of **2a**-**2u**.



Scheme 3. Reaction of **1e** and **1f**.

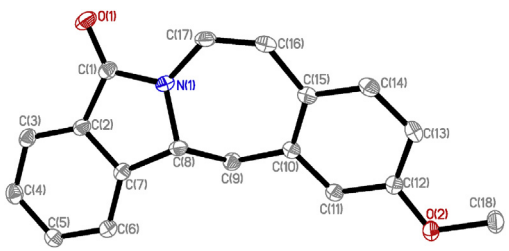


Fig. 2. The molecular structure of **4b**.

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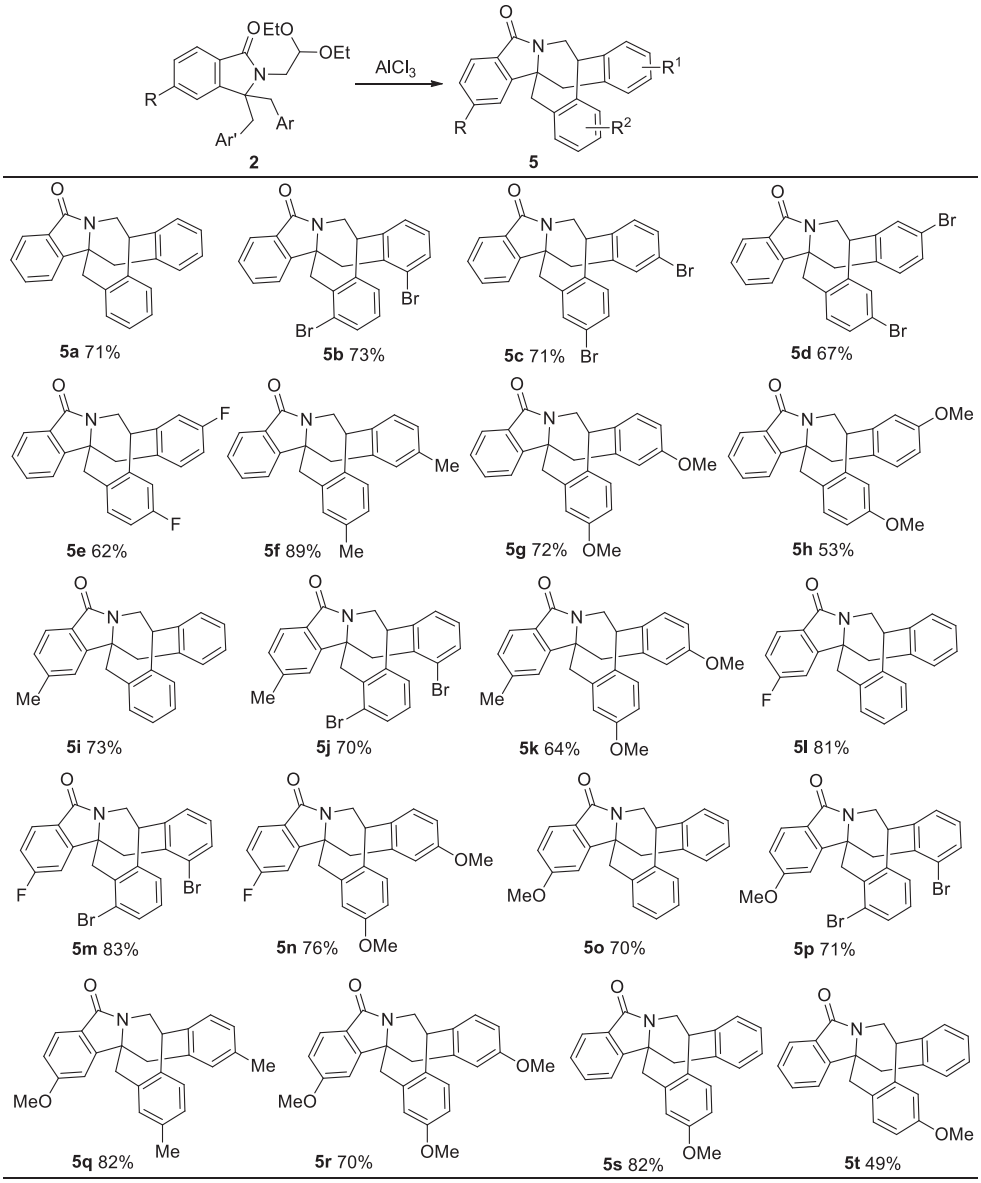
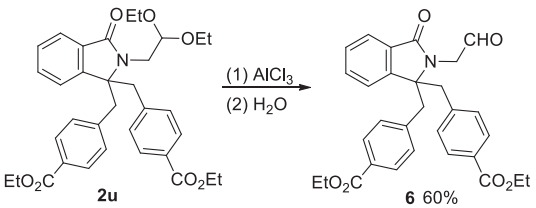
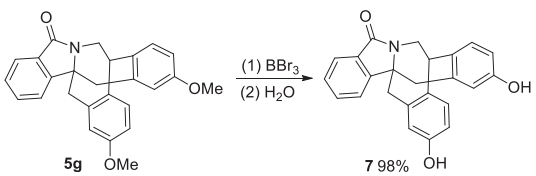


Scheme 4. Synthesis of **5a**-**5t**.



Scheme 5. Reaction of **2u** with $AlCl_3$.



Scheme 6. Reaction of **5g** with BBr_3.

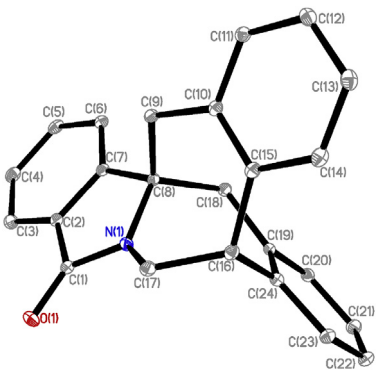


Fig. 3. The molecular structure of **5a**.

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Table 1
Antifungal activity of **5** and **7** (Percent inhibition, 50 μg/mL in DMF).

Comp.	*Sclerotinia sclerotiorum*	*Botrytis cinerea*	*Cercospora arachidicola*	*Alternaria solani*	*Rhizoctonia cerealis*
5a	0	17	0	0	20
5b	0	22	72	58	2
5c	70	22	0	0	0
5d	10	12	0	0	0
5e	75	32	0	21	53
5f	0	24	0	0	18
5g	0	37	0	0	0
5h	65	27	0	15	45
5i	58	66	0	0	49
5j	47	37	0	0	0
5k	56	24	0	0	6
5l	61	29	0	0	0
5m	47	27	0	0	0
5n	56	29	0	0	59
5o	72	49	40	36	71
5p	53	7	24	27	59
5q	69	20	32	27	69
5r	61	41	28	30	73
5s	75	49	8	21	57
5t	61	54	0	6	59
7	50	12	24	24	45
boscalid	100	100	100	91	73

3. Experimental

3.1. General

Solvents were dried by standard methods and freshly distilled prior to use. All reactions were carried out under an argon atmosphere. NMR (^{1}H and ^{13}C) were recorded on a Bruker 400 spectrometer using $CDCl_3$ as the solvent unless otherwise noted, and the chemical shifts were reported in ppm with respect to the reference (internal $SiMe_4$ for ^{1}H and ^{13}C NMR spectra). HR mass spectra were obtained on a Varian QFT-ESI spectrometer. Preliminary *in vitro* tests for fungicidal activity of compounds have been carried out by the fungi growth inhibition method [22]. The synthesis of aromatic imines is provided in the supporting information.

3.2. Typical procedure for the synthesis of ***1a*–*1f***

A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2 mmol) was slowly added to the stirred solution of aromatic imine (2 mmol) in THF (30 mL) at −78 °C. After continuously stirring for half an hour, carbon monoxide was bubbled into the solution. The carbon monoxide atmosphere was kept with a balloon at the exit. The reaction mixture was continuously stirred at low temperature for 1 h, then water (0.2 mL) or benzyl bromide (2 mmol) was slowly added dropwise with syringe. The reaction mixture was allowed to reach room temperature slowly and stirred for 2 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 2:5) as the eluent to afford products **1a**–**1f**.

*Data of **1a*** [23]. Yellow oil. This compound was also obtained in 47% (1.19 g) yield in 10 mmol scale. ^{1}H NMR δ 1.21 (t, J = 7.0 Hz, 6H), 3.53–3.60 (m, 2H), 3.73 (d, J = 5.6 Hz, 2H), 3.75–3.80 (m, 2H), 4.55 (s, 2H), 4.70 (t, J = 5.4 Hz, 1H), 7.46 (t, J = 7.3 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.85 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ 15.4, 45.5, 51.8, 63.2, 101.3, 122.7, 123.6, 127.9, 131.3, 132.5, 141.9, 168.8; HRMS (ESI) calcd for $C_{14}H_{19}NNaO_3$ $[M+Na]^+$: 272.1263, found: 272.1261.

*Data of **1b***. Yellow oil. ^{1}H NMR δ 1.20 (t, J = 7.0 Hz, 6H), 2.45 (s, 3H), 3.52–3.59 (m, 2H), 3.70 (d, J = 5.4 Hz, 2H), 3.73–3.79 (m, 2H), 4.49 (s, 2H), 4.69 (t, J = 5.4 Hz, 1H), 7.24–7.26 (m, 2H), 7.72 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 15.4, 21.9, 45.4, 51.6, 63.1, 101.3, 123.2, 123.4, 128.9, 130.0, 141.9, 142.3, 168.8; HRMS (ESI) calcd for $C_{15}H_{22}NO_3$ $[M+H]^+$: 264.1600, found: 264.1595.

*Data of **1c***. Yellow oil. ^{1}H NMR δ 1.21 (t, J = 7.0 Hz, 6H), 3.52–3.60 (m, 2H), 3.69 (d, J = 5.4 Hz, 2H), 3.73–3.79 (m, 2H), 3.87 (s, 3H), 4.49 (s, 2H), 4.68 (t, J = 5.4 Hz, 1H), 6.93 (s, 1H), 6.97 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 15.4, 45.4, 51.6, 55.6, 63.1, 101.4, 107.5, 114.5, 124.9, 125.2, 144.1, 162.6, 168.6; HRMS (ESI) calcd for $C_{15}H_{22}NO_4$ $[M+H]^+$: 280.1549, found: 280.1541.

*Data of **1d***. Yellow oil. ^{1}H NMR δ 1.21 (t, J = 7.0 Hz, 6H), 3.53–3.61 (m, 2H), 3.71 (d, J = 5.4 Hz, 2H), 3.74–3.80 (m, 2H), 4.53 (s, 2H), 4.69 (t, J = 5.4 Hz, 1H), 7.13–7.17 (m, 2H), 7.82 (dd, J = 8.0, 5.4 Hz, 1H); ^{13}C NMR δ 15.4, 45.4, 51.4, 63.2, 101.2, 110.0 (d, $J_{F\text{-}C}$ = 24.2 Hz), 115.6 (d, $J_{F\text{-}C}$ = 23.5 Hz), 125.4 (d, $J_{F\text{-}C}$ = 9.8 Hz), 128.6, 144.2 (d, $J_{F\text{-}C}$ = 10.1 Hz), 165.0 (d, $J_{F\text{-}C}$ = 250.8 Hz), 167.7; HRMS (ESI) calcd for $C_{14}H_{18}FNNaO_3$ $[M+Na]^+$: 290.1168, found: 290.1160.

*Data of **1e***. Yellow oil. ^{1}H NMR δ 1.18 (t, J = 7.0 Hz, 3H), 1.26 (t, J = 7.0 Hz, 3H), 2.74 (dd, J = 13.6, 8.5 Hz, 1H), 3.32 (dd, J = 14.4, 6.9 Hz, 1H), 3.44–3.54 (m, 2H), 3.62–3.69 (m, 1H), 3.73–3.82 (m, 2H), 4.27 (dd, J = 14.4, 3.5 Hz, 1H), 4.71 (dd, J = 6.8, 3.5 Hz, 1H), 5.06 (dd, J = 8.5, 4.1 Hz, 1H), 6.86–6.89 (m, 1H), 7.03–7.05 (m, 2H), 7.21–7.25 (m, 3H), 7.37–7.40 (m, 2H), 7.76–7.79 (m, 1H); ^{13}C NMR δ 15.4 (2 C), 37.7, 40.1, 61.5, 63.3, 63.9, 101.5, 123.0, 123.5, 126.9, 128.0, 128.4, 129.6, 130.9, 131.9, 136.1, 145.5, 168.5; HRMS (ESI) calcd for $C_{21}H_{25}NNaO_3$ $[M+Na]^+$: 362.1732, found: 362.1726.

*Data of **1f***. Yellow oil. ^{1}H NMR δ 1.18 (t, J = 7.0 Hz, 3H), 1.26 (t, J = 7.0 Hz, 3H), 2.71 (dd, J = 13.6, 8.5 Hz, 1H), 3.31 (dd, J = 14.4, 6.8 Hz, 1H), 3.46–3.52 (m, 2H), 3.61–3.67 (m, 1H), 3.69 (s, 3H), 3.74–3.81 (m, 2H), 4.27 (dd, J = 14.4, 3.5 Hz, 1H), 4.71 (dd, J = 6.8, 3.5 Hz, 1H), 5.06 (dd, J = 8.5, 4.0 Hz, 1H), 6.56 (d, J = 1.8 Hz, 1H), 6.65 (d, J = 7.6 Hz, 1H), 6.75 (dd, J = 8.2, 2.3 Hz, 1H), 6.93–6.96 (m, 1H), 7.15 (t, J = 7.9 Hz, 1H), 7.38–7.42 (m, 2H), 7.77–7.80 (m, 1H); ^{13}C NMR δ 15.4 (2 C), 37.7, 43.0, 55.1, 61.3, 63.2, 63.8, 101.4, 112.4, 115.0, 121.9, 123.1, 123.5, 128.0, 129.4, 131.0, 131.9, 137.6, 145.5, 159.5, 168.5; HRMS (ESI) calcd for $C_{22}H_{27}NNaO_4$ $[M+Na]^+$: 392.1838, found: 392.1829.

3.3. Typical procedure for the synthesis of ***2a*–*2u***

A THF solution of KHMDS (1.0 M, 2.2 mL, 2.2 mmol) was slowly added to the stirred solution of **1a**–**1d** (1 mmol) or **1e** (2 mmol) in THF (20 mL) at room temperature. After continuously stirring for

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half an hour, $ArCH_2Br$ (2 mmol) was added. The reaction mixture was stirred at room temperature overnight. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*V*/*V* = 1:3) as the eluent to afford products **2a**–**2u**.

Data of ***2a***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.16 (d, J = 14.1 Hz, 2H), 3.48 (d, J = 14.1 Hz, 2H), 3.58–3.65 (m, 2H), 3.69 (d, J = 5.1 Hz, 2H), 3.79–3.86 (m, 2H), 5.11 (t, J = 5.0 Hz, 1H), 6.79–6.81 (m, 5H), 7.08–7.14 (m, 6H), 7.28–7.36 (m, 2H), 7.57 (d, J = 7.0 Hz, 1H); ^{13}C NMR δ 15.4, 43.6, 46.0, 64.4, 69.8, 100.8, 123.0, 124.1, 126.8, 127.9, 128.0, 130.3, 130.4, 132.0, 135.5, 146.9, 169.0; HRMS (ESI) calcd for $C_{28}H_{32}NO_3$ $[M+H]^+$: 430.2382, found: 430.2372.

Data of ***2b***. Yellow oil. ^{1}H NMR δ 1.17 (t, J = 7.0 Hz, 6H), 3.51 (d, J = 14.8 Hz, 2H), 3.56–3.64 (m, 2H), 3.73 (d, J = 5.1 Hz, 2H), 3.77–3.85 (m, 4H), 5.17 (t, J = 5.1 Hz, 1H), 6.77–6.81 (m, 3H), 6.95 (td, J = 7.6, 1.5 Hz, 2H), 7.02 (t, J = 7.0 Hz, 2H), 7.22 (t, J = 7.4 Hz, 1H), 7.27 (t, J = 7.2 Hz, 1H), 7.40 (d, J = 7.2 Hz, 2H), 7.63 (d, J = 7.3 Hz, 1H); ^{13}C NMR δ 15.3, 41.8, 45.9, 63.9, 69.7, 100.5, 122.9, 123.7, 126.3, 127.0, 128.1, 128.4, 130.7, 130.8, 131.8, 132.9, 135.5, 146.3, 169.3; HRMS (ESI) calcd for $C_{28}H_{29}Br_2NNaO_3$ $[M+Na]^+$: 610.0391, found: 610.0378.

Data of ***2c***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.8 Hz, 6H), 3.17 (d, J = 14.2 Hz, 2H), 3.39 (d, J = 14.1 Hz, 2H), 3.58–3.66 (m, 4H), 3.79–3.87 (m, 2H), 5.08 (t, J = 4.2 Hz, 1H), 6.75 (d, J = 7.6 Hz, 2H), 6.87 (d, J = 7.5 Hz, 1H), 6.93 (s, 2H), 6.97 (td, J = 7.9, 1.4 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 15.3, 43.0, 46.0, 64.3, 69.4, 100.7, 121.9, 123.4, 123.6, 128.5, 128.7, 129.5, 130.0, 130.8, 131.9, 133.2, 137.6, 146.2, 168.9; HRMS (ESI) calcd for $C_{28}H_{30}Br_2NO_3$ $[M+H]^+$: 588.0572, found: 588.0560.

Data of ***2d***. Yellow oil. ^{1}H NMR δ 1.18 (t, J = 7.0 Hz, 6H), 3.14 (d, J = 14.2 Hz, 2H), 3.38 (d, J = 14.2 Hz, 2H), 3.57–3.64 (m, 4H), 3.79–3.86 (m, 2H), 5.09 (t, J = 4.8 Hz, 1H), 6.67 (d, J = 7.7 Hz, 4H), 6.85 (d, J = 7.3 Hz, 1H), 7.22 (d, J = 7.4 Hz, 4H), 7.32–7.41 (m, 2H), 7.60 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 15.3, 42.9, 46.0, 64.4, 69.3, 100.7, 121.0, 123.4, 123.6, 128.4, 130.7, 131.1, 131.8, 131.9, 134.3, 146.3, 168.9; HRMS (ESI) calcd for $C_{28}H_{30}Br_2NO_3$ $[M+H]^+$: 588.0572, found: 588.0551.

Data of ***2e***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.17 (d, J = 14.2 Hz, 2H), 3.41 (d, J = 14.2 Hz, 2H), 3.61–3.64 (m, 2H), 3.65 (d, J = 5.0 Hz, 2H), 3.79–3.87 (m, 2H), 5.10 (t, J = 5.1 Hz, 1H), 6.76–6.84 (m, 9H), 7.31–7.40 (m, 2H), 7.59 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ 15.3, 42.6, 46.0, 64.4, 69.6, 100.7, 114.8 (d, $J_{F\text{-}C}$ = 21.1 Hz), 123.3, 123.7, 128.2, 130.6, 131.1 (d, $J_{F\text{-}C}$ = 3.3 Hz), 131.6 (d, $J_{F\text{-}C}$ = 7.9 Hz), 132.0, 146.5, 161.8 (d, $J_{F\text{-}C}$ = 245.6 Hz), 169.0; HRMS (ESI) calcd for $C_{28}H_{30}F_2NO_3$ $[M+H]^+$: 466.2194, found: 466.2179.

Data of ***2f***. Yellow oil. ^{1}H NMR δ 1.20 (t, J = 7.9 Hz, 6H), 2.17 (s, 6H), 3.09 (d, J = 14.0 Hz, 2H), 3.45 (d, J = 14.0 Hz, 2H), 3.62–3.66 (m, 4H), 3.79–3.86 (m, 2H), 5.10 (t, J = 4.0 Hz, 1H), 6.60–6.62 (m, 4H), 6.81 (d, J = 7.3 Hz, 1H), 6.93 (d, J = 7.3 Hz, 2H), 6.99 (t, J = 7.3 Hz, 2H), 7.32–7.37 (m, 2H), 7.59 (d, J = 7.0 Hz, 1H); ^{13}C NMR δ 15.4, 21.3, 43.6, 46.0, 64.3, 69.8, 100.9, 122.9, 124.3, 127.3, 127.5, 127.7, 127.9, 130.1, 131.2, 132.1, 135.5, 137.3, 147.1, 169.0; HRMS (ESI) calcd for $C_{30}H_{36}NO_3$ $[M+H]^+$: 458.2695, found: 458.2676.

Data of ***2g***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.13 (d, J = 14.1 Hz, 2H), 3.48 (d, J = 14.1 Hz, 2H), 3.58 (s, 6H), 3.60–3.66 (m, 4H), 3.78–3.84 (m, 2H), 5.09 (t, J = 5.0 Hz, 1H), 6.27 (s, 2H), 6.47 (d, J = 7.5 Hz, 2H), 6.67 (d, J = 8.2 Hz, 2H), 6.90 (d, J = 7.4 Hz, 1H), 7.04 (t, J = 7.9 Hz, 2H), 7.34–7.39 (m, 2H), 7.61 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ 15.4, 43.7, 46.0, 55.0, 64.3, 69.7, 100.8, 112.6, 115.6, 122.8, 123.1, 124.1, 128.1, 128.8, 130.3, 132.2, 137.0, 147.1, 159.0, 168.9; HRMS (ESI) calcd for $C_{30}H_{35}NNaO_5$ $[M+Na]^+$: 512.2413, found: 512.2408.

Data of ***2h***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.07 (d, J = 14.2 Hz, 2H), 3.41 (d, J = 14.2 Hz, 2H), 3.58–3.66 (m, 4H), 3.70 (s, 6H), 3.79–3.86 (m, 2H), 5.10 (t, J = 5.0 Hz, 1H), 6.63 (d, J = 8.4 Hz, 4H), 6.72 (d, J = 8.5 Hz, 4H), 6.83 (d, J = 7.2 Hz, 1H), 7.29–7.37 (m, 2H), 7.58 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ 15.4, 42.6, 46.0, 55.1, 64.3, 69.9, 100.9, 113.3, 123.0, 124.0, 127.5, 127.9, 130.3, 131.2, 132.1, 147.2, 158.4, 169.1; HRMS (ESI) calcd for $C_{30}H_{35}NO_5$ $[M+H]^+$: 490.2593, found: 490.2580.

Data of ***2i***. Yellow oil. ^{1}H NMR δ 1.10 (t, J = 7.0 Hz, 6H), 2.24 (s, 3H), 3.06 (d, J = 14.1 Hz, 2H), 3.39 (d, J = 14.1 Hz, 2H), 3.53–3.56 (m, 2H), 3.57 (d, J = 5.0 Hz, 2H), 3.70–3.78 (m, 2H), 5.01 (t, J = 5.1 Hz, 1H), 6.48 (s, 1H), 6.73 (dd, J = 7.4, 1.7 Hz, 4H), 7.00–7.05 (m, 7H), 7.38 (d, J = 7.7 Hz, 1H); ^{13}C NMR δ 15.4, 22.0, 43.7, 46.0, 64.3, 69.4, 100.9, 122.8, 124.6, 126.8, 127.8, 128.9, 129.5, 130.3, 135.7, 140.8, 147.2, 169.1; HRMS (ESI) calcd for $C_{29}H_{34}NO_3$ $[M+H]^+$: 444.2539, found: 444.2525.

Data of ***2j***. Yellow oil. ^{1}H NMR δ 1.17 (t, J = 7.0 Hz, 6H), 2.21 (s, 3H), 3.49 (d, J = 14.8 Hz, 2H), 3.54–3.62 (m, 2H), 3.70 (d, J = 5.0 Hz, 2H), 3.74 (d, J = 14.8 Hz, 2H), 3.76–3.84 (m, 2H), 5.14 (t, J = 5.0 Hz, 1H), 6.57 (s, 1H), 6.80 (d, J = 7.6 Hz, 2H), 6.96 (t, J = 7.6 Hz, 2H), 7.01–7.08 (m, 3H), 7.41 (d, J = 7.9 Hz, 2H), 7.50 (d, J = 7.7 Hz, 1H); ^{13}C NMR δ 15.3, 21.8, 41.9, 45.8, 63.9, 69.4, 100.6, 122.6, 124.3, 126.3, 127.0, 128.3, 129.0, 129.2, 130.7, 132.8, 135.6, 141.2, 146.5, 169.5; HRMS (ESI) calcd for $C_{29}H_{32}Br_2NO_3$ $[M+H]^+$: 602.0728, found: 602.0717.

Data of ***2k***. Yellow oil. ^{1}H NMR δ 1.18 (t, J = 7.0 Hz, 6H), 2.34 (s, 3H), 3.11 (d, J = 14.1 Hz, 2H), 3.45 (d, J = 14.1 Hz, 2H), 3.59 (s, 6H), 3.60–3.64 (m, 2H), 3.77–3.85 (m, 2H), 5.07 (t, J = 5.0 Hz, 1H), 6.28 (s, 2H), 6.47 (d, J = 7.5 Hz, 2H), 6.67–6.69 (m, 3H), 7.04 (t, J = 7.9 Hz, 2H), 7.15 (d, J = 7.7 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H); ^{13}C NMR δ 15.4, 21.9, 43.7, 45.9, 55.0, 64.3, 69.4, 100.9, 112.7, 115.5, 122.8, 122.9, 124.6, 128.8, 128.9, 129.7, 137.1, 140.7, 147.5, 159.0, 169.0; HRMS (ESI) calcd for $C_{31}H_{38}NO_5$ $[M+H]^+$: 504.2750, found: 504.2743.

Data of ***2l***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.18 (d, J = 14.1 Hz, 2H), 3.45 (d, J = 14.1 Hz, 2H), 3.61–3.67 (m, 2H), 3.68 (d, J = 5.1 Hz, 2H), 3.79–3.86 (m, 2H), 5.08 (t, J = 5.1 Hz, 1H), 6.45 (dd, J = 8.7, 2.1 Hz, 1H), 6.83 (dd, J = 7.2, 2.2 Hz, 4H), 6.99 (td, J = 8.8, 2.2 Hz, 1H), 7.10–7.15 (m, 6H), 7.53 (dd, J = 8.3, 5.1 Hz, 1H); ^{13}C NMR δ 15.4, 43.4, 46.1, 64.3, 69.5, 100.7, 111.4 (d, $J_{F\text{-}C}$ = 24.4 Hz), 115.6, 115.8, 125.0 (d, $J_{F\text{-}C}$ = 9.7 Hz), 127.0, 128.0, 130.2, 135.1, 149.4 (d, $J_{F\text{-}C}$ = 9.1 Hz), 164.1 (d, $J_{F\text{-}C}$ = 250.6 Hz), 167.9; HRMS (ESI) calcd for $C_{28}H_{31}FNO_3$ $[M+H]^+$: 448.2288, found: 448.2280.

Data of ***2m***. Yellow oil. ^{1}H NMR δ 1.18 (t, J = 7.0 Hz, 6H), 3.49 (d, J = 14.7 Hz, 2H), 3.57–3.65 (m, 2H), 3.73 (d, J = 5.1 Hz, 2H), 3.76 (d, J = 14.7 Hz, 2H), 3.80–3.86 (m, 2H), 5.16 (t, J = 5.1 Hz, 1H), 6.42 (dd, J = 8.8, 2.1 Hz, 1H), 6.88 (dd, J = 7.7, 1.5 Hz, 2H), 6.93–7.02 (m, 3H), 7.08 (t, J = 7.5 Hz, 2H), 7.43 (dd, J = 7.9, 1.2 Hz, 2H), 7.58 (dd, J = 8.3, 5.1 Hz, 1H); ^{13}C NMR δ 15.3, 41.6, 45.9, 64.0, 69.3, 100.4, 111.3 (d, $J_{F\text{-}C}$ = 24.9 Hz), 115.8 (d, $J_{F\text{-}C}$ = 23.4 Hz), 124.8 (d, $J_{F\text{-}C}$ = 9.6 Hz), 126.3, 127.2, 127.7, 128.7, 130.7, 133.1, 135.1, 148.6 (d, $J_{F\text{-}C}$ = 9.8 Hz), 164.3 (d, $J_{F\text{-}C}$ = 250.9 Hz), 168.3; HRMS (ESI) calcd for $C_{28}H_{28}Br_2FNNaO_3$ $[M+Na]^+$: 628.0297, found: 628.0322.

Data of ***2n***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.14 (d, J = 14.1 Hz, 2H), 3.43 (d, J = 14.1 Hz, 2H), 3.57–3.66 (m, 10H), 3.78–3.86 (m, 2H), 5.07 (t, J = 5.1 Hz, 1H), 6.32 (s, 2H), 6.46 (d, J = 7.5 Hz, 2H), 6.56 (dd, J = 8.7, 2.0 Hz, 1H), 6.69 (dd, J = 8.2, 2.0 Hz, 2H), 7.00–7.08 (m, 3H), 7.57 (dd, J = 8.3, 5.1 Hz, 1H); ^{13}C NMR δ 15.4, 43.5, 46.0, 55.1, 64.3, 69.4, 100.7, 111.4 (d, $J_{F\text{-}C}$ = 24.4 Hz), 112.7, 115.68, 115.7 (d, $J_{F\text{-}C}$ = 23.4 Hz), 122.7, 125.1 (d, $J_{F\text{-}C}$ = 9.6 Hz), 128.2, 129.0, 136.6, 149.6 (d, $J_{F\text{-}C}$ = 9.3 Hz), 159.1, 164.1 (d, $J_{F\text{-}C}$ = 252.2 Hz), 167.9; HRMS (ESI) calcd for $C_{30}H_{34}FNNaO_5$ $[M+Na]^+$: 530.2319, found: 530.2307.

Data of ***2o***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.14 (d, J = 14.1 Hz, 2H), 3.47 (d, J = 14.1 Hz, 2H), 3.63–3.65 (m, 4H), 3.67 (s, 3H), 3.78–3.86 (m, 2H), 5.08 (t, J = 5.1 Hz, 1H), 6.21 (d, J = 2.1 Hz, 1H), 6.82–6.86 (m, 5H), 7.09–7.13 (m, 6H), 7.49 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 15.4, 43.7, 46.0, 55.4, 64.4, 69.2, 100.9, 108.5, 115.1, 124.3, 124.7, 126.9, 127.9, 130.3, 135.6, 149.1, 161.6, 168.8; HRMS (ESI) calcd for $C_{29}H_{34}NO_4$ $[M+H]^+$: 460.2488, found: 460.2478.

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*Data of **2p***. Yellow oil. ^{1}H NMR δ 1.18 (t, J = 7.0 Hz, 6H), 3.48 (d, J = 14.7 Hz, 2H), 3.59 (s, 3H), 3.60–3.66 (m, 2H), 3.71 (d, J = 5.1 Hz, 2H), 3.77 (d, J = 14.7 Hz, 2H), 3.80–3.86 (m, 2H), 5.17 (t, J = 5.1 Hz, 1H), 6.23 (d, J = 2.1 Hz, 1H), 6.76 (dd, J = 8.4, 2.2 Hz, 1H), 6.90 (dd, J = 7.7, 1.6 Hz, 2H), 6.97 (td, J = 7.8, 1.6 Hz, 2H), 7.06 (td, J = 7.5, 1.2 Hz, 2H), 7.42 (dd, J = 8.0, 1.1 Hz, 2H), 7.50 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 15.3, 41.7, 45.8, 55.3, 64.0, 69.2, 100.7, 107.4, 116.0, 124.1, 124.3, 126.5, 127.1, 128.4, 130.9, 132.9, 135.6, 148.5, 161.8, 169.3; HRMS (ESI) calcd for $C_{29}H_{32}Br_2NO_4$ $[M+H]^+$: 618.0678, found: 618.0698.

*Data of **2q***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 2.19 (s, 6H), 3.08 (d, J = 14.0 Hz, 2H), 3.44 (d, J = 14.0 Hz, 2H), 3.57–3.63 (m, 4H), 3.67 (s, 3H), 3.78–3.86 (m, 2H), 5.07 (t, J = 5.0 Hz, 1H), 6.24 (d, J = 2.1 Hz, 1H), 6.63–6.65 (m, 4H), 6.85 (dd, J = 8.4, 2.2 Hz, 1H), 6.94 (d, J = 7.5 Hz, 2H), 7.01 (t, J = 7.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 15.4, 21.3, 43.7, 45.9, 55.4, 64.3, 69.2, 101.0, 108.6, 115.2, 124.2, 124.8, 127.4, 127.6, 127.7, 131.2, 135.5, 137.3, 149.3, 161.6, 168.8; HRMS (ESI) calcd for $C_{31}H_{38}NO_4$ $[M+H]^+$: 488.2801, found: 488.2802.

*Data of **2r***. Yellow oil. ^{1}H NMR δ 1.19 (t, J = 7.0 Hz, 6H), 3.10 (d, J = 14.1 Hz, 2H), 3.45 (d, J = 14.1 Hz, 2H), 3.57–3.64 (m, 10H), 3.69 (s, 3H), 3.79–3.83 (m, 2H), 5.06 (t, J = 5.1 Hz, 1H), 6.30 (d, J = 2.1 Hz, 1H), 6.33 (s, 2H), 6.49 (d, J = 7.6 Hz, 2H), 6.68 (dd, J = 8.2, 2.2 Hz, 2H), 6.86 (dd, J = 8.4, 2.2 Hz, 1H), 7.05 (t, J = 7.9 Hz, 2H), 7.52 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 15.4, 43.8, 45.9, 55.0, 55.4, 64.3, 69.1, 100.9, 108.6, 112.5, 115.2, 115.8, 122.8, 124.4, 124.8, 128.8, 137.0, 149.3, 159.0, 161.7, 168.7; HRMS (ESI) calcd for $C_{31}H_{38}NO_6$ $[M+H]^+$: 520.2699, found: 520.2685.

*Data of **2s***. Yellow oil. ^{1}H NMR δ 1.16–1.21 (m, 6H), 3.15 (d, J = 14.1 Hz, 2H), 3.44–3.51 (m, 2H), 3.57 (s, 3H), 3.59–3.64 (m, 2H), 3.67 (d, J = 5.1 Hz, 2H), 3.78–3.86 (m, 2H), 5.10 (t, J = 5.0 Hz, 1H), 6.25 (s, 1H), 6.46 (d, J = 7.5 Hz, 1H), 6.66 (d, J = 9.9 Hz, 1H), 6.61–6.68 (m, 3H), 7.03 (t, J = 7.9 Hz, 1H), 7.09–7.12 (m, 3H), 7.32–7.38 (m, 2H), 7.59 (d, J = 7.3 Hz, 1H); ^{13}C NMR δ 15.35, 15.37, 43.6, 43.7, 46.0, 55.0, 64.3, 69.7, 100.8, 112.6, 115.6, 122.8, 123.1, 124.1, 126.8, 127.9, 128.0, 128.8, 130.29, 130.34, 132.1, 135.6, 137.0, 147.0, 159.0, 168.9; HRMS (ESI) calcd for $C_{29}H_{33}NNaO_4$ $[M+Na]^+$: 482.2307, found: 482.2305.

*Data of **2t***. Yellow oil. ^{1}H NMR δ 1.16–1.22 (m, 6H), 3.09 (d, J = 14.2 Hz, 1H), 3.14 (d, J = 14.1 Hz, 1H), 3.42 (d, J = 14.2 Hz, 1H), 3.47 (d, J = 14.1 Hz, 1H), 3.58–3.68 (m, 4H), 3.72 (s, 3H), 3.78–3.86 (m, 2H), 5.10 (t, J = 5.1 Hz, 1H), 6.63 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 7.7 Hz, 3H), 7.08–7.12 (m, 3H), 7.30–7.38 (m, 2H), 7.58 (d, J = 6.7 Hz, 1H); ^{13}C NMR δ 15.34, 15.38, 42.7, 43.5, 46.0, 55.1, 64.3, 69.8, 100.8, 113.3, 123.0, 124.0, 126.8, 127.4, 127.86, 127.94, 130.26, 130.33, 131.2, 132.0, 135.7, 147.0, 158.4, 169.0; HRMS (ESI) calcd for $C_{29}H_{33}NNaO_4$ $[M+Na]^+$: 482.2307, found: 482.2294.

*Data of **2u***. Yellow oil. ^{1}H NMR δ 1.18 (t, J = 7.0 Hz, 6H), 1.35 (t, J = 7.1 Hz, 6H), 3.31 (d, J = 14.0 Hz, 2H), 3.51 (d, J = 14.0 Hz, 2H), 3.58–3.65 (m, 2H), 3.68 (d, J = 5.0 Hz, 2H), 3.80–3.87 (m, 2H), 4.32 (q, J = 7.1 Hz, 4H), 5.09 (t, J = 5.0 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 6.89 (d, J = 8.2 Hz, 4H), 7.30–7.40 (m, 2H), 7.58 (d, J = 7.2 Hz, 1H), 7.79 (d, J = 8.2 Hz, 4H); ^{13}C NMR δ 14.3, 15.3, 43.5, 46.0, 60.9, 64.4, 69.4, 100.7, 123.3, 123.6, 128.4, 129.08, 129.13, 130.1, 130.8, 131.8, 140.6, 146.2, 166.3, 168.8; HRMS (ESI) calcd for $C_{34}H_{39}NNaO_7$ $[M+Na]^+$: 596.2624, found: 596.2624.

3.4. Gram-scale synthesis of **2c**

A THF solution of KHMDS (1.0 M, 10.5 mL, 10.5 mmol) was slowly added to the stirred solution of **1a** (1.18 g, 4.75 mmol) in THF (30 mL) at room temperature. After continuously stirring for half an hour, the solution of 3-bromobenzyl bromide (2.62 g, 10.5 mmol) in THF (5 mL) was slowly added. The reaction mixture was stirred at room temperature overnight. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 1:3) as the eluent to afford 1.54 g (55%) of **2c**.

3.5. Reaction of **1e** with CF_3CO_2H

Trifluoroacetic acid (0.14 mL, 1.9 mmol) was added the solution of **1e** (325 mg, 0.96 mmol) in CH_2Cl_2 (30 mL). The reaction mixture was stirred overnight at room temperature, and quenched with saturated aqueous sodium carbonate solution (10 mL). The aqueous layer was extracted with ethyl acetate (10 mL × 3), and the combined extracts were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 3:2) as the eluent to afford 207 mg (82%) of **3** as yellow oil. [20] ^{1}H NMR δ 3.00 (dd, J = 14.0, 7.0 Hz, 1H), 3.14 (dd, J = 14.0, 6.4 Hz, 1H), 3.99 (d, J = 18.9 Hz, 1H), 4.63 (d, J = 18.9 Hz, 1H), 4.98 (t, J = 6.7 Hz, 1H), 7.06–7.11 (m, 3H), 7.25–7.30 (m, 3H), 7.42–7.50 (m, 2H), 7.83 (dd, J = 6.4, 1.5 Hz, 1H), 9.54 (s, 1H); ^{13}C NMR δ 39.2, 51.3, 61.4, 122.9, 123.9, 127.3, 128.4, 128.8, 129.3, 131.1, 131.7, 136.0, 145.5, 169.0, 196.9.

3.6. Synthesis of **4a**

Powdery $AlCl_3$ (72 mg, 0.54 mmol) was added to the solution of **1e** (41 mg, 0.12 mmol) in CH_2Cl_2 (3 mL) at room temperature. The reaction mixture was stirred for 12 h, and quenched with aqueous sodium hydroxide solution (40%, 10 mL). The aqueous layer was extracted with ethyl acetate (10 mL × 3), and the combined extracts were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 1:6) as the eluent to afford 21 mg (71%) of **4a** as yellow oil [20], which solidifies during storage. ^{1}H NMR δ 3.09 (dd, J = 15.4, 9.8 Hz, 1H), 3.53 (d, J = 15.3 Hz, 1H), 4.82 (d, J = 9.8 Hz, 1H), 5.84 (d, J = 10.3 Hz, 1H), 7.18–7.26 (m, 5H), 7.52 (t, J = 7.4 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.66 (td, J = 7.5, 1.1 Hz, 1H), 7.89 (d, J = 7.6 Hz, 1H); ^{13}C NMR δ 42.0, 60.5, 109.8, 121.3, 122.3, 124.2, 126.9, 127.3, 128.9, 129.8, 130.7, 131.1, 132.9, 135.3, 135.8, 144.4, 165.7. HRMS (ESI) calcd for $C_{17}H_{14}NO$ $[M+H]^+$: 248.1075, found: 248.1073.

3.7. Synthesis of **4b**

When **1f** was used as the substrate instead of **1e** as described above for **3**, compound **4b** was obtained as a white solid in 63% yield. This compound has also been directly obtained from aromatic imine as follows. A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2 mmol) was slowly added to the stirred solution of N-(2-bromobenzylidene)-2,2-diethoxyethanamine (0.6 g, 2 mmol) in THF (30 mL) at −78 °C. After continuously stirring for half an hour, carbon monoxide was bubbled into the solution. The carbon monoxide atmosphere was kept with a balloon at the exit. The reaction mixture was continuously stirred at low temperature for 1 h, 3-methoxybenzyl bromide (0.28 mL, 2 mmol) was slowly added dropwise with syringe. The reaction mixture was warmed to room temperature slowly and stirred for 5 h. The solvent was removed in vacuo, and the residual was redissolved in CH_2Cl_2 (30 mL). Trifluoroacetic acid (2.6 mL, 4 mmol) was added. The reaction mixture was stirred overnight at room temperature, and quenched with saturated aqueous sodium carbonate solution (30 mL). The aqueous layer was extracted with ethyl acetate (20 mL × 3), and the combined extracts were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 1:5) as the eluent to afford **4b** (262 mg,

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50%). ^{1}H NMR δ 3.08 (dd, J = 15.4, 9.9 Hz, 1H), 3.46 (d, J = 15.4 Hz, 1H), 3.84 (s, 3H), 4.80 (d, J = 9.8 Hz, 1H), 5.79 (d, J = 10.3 Hz, 1H), 6.78–6.81 (m, 2H), 7.11 (d, J = 10.2 Hz, 1H), 7.17 (d, J = 9.2 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.58 (d, J = 7.4 Hz, 1H), 7.64 (t, J = 7.1 Hz, 1H), 7.88 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 42.1, 55.4, 60.3, 109.7, 112.2, 115.7, 119.3, 122.2, 124.1, 128.0, 128.8, 130.9, 132.5, 132.7, 137.3, 144.2, 158.5, 165.5. HRMS (ESI) calcd for $C_{18}H_{16}NO_2$ $[M+H]^+$: 278.1181, found: 278.1176.

3.8. Typical procedure for the synthesis of **5a**–**5t** and **6**

Powdery $AlCl_3$ (3.5 mmol) was added to the solution of **2a**–**2u** (1 mmol) in CH_2Cl_2 (40 mL) at room temperature. The reaction mixture was stirred overnight, and quenched with aqueous sodium hydroxide solution (40%, 10 mL). Then, the mixture was extracted with CH_2Cl_2 (20 mL × 3). The extracts were combined and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 1:2) as the eluent to afford products **5a**–**5t** and **6**.

*Data of **5a***. White solid. ^{1}H NMR δ 3.29 (d, J = 16.7 Hz, 2H), 3.58 (d, J = 16.7 Hz, 2H), 4.20 (d, J = 2.9 Hz, 2H), 4.48 (t, J = 2.9 Hz, 1H), 7.04 (d, J = 7.4 Hz, 2H), 7.13 (t, J = 7.4 Hz, 2H), 7.20 (t, J = 7.3 Hz, 2H), 7.32 (d, J = 7.4 Hz, 2H), 7.48 (t, J = 7.3 Hz, 1H), 7.59 (d, J = 7.5 Hz, 1H), 7.66 (t, J = 7.5 Hz, 1H), 7.79 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 45.3, 45.7, 50.2, 65.1, 120.8, 123.6, 127.0, 127.4, 128.3, 130.4, 130.8, 130.9, 132.5, 135.9, 139.2, 153.6, 169.0; HRMS (ESI) calcd for $C_{24}H_{20}NO$ $[M+H]^+$: 338.1545, found: 338.1543.

*Data of **5b***. Yellow solid. ^{1}H NMR δ 3.38 (d, J = 17.7 Hz, 2H), 3.71 (d, J = 17.7 Hz, 2H), 4.21 (s, 2H), 4.50 (s, 1H), 6.99 (d, J = 7.5 Hz, 2H), 7.23 (d, J = 7.3 Hz, 2H), 7.42 (d, J = 7.7 Hz, 2H), 7.45–7.53 (m, 1H), 7.65–7.69 (m, 2H), 7.81 (d, J = 7.1 Hz, 1H); ^{13}C NMR δ 45.5, 45.6, 51.1, 64.6, 120.9, 123.7, 126.9, 128.5, 128.6, 130.0, 130.1, 132.1, 132.9, 135.0, 141.4, 153.6, 168.9; HRMS (ESI) calcd for $C_{24}H_{18}Br_2NO$ $[M+H]^+$: 495.9735, found: 495.9739.

*Data of **5c***. Yellow oil. ^{1}H NMR δ 3.24 (d, J = 16.8 Hz, 2H), 3.51 (d, J = 16.9 Hz, 2H), 4.14 (d, J = 3.4 Hz, 2H), 4.40 (t, J = 3.4 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.21 (s, 2H), 7.32 (dd, J = 8.1, 1.9 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 44.8, 45.2, 49.1, 64.6, 120.7, 120.9, 123.8, 127.7, 128.6, 130.5, 131.9, 132.8, 133.6, 137.7, 138.0, 152.9, 168.9; HRMS (ESI) calcd for $C_{24}H_{18}Br_2NO$ $[M+H]^+$: 495.9735, found: 495.9724.

*Data of **5d***. Yellow oil. ^{1}H NMR δ 3.22 (d, J = 16.8 Hz, 2H), 3.49 (d, J = 16.8 Hz, 2H), 4.16 (d, J = 3.4 Hz, 2H), 4.35 (t, J = 3.4 Hz, 1H), 6.93 (d, J = 8.1 Hz, 2H), 7.26–7.32 (m, 2H), 7.46 (d, J = 1.8 Hz, 2H), 7.49 (t, J = 7.5 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.66 (t, J = 7.5 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 44.7, 45.3, 49.5, 64.6, 120.7, 121.1, 123.8, 128.5, 130.3, 130.5, 132.6, 132.7, 133.1, 134.9, 140.5, 153.1, 168.9; HRMS (ESI) calcd for $C_{24}H_{18}Br_2NO$ $[M+H]^+$: 495.9735, found: 495.9724.

*Data of **5e***. Yellow oil. ^{1}H NMR δ 3.25 (d, J = 16.7 Hz, 2H), 3.52 (d, J = 16.6 Hz, 2H), 4.18 (d, J = 3.5 Hz, 2H), 4.36 (t, J = 3.5 Hz, 1H), 6.85 (td, J = 8.3, 2.6 Hz, 2H), 7.00–7.03 (m, 4H), 7.49 (t, J = 7.4 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.66 (td, J = 7.6, 0.9 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 44.4, 45.2, 49.9, 64.8, 114.1 (d, $J_{F\text{-}C}$ = 20.8 Hz), 116.9 (d, $J_{F\text{-}C}$ = 21.2 Hz), 120.7, 123.7, 128.4, 130.6, 131.6 (d, $J_{F\text{-}C}$ = 3.1 Hz), 132.5 (d, $J_{F\text{-}C}$ = 7.9 Hz), 132.7, 140.4 (d, $J_{F\text{-}C}$ = 6.9 Hz), 153.3, 161.9 (d, $J_{F\text{-}C}$ = 248.8 Hz), 168.9; HRMS (ESI) calcd for $C_{24}H_{18}F_2NO$ $[M+H]^+$: 374.1356, found: 374.1349.

*Data of **5f***. Yellow oil. ^{1}H NMR δ 2.23 (s, 6H), 3.22 (d, J = 16.7 Hz, 2H), 3.53 (d, J = 16.7 Hz, 2H), 4.15 (d, J = 3.3 Hz, 2H), 4.39 (t, J = 3.3 Hz, 1H), 6.84 (s, 2H), 6.98 (d, J = 7.4 Hz, 2H), 7.18 (d, J = 7.7 Hz, 2H), 7.45 (d, J = 7.3 Hz, 1H), 7.56 (d, J = 7.5 Hz, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.78 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 20.8, 45.2, 46.0, 49.4, 65.2, 120.8, 123.5, 128.1, 128.2, 130.2, 130.8, 131.6, 132.4, 135.6, 136.5, 136.6, 153.8, 169.0; HRMS (ESI) calcd for $C_{26}H_{24}NO$ $[M+H]^+$: 366.1858, found: 366.1849.

*Data of **5g***. White solid. ^{1}H NMR δ 3.24 (d, J = 16.7 Hz, 2H), 3.55 (d, J = 16.7 Hz, 2H), 3.73 (s, 6H), 4.14 (d, J = 3.3 Hz, 2H), 4.38 (t, J = 3.4 Hz, 1H), 6.57 (s, 2H), 6.73 (dd, J = 8.4, 2.5 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.65 (t, J = 7.4 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 45.4, 46.2, 48.5, 55.3, 65.0, 112.6, 116.2, 120.8, 123.6, 128.2, 130.8, 131.2, 132.2, 132.4, 136.9, 153.6, 158.3, 169.0; HRMS (ESI) calcd for $C_{26}H_{24}NO_3$ $[M+H]^+$: 398.1756, found: 398.1753.

*Data of **5h***. Yellow oil. ^{1}H NMR δ 3.20 (d, J = 16.5 Hz, 2H), 3.51 (d, J = 16.5 Hz, 2H), 3.78 (s, 6H), 4.18 (d, J = 3.5 Hz, 2H), 4.34 (t, J = 3.4 Hz, 1H), 6.68 (dd, J = 8.4, 2.7 Hz, 2H), 6.85 (d, J = 2.6 Hz, 2H), 6.95 (d, J = 8.4 Hz, 2H), 7.46 (t, J = 7.4 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.64 (t, J = 7.9 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 44.4, 45.5, 50.6, 55.3, 65.2, 112.2, 115.8, 120.7, 123.5, 128.0, 128.1, 130.8, 132.0, 132.4, 140.2, 153.7, 158.7, 169.0; HRMS (ESI) calcd for $C_{26}H_{24}NO_3$ $[M+H]^+$: 398.1756, found: 398.1746.

*Data of **5i***. White solid. ^{1}H NMR δ 2.53 (s, 3H), 3.27 (d, J = 16.7 Hz, 2H), 3.55 (d, J = 16.7 Hz, 2H), 4.17 (d, J = 3.5 Hz, 2H), 4.45 (t, J = 3.5 Hz, 1H), 7.03 (d, J = 7.2 Hz, 2H), 7.11 (td, J = 7.4, 1.4 Hz, 2H), 7.18 (td, J = 7.4, 1.2 Hz, 2H), 7.27 (d, J = 7.8 Hz, 1H), 7.30 (d, J = 7.5 Hz, 2H), 7.39 (s, 1H), 7.66 (d, J = 7.7 Hz, 1H); ^{13}C NMR δ 22.2, 45.3, 45.7, 50.3, 64.9, 121.4, 123.3, 127.0, 127.4, 128.2, 129.2, 130.4, 130.9, 136.0, 139.3, 143.2, 154.1, 169.1; HRMS (ESI) calcd for $C_{25}H_{22}NO$ $[M+H]^+$: 352.1701, found: 352.1700.

*Data of **5j***. Yellow oil. ^{1}H NMR δ 2.57 (s, 3H), 3.38 (d, J = 17.6 Hz, 2H), 3.69 (d, J = 17.6 Hz, 2H), 4.21 (d, J = 3.6 Hz, 2H), 4.51 (t, J = 3.6 Hz, 1H), 7.04 (t, J = 7.8 Hz, 2H), 7.24 (t, J = 7.0 Hz, 2H), 7.31 (d, J = 7.8 Hz, 1H), 7.45 (d, J = 1.2 Hz, 1H), 7.47 (s, 2H), 7.69 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 22.3, 45.5 (2 C), 51.3, 64.4, 121.3, 123.5, 126.9, 127.5, 128.4, 129.6, 129.9, 132.1, 135.1, 141.4, 143.7, 154.0, 169.0; HRMS (ESI) calcd for $C_{25}H_{20}Br_2NO$ $[M+H]^+$: 509.9891, found: 509.9885.

*Data of **5k***. White solid. ^{1}H NMR δ 2.53 (s, 3H), 3.22 (d, J = 16.7 Hz, 2H), 3.53 (d, J = 16.7 Hz, 2H), 3.71 (s, 6H), 4.12 (d, J = 3.5 Hz, 2H), 4.36 (t, J = 3.5 Hz, 1H), 6.57 (d, J = 2.6 Hz, 2H), 6.72 (dd, J = 8.4, 2.7 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.1 Hz, 1H), 7.38 (s, 1H), 7.67 (d, J = 7.7 Hz, 1H); ^{13}C NMR δ 22.1, 45.5, 46.1, 48.5, 55.2, 64.8, 112.6, 116.2, 121.3, 123.3, 128.2, 129.2, 131.2, 132.3, 137.0, 143.1, 154.0, 158.2, 169.1; HRMS (ESI) calcd for $C_{27}H_{26}NO_3$ $[M+H]^+$: 412.1913, found: 412.1912.

*Data of **5l***. Yellow solid. ^{1}H NMR δ 3.27 (d, J = 16.7 Hz, 2H), 3.54 (d, J = 16.7 Hz, 2H), 4.17 (d, J = 3.2 Hz, 2H), 4.47 (t, J = 3.2 Hz, 1H), 7.04 (t, J = 7.48 Hz, 2H), 7.11–7.16 (m, 3H), 7.20–7.25 (m, 2H), 7.28–7.32 (m, 3H), 7.75–7.78 (m, 1H); ^{13}C NMR δ 45.1, 45.8, 50.2, 64.9, 108.4 (d, $J_{F\text{-}C}$ = 24.1 Hz), 116.0 (d, $J_{F\text{-}C}$ = 23.5 Hz), 125.7 (d, $J_{F\text{-}C}$ = 9.5 Hz), 126.8, 127.1, 127.5, 130.4, 130.9, 135.5, 139.1, 155.9 (d, $J_{F\text{-}C}$ = 8.8 Hz), 165.8 (d, $J_{F\text{-}C}$ = 252.4 Hz), 167.9; HRMS (ESI) calcd for $C_{24}H_{19}FNO$ $[M+H]^+$: 356.1451, found: 356.1445.

*Data of **5m***. Yellow oil. ^{1}H NMR δ 3.40 (d, J = 17.6 Hz, 2H), 3.67 (d, J = 17.6 Hz, 2H), 4.19 (d, J = 3.5 Hz, 2H), 4.52 (t, J = 3.5 Hz, 1H), 7.04 (t, J = 7.8, 2H), 7.19 (td, J = 8.8, 2.2 Hz, 1H), 7.25 (d, J = 7.1 Hz, 2H), 7.39 (dd, J = 8.1, 2.1 Hz, 1H), 7.46 (dd, J = 8.0, 1.1 Hz, 2H), 7.79 (dd, J = 8.3, 5.0 Hz, 1H); ^{13}C NMR δ 45.3, 45.6, 51.1, 64.3, 108.5 (d, $J_{F\text{-}C}$ = 24.3 Hz), 116.4 (d, $J_{F\text{-}C}$ = 23.4 Hz), 125.9 (d, $J_{F\text{-}C}$ = 9.8 Hz), 126.2 (d, $J_{F\text{-}C}$ = 1.8 Hz), 126.9, 128.6, 129.9, 132.1, 134.7, 141.3, 155.9 (d, $J_{F\text{-}C}$ = 8.9 Hz), 165.9 (d, $J_{F\text{-}C}$ = 253.2 Hz), 167.8; HRMS (ESI) calcd for $C_{24}H_{17}Br_2FNO$ $[M+H]^+$: 513.9640, found: 513.9632.

*Data of **5n***. White solid. ^{1}H NMR δ 3.23 (d, J = 16.7 Hz, 2H), 3.51 (d, J = 16.7 Hz, 2H), 3.72 (s, 6H), 4.11 (d, J = 3.5 Hz, 2H), 4.37 (t, J = 3.5 Hz, 1H), 6.57 (d, J = 2.6 Hz, 2H), 6.73 (dd, J = 8.4, 2.7 Hz, 2H), 7.13–7.18 (m, 1H), 7.20 (d, J = 8.4 Hz, 2H), 7.25–7.27 (m, 1H), 7.77 (dd, J = 8.3, 5.0 Hz, 1H); ^{13}C NMR δ 45.3, 46.3, 48.4, 55.3, 64.8, 108.4 (d, $J_{F\text{-}C}$ = 24.2 Hz), 112.7, 116.0 (d, $J_{F\text{-}C}$ = 23.4 Hz), 116.2, 125.7 (d, $J_{F\text{-}$

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$_C$ = 9.7 Hz), 126.8 (d, J_{F-C} = 1.7 Hz), 131.3, 132.1, 136.5, 155.9 (d, J_{F-C} = 9.0 Hz), 158.3, 165.7 (d, J_{F-C} = 252.2 Hz), 167.9; HRMS (ESI) calcd for $C_{26}H_{23}FNO_3$ $[M+H]^+$: 416.1662, found: 416.1656.

Data of ***5o***. White solid. ^{1}H NMR δ 3.28 (d, J = 16.7 Hz, 2H), 3.53 (d, J = 16.7 Hz, 2H), 3.94 (s, 3H), 4.16 (d, J = 3.5 Hz, 2H), 4.46 (t, J = 3.5 Hz, 1H), 6.98 (dd, J = 8.4, 2.2 Hz, 1H), 7.03–7.05 (m, 3H), 7.12 (td, J = 7.4, 1.4 Hz, 2H), 7.19 (td, J = 7.4, 1.2 Hz, 2H), 7.30 (dd, J = 7.5, 0.9 Hz, 2H), 7.70 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ 45.4, 45.7, 50.3, 55.8, 64.8, 106.0, 114.4, 123.4, 125.0, 127.0, 127.4, 130.4, 130.9, 135.9, 139.3, 155.9, 163.6, 168.9; HRMS (ESI) calcd for $C_{25}H_{22}NO_2$ $[M+H]^+$: 368.1651, found: 368.1648.

Data of ***5p***. Yellow oil. ^{1}H NMR δ 3.31 (d, J = 17.6 Hz, 2H), 3.58 (d, J = 17.6 Hz, 2H), 3.88 (s, 3H), 4.10 (d, J = 3.5 Hz, 2H), 4.42 (t, J = 3.5 Hz, 1H), 6.92–6.96 (m, 3H), 7.06 (d, J = 2.1 Hz, 1H), 7.12–7.17 (m, 2H), 7.36 (dd, J = 8.0, 1.1 Hz, 2H), 7.65 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 45.48, 45.53, 51.3, 55.9, 64.3, 106.3, 114.5, 122.7, 125.2, 126.9, 128.4, 129.9, 132.0, 135.0, 141.4, 155.8, 163.8, 168.8; HRMS (ESI) calcd for $C_{25}H_{20}Br_2NO_2$ $[M+H]^+$: 525.9840, found: 525.9841.

Data of ***5q***. Yellow oil. ^{1}H NMR δ 2.21 (s, 6H), 3.21 (d, J = 16.7 Hz, 2H), 3.48 (d, J = 16.7 Hz, 2H), 3.91 (s, 3H), 4.11 (d, J = 3.4 Hz, 2H), 4.36 (t, J = 3.4 Hz, 1H), 6.83 (s, 2H), 6.95–6.97 (m, 3H), 7.04 (d, J = 2.1 Hz, 1H), 7.16 (d, J = 7.7 Hz, 2H), 7.69 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 20.8, 45.4, 46.0, 49.4, 55.8, 64.9, 106.0, 114.5, 123.5, 124.9, 128.0, 130.2, 131.6, 135.6, 136.4, 136.7, 156.1, 163.6, 168.9; HRMS (ESI) calcd for $C_{27}H_{26}NO_2$ $[M+H]^+$: 396.1964, found: 396.1966.

Data of ***5r***. White solid. ^{1}H NMR δ 3.21 (d, J = 16.8 Hz, 2H), 3.50 (d, J = 16.8 Hz, 2H), 3.68 (s, 6H), 3.91 (s, 3H), 4.08 (d, J = 3.4 Hz, 2H), 4.33 (t, J = 3.4 Hz, 1H), 6.56 (d, J = 2.5 Hz, 2H), 6.70 (dd, J = 8.4, 2.6 Hz, 2H), 6.96 (dd, J = 8.4, 2.1 Hz, 1H), 7.04 (d, J = 1.9 Hz, 1H), 7.17 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 45.5, 46.1, 48.5, 55.2, 55.8, 64.7, 106.0, 112.6, 114.5, 116.2, 123.4, 124.9, 131.3, 132.3, 136.9, 155.9, 158.2, 163.6, 168.8; HRMS (ESI) calcd for $C_{27}H_{26}NO_4$ $[M+H]^+$: 428.1862, found: 428.1851.

Data of ***5s***. Yellow oil. ^{1}H NMR δ 3.26 (dd, J = 16.7, 11.1 Hz, 2H), 3.56 (dd, J = 16.7, 13.7 Hz, 2H), 3.72 (s, 3H), 4.17 (dd, J = 3.5, 1.5 Hz, 2H), 4.42 (t, J = 3.5 Hz, 1H), 6.58 (d, J = 2.6 Hz, 1H), 6.73 (dd, J = 8.4, 2.7 Hz, 1H), 7.02 (d, J = 7.4 Hz, 1H), 7.11 (td, J = 7.4, 1.4 Hz, 1H), 7.18 (t, J = 6.8 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.29 (d, J = 6.5 Hz, 1H), 7.47 (td, J = 7.4, 0.9 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.65 (td, J = 7.5, 1.1 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 45.2, 45.5, 45.9, 49.4, 55.3, 65.1, 112.6, 116.2, 120.8, 123.6, 126.9, 127.4, 128.3, 130.2, 130.8, 130.9, 131.4, 131.7, 132.5, 135.7, 137.1, 139.7, 153.6, 158.3, 169.0; HRMS (ESI) calcd for $C_{25}H_{22}NO_2$ $[M+H]^+$: 368.1651, found: 368.1649.

Data of ***5t***. Yellow oil. ^{1}H NMR δ 3.21 (d, J = 16.6 Hz, 1H), 3.27 (d, J = 16.8 Hz, 1H), 3.51 (d, J = 16.5 Hz, 1H), 3.58 (d, J = 16.7 Hz, 1H), 3.77 (s, 3H), 4.19 (dd, J = 6.1, 3.6 Hz, 2H), 4.41 (t, J = 3.5 Hz, 1H), 6.68 (dd, J = 8.4, 2.7 Hz, 1H), 6.84 (d, J = 2.7 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 7.4 Hz, 1H), 7.12 (td, J = 7.4, 1.4 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 7.31 (d, J = 8.6 Hz, 1H), 7.46 (td, J = 7.4, 0.9 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.64 (td, J = 7.5, 1.1 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 44.5, 45.1, 45.6, 50.4, 55.3, 65.2, 112.3, 115.8, 120.8, 123.5, 127.1, 127.4, 127.9, 128.2, 130.3, 130.75, 130.82, 132.0, 132.4, 136.0, 139.1, 140.3, 153.7, 158.7, 169.0; HRMS (ESI) calcd for $C_{25}H_{22}NO_2$ $[M+H]^+$: 368.1651, found: 368.1645.

Data of ***6***. Yellow oil. ^{1}H NMR δ 1.28 (t, J = 7.1 Hz, 6H), 3.18 (d, J = 14.0 Hz, 2H), 3.43 (d, J = 14.0 Hz, 2H), 4.09 (s, 1H), 4.25 (q, J = 7.1 Hz, 4H), 6.71 (d, J = 8.2 Hz, 4H), 7.18 (d, J = 7.7 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.50–7.56 (m, 2H), 7.70 (d, J = 8.2 Hz, 4H), 9.15 (s, 1H); ^{13}C NMR δ 14.3, 43.8, 49.9, 61.0, 69.2, 123.1, 124.1, 129.0, 129.5, 129.6, 129.8, 131.4, 131.7, 139.2, 146.5, 166.1, 168.7, 197.6; HRMS (ESI) calcd for $C_{30}H_{30}NO_6$ $[M+H]^+$: 500.2073, found: 500.2070.

3.9. Gram-scale synthesis of *5c*

Powdery $AlCl_3$ (1.23 g, 9.21 mmol) was slowly added to the stirred solution of **2c** (1.54 g, 2.63 mmol) in CH_2Cl_2 (80 mL) at room temperature. The reaction mixture was stirred overnight, and quenched with aqueous sodium hydroxide solution (40%, 25 mL). The mixture was extracted with CH_2Cl_2 (30 mL × 3). The extracts were combined and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 2:3) as the eluent to afford 0.911 g (70%) of **5c** as yellow oil.

3.10. Reaction of *5g* with BBr_3

BBr_3 (0.12 mL, 1.26 mmol) was added to the stirred solution of **5g** (125 mg, 0.31 mmol) in CH_2Cl_2 (25 mL) at −78 °C. The reaction mixture was warmed to room temperature, stirred overnight, and quenched with H_2O (10 mL). The mixture was transferred to a separatory funnel and extracted with ethyl acetate (20 mL × 3). The combined organic extracts were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 3:2) as the eluent to afford 113 mg (98%) of **7** as a white solid. ^{1}H NMR (DMSO-d_6) δ 3.07 (d, J = 16.9 Hz, 2H), 3.51 (d, J = 16.9 Hz, 2H), 3.92 (d, J = 2.4 Hz, 2H), 4.38 (s, 1H), 6.48 (s, 2H), 6.57 (dd, J = 8.1, 1.8 Hz, 2H), 7.12 (d, J = 8.2 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.62 (d, J = 7.4 Hz, 1H), 7.72 (t, J = 7.4 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 9.22 (s, 2H); ^{13}C NMR (DMSO-d_6) δ 44.4, 45.9, 47.0, 64.5, 113.6, 117.1, 121.8, 122.4, 128.1, 130.1, 130.8, 131.0, 132.6, 137.0, 153.9, 155.6, 167.8. HRMS (ESI) calcd for $C_{24}H_{20}NO_3$ $[M+H]^+$: 370.1443, found: 370.1438.

CCDC 1998409–1998410 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Crystal structure determinations of **4b** and **5a** along with their data and the synthesis of aromatic imines as well as ^{1}H and ^{13}C NMR spectra of all compounds are provided.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131341.

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