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ARTICLE

Synthesis of Unnatural α-Amino Acid Derivatives *via* Selective *o*-C-H Functionalization

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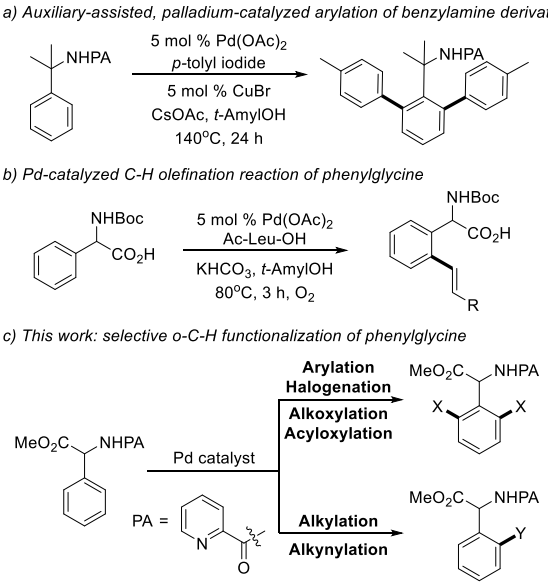
Pd-catalyzed *o*-C-H functionalization of α-phenylglycine, 4-hydroxyphenylglycine and phenylalanine using picolinamide as a directing group is reported. We have developed different protocols for the arylation, alkylation, alkynylation, halogenation, alkoxylation, and acyloxylation of these amino acids. The reactions exhibit high selectivity, broad substrate scope, and compatibility with different functional groups in moderate to high yields. They provide a rapid and efficient access to a variety of phenyl based amino acid derivatives which can be further modified and have broad spectrum of applications in medicinal chemistry.

Introduction

α-Amino acids (α-AAs) are pivotal structural motifs of peptides, peptidomimetics and many other pharmaceutically important compounds.[1] The interest in biologics containing non-proteinogenic amino acids or non-natural linkages has increased dramatically.[2] Coordination-directed C–H bond functionalization of nitrogen-containing compounds, such as α-amino acids, is particularly attractive given their prevalence in natural products and therapeutic agents.[3] Therefore it is significant to develop new methodologies for the efficient molecular chemical modifications of amino acids due to the limited number of natural amino acids and their high potential application value. In this context, the use of transition-metal catalysis to modify small molecules in a tailored manner through C-C or C-X bond formation in aromatic rings could provide an attractive way to target amino acids that display this structural motif.[4]

In recent years, synthetic methods based on transition-metal catalyzed directed C-H functionalization to access unnatural counterparts have been investigated. Compared with traditional cross-coupling reactions, transition-metal catalyzed directed C-H activation has proven to be a powerful approach to utilize existing functional groups in a molecule to guide C–H cleavage at a particular site in a highly selective manner.[5] In 2006, Corey et al. first applied the AQ auxiliary for Pd-catalyzed *β*-C–H acetoxylation of alanine.[6] Inspired by this seminal work, significant progress has been made in this area. Reports by several groups on metal-catalyzed halogenation,[7] arylation,[8,18]



Scheme 1 Pd-catalyzed C-H functionalization of benzylamine and α-phenylglycine.

alkylation,[9] borylation,[10] alkoxylation,[11] alkenylation,[12] and acetoxylation[13] reactions for the synthesis of unnatural amino acids have been published. Considering most work are focused on phenylalanine (Phe), tyrosine (Tyr), tryptophan (Trp), and histidine (His), we chose α-phenylglycine as our substrate and tried to develop protocols for the synthesis of its derivatives. Notably, these scaffolds have already been found in many pharmaceutical drugs (e.g., cephalexin,[14] clopidogrel,[15] ampicillin[16]), and direct functionalization may expand the scope of these classes of compounds for further medicinal investigation. In 2013, Daugulis reported the scope of palladium-catalyzed, picolinamide-assisted direct arylation and alkylation of sp^2 C–H bonds of benzyl amines derivatives

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(Scheme 1a).[17] In 2015, Yu and co-workers described the Pd-catalyzed C–H olefination of α-phenylglycine, in which a monoprotected amino acids (MPAA) ligand was employed to achieve the monoselectivity (Scheme 1b).[18] Herein, we report a variety of *o*-C–H functionalizations of α-phenylglycine, 4-hydroxyphenylglycine and phenylalanine including selective bis-arylation, halogenation, alkoxylation, acyloxylation and selective mono-alkylation, alkynylation with the yield up to 99% (**Scheme 1c**). The site-selectivity in this method was controlled by a removable bidentate directing group of picolinamide.[19]

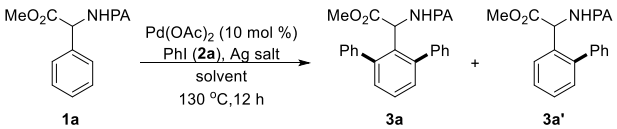
Results and discussion

Arylation of α-phenylglycine, 4-hydroxyphenylglycine and phenylalanine. Based on one of our previous work of vinylic C-H arylation of unsubstituted acrylamide,[20] we began our investigation by studying C-H arylation of **1a** with phenyl iodide in the presence of a Pd catalyst under various reaction conditions (Table 1). The initial optimization experiments were aimed at varying the equivalence of phenyl iodide (**2a**), which plays a crucial role in mono- or di-selectivity (entries 1-4). Next, we investigated the influence of different solvents including 1,4-dioxane, toluene and CH_3CN (entries 5-7). Among the solvents investigated, the initially used *t*-AmylOH provided the best result. The amount of silver acetate is crucial for improving the yields and selectivity of the di-arylated product. Eventually, the optimized bis-arylation conditions include 2.5 equiv. of AgOAc in *t*-AmylOH solvent, 10 mol % of $Pd(OAc)_2$, and 5 equiv. of aryl iodide at 130 °C.

Subsequently, the scope of aryl iodides **2** with diverse functional groups was examined under the optimized conditions (Table 2). As shown in Table 2, we found that a variety of different functional groups on the arenes were tolerated including electron-donating groups such as alkyls (**3b**, **3k**), methoxyl (**3c** and **3l**), and phenyl (**3d**), as well as electron-withdrawing groups such as trifluoromethyl (**3h**, **3p**), cyano(**3i**), and methoxycarbonyl (**3j**). Halides including fluoro (**3e**, **3m**), chloro (**3f**, **3n**), and bromo (**3g**, **3o**) in the meta- or para- position also worked well and can be used for further synthetic elaborations. Most of the substrates gave good to excellent yields even though some of the mono-arylated products were observed.

Next, we expanded the amino acid substrate scope to 4-hydroxyphenylglycine (Table 3) and phenylalanine (Table 4). In Table 3, Aryl iodides bearing methoxyl and phenyl groups gave moderate to good yields with extended reaction time, while aryl iodides with electron-withdrawing groups (e.g., 4-CO_2CF_3, 3-F,

Table 1 Optimization of the reaction conditions for di-arylation of α-phenylglycine[a]

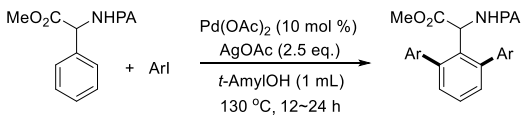


1a 3a 3a'

Entry	Ag salt (eq.)	Solvent (0.5 mL)	PhI (eq.)	Yield[b] of **3a**	Rtio[b] (**3a**/**3a'**)
1	AgOAc(1.5)	*t*-AmylOH	3	34	100/137
2	AgOAc(1.5)	*t*-AmylOH	4	33	100/142
3	AgOAc(1.5)	*t*-AmylOH	5	41	100/100
4	AgOAc(1.5)	*t*-AmylOH	6	35	100/89
5	AgOAc(1.5)	toluene	5	36	100/91
6	AgOAc(1.5)	dioxane	5	32	100/96
7	AgOAc(1.5)	CH_3CN	5	33	100/91
8	AgOAc(2)	*t*-AmylOH	5	54	100/38
9	AgOAc(2.5)	*t*-AmylOH	5	82	100/5
10	AgOAc(3)	*t*-AmylOH	5	78	100/8

[a] Unless otherwise noted, all reactions were carried on a 0.1 mmol scale in 0.5 ml solvent. [b] Determined by ^{1}HNMR analysis of the crude products which only contains **3a**/**3a'**.

Table 2 C-H arylation of α-phenylglycine[a]

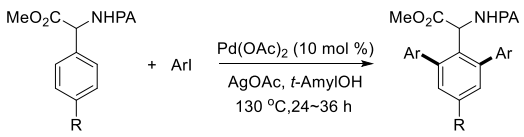


1a 2 3

Entry	Ar-	Product (**3**)	Yield[b] (%)
1	Ph	**3a**	82
2	4-MeC_6H_4	**3b**	70
3	4-$MeOC_6H_4$	**3c**	70
4	4-PhC_6H_4	**3d**	72
5	4-FC_6H_4	**3e**	55 (**3e'**, 16)
6	4-ClC_6H_4	**3f**	80
7	4-BrC_6H_4	**3g**	87
8	4-$CF_3C_6H_4$	**3h**	66
9	4-CNC_6H_4	**3i**	67
10[c]	4-$MeCO_2C_6H_4$	**3j**	70 (**3j'**, 20)
11	3-MeC_6H_4	**3k**	72
12	3-$MeOC_6H_4$	**3l**	87
13	3-FC_6H_4	**3m**	85
14	3-ClC_6H_4	**3n**	73
15	3-BrC_6H_4	**3o**	73
16	3-$CF_3C_6H_4$	**3p**	63 (**3p'**, 21)
17	3-F-4-BrC_6H_4	**3q**	75

[a] Conditions: all reactions were carried on a 0.1 mmol scale. [b] Isolated yield, mono-arylated product in the parenthesis. [c] Conditions: $Pd(TFA)_2$ (10 mol %), AgOAc (3.5 equiv.).

Table 3 C-H arylation of 4-hydroxyphenylglycine[a]



1b, R = OTBS
1c, R = OBn
2 **3**

Entry	Substrate	Ar-	Product	Yield[b] (%)
1	**1b**	4-$MeOC_6H_4$	**3r**	53 (**3r'**, 36)
2	**1b**	4-PhC_6H_4	**3s**	50
3	**1c**	4-$MeOC_6H_4$	**3t**	81
4	**1c**	4-PhC_6H_4	**3u**	68

[a] Conditions: **1b**/**1c** (0.1 mmol), ArI (5 equiv.), $Pd(OAc)_2$ (10 mol %), AgOAc (2.5 equiv.), *t*-AmylOH (1 mL), 130 °C, 24~36 h. [b] Isolated yield.

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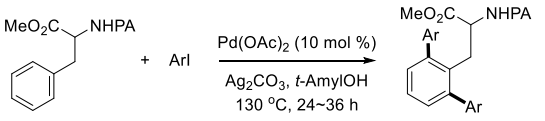
Table 4 C-H arylation of phenylalanine[a]

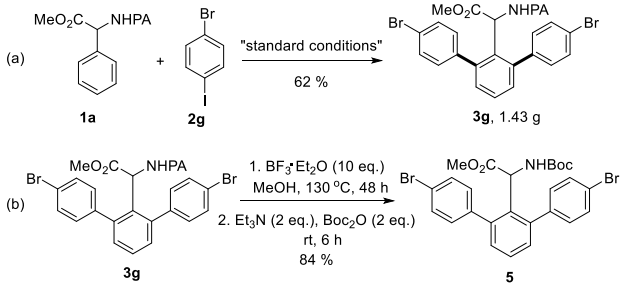


Entry	Ar-	Product (**4**)	Yield[b] (%)
1	Ph	**4a**	78
2	4-MeC_6H_4	**4b**	70
3	4-$MeOC_6H_4$	**4c**	86
4	4-PhC_6H_4	**4d**	85
5	4-FC_6H_4	**4e**	58
6	4-BrC_6H_4	**4f**	75
7	4-$CF_3C_6H_4$	**4g**	52
8	4-$COOMeC_6H_4$	**4h**	34 (**4h'**, 25)
9	3-ClC_6H_4	**4i**	65

[a] Conditions: substrate **1d** (0.1 mmol), ArI (5 equiv.), $Pd(OAc)_2$ (10 mol %), Ag_2CO_3 (2.5 equiv.), *t*-AmylOH (1 mL), 130 °C, 24~36 h. [b] Isolated yield.

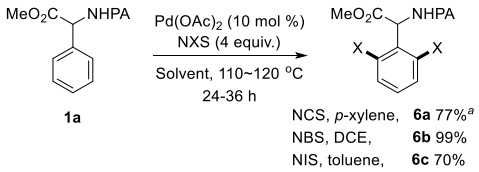
4-CO_2Me) were not effective. Phenylalanine was also compatible with this protocol when Ag_2CO_3 was added instead of AgOAc (Table 4). Despite significant progress in the C-H functionalization of phenylalanine, there are no reports on the selective *o*-C-H bis-arylation of phenylalanines.[6,8e,21]

To further explore the potential application, the C-H arylation reaction of **1a** with 4-bromo-iodobenzene (**2g**) was scaled up to 4.0 mmol. 1.43 gram of product **3g** was successfully obtained in 62% yield (Scheme 2a). Then, we attempted the removal of the picolinamide directing group. Upon treatment with $BF_3{\cdot}Et_2O$ in dichloromethane for 48 h, the directing group was removed and protected with Boc group to afford compound **5**.[22]

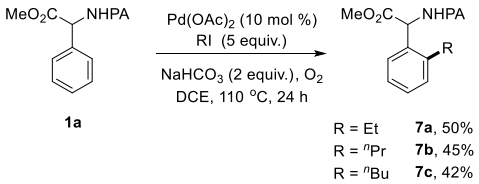


Scheme 2 (a) Gram-scale synthesis; (b) directing group cleavage.

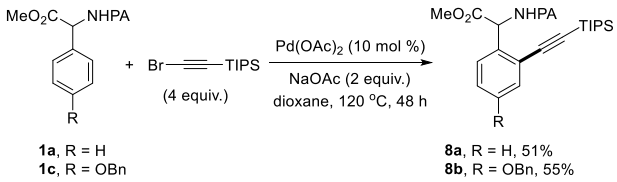
Halogenation, alkylation and alkynylation of *α*-phenylglycine and 4-hydroxyphenylglycine. A palladium-catalyzed halogenation of α-phenylglycine with *N*-halosuccinimides was also developed to give halo substituted α-phenylglycines, which provides an efficient and practical entry for further derivatization.[23] With NCS, NBS and NIS as the halogenation reagents, dihalogenation product **6a**, **6b** and **6c** were obtained in 77%, 99% and 70% yields (Scheme 3) using different solvent.



Scheme 3 C-H halogenation of α-phenylglycine. [a] AgF (3 equiv.) was added.



Scheme 4 C-H alkylation of α-phenylglycine.



Scheme 5 C-H alkynylation of α-phenylglycine.

AgF was added to achieve the successful chlorination reaction, otherwise, only trace amount of product was observed. The fluorination reaction was also attempted with NFSI, but no fluorinated products were observed.

C–H alkylation and alkynylation of α-phenylglycine was also studied using different alkyl iodides. With extensive optimization of the conditions, the alkylation reactions were less efficient, affording moderate yields of the mono-alkylated products **7a**, **7b** and **7c** as shown in Scheme 4. $NaHCO_3$ was employed as a base and additive in the reaction, and an oxygen atmosphere was required for the reaction. Employing a 1-bromo-alkyne reagent, the mono-selective ortho alkynylated products **8a**, **8b** were obtained in moderate yields using NaOAc as a promoter (Scheme 5).[24]

Alkoxylation and acyloxylation of α-phenylglycine and 4-hydroxyphenylglycine. Palladium-catalyzed alkoxylation of α-phenylglycine with primary or secondary alcohols was also developed which was rarely studied on α-phenylglycine and offers a late-stage strategy to synthesize α-phenylglycine derivatives. Since alcohols can be used as a solvent in palladium-catalyzed C–H bond functionalization,[19a,25] we performed the reaction of **1a** with 5 mol % of Pd-catalyst and 3.5 equiv. of $PhI(OAc)_2$ in methanol in a sealed tube (Table 5). To our delight, the desired product was obtained in a good yield of 86% when $Pd(OAc)_2$ was applied as the catalyst (entry 1). Other palladium catalysts only led to inferior results (entries 2-4). A mixed solvent of MeOH: toluene in 4 : 1 gave increased yield and

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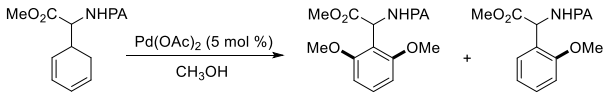
Table 5 Optimization of the reaction conditions for di-alkoxylationa of α-phenylglycine[a]



Entry	Catalyst	Solvent	T (℃)	Yield[b] (%)
1	$Pd(OAc)_2$	MeOH	80	86 (10)
2	$Pd(CH_3CN)_2Cl_2$	MeOH	80	43 (41)
3	$Pd(TFA)_2$	MeOH	80	37 (34)
4	$PdCl_2$	MeOH	80	27 (19)
5	$Pd(OAc)_2$	MeOH:Toluene	80	89
6	$Pd(OAc)_2$	MeOH:Toluene	120	89
7[c]	$Pd(OAc)_2$	MeOH:Toluene	80	nr
8	no $Pd(OAc)_2$	MeOH:Toluene	80	trace

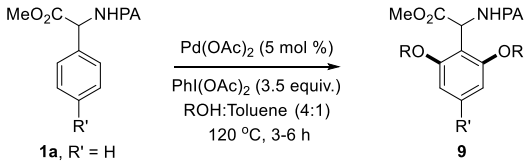
[a] Conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (5 mol %), $PhI(OAc)_2$ (3.5 equiv.), solvent (1 mL), mixed solvent MeOH: Toluene = 4:1, 3 h. [b] Isolated yield. [c] No PhI(OAc).

higher selectivity of di-methoxylation product (entry 5). Increasing reaction temperature did not further improve the yield (entry 6). The alkoxylation did not proceed in the absence of either $Pd(OAc)_2$ or $PhI(OAc)_2$ (entry 7 and entry 8). We then assessed the scope of the reaction with several alcohols under the optimized reaction conditions with α-phenylglycine substrate **1a** and 4-hydroxyphenylglycine substrate **1b** with TBS protection. As shown in Table 6, the protocol was feasible for both primary and secondary alcohols, and the desired di-alkoxylated products were obtained in moderate to good yields.

Additionally, the study of the acyloxylation of α-phenylglycine using $PhI(OAc)_2$ was carried out with $Pd(OAc)_2$ as the catalyst and Ag_2CO_3 as the base and promoter (Scheme 6).[27] After optimization, the di-acyloxylated products were obtained in 69% yield with 10 equiv. of Ac_2O added. Based on the optimized conditions, the benzoxylation of α-phenylglycine with iodobenzene dibenzoate was also achieved as shown in Scheme 6.

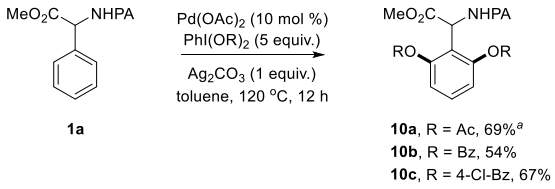
Conclusions

Table 6 C-H alkoxylation of α-phenylglycine[a]



R (**1a** as substrate)	Yield[b] (%)	R (**1b** as substrate)	Yield[b] (%)
OMe (**9a**)	89	OMe (**9e**)	93
O^{n}Pr (**9b**)	91	O^{n}Pr (**9f**)	91
O^{n}Bu (**9c**)	89	O^{n}Bu (**9g**)	85
O^{i}Bu (**9d**)	82	O^{i}Bu (**9h**)	82

[a] Conditions: **1a**/**1b** (0.1 mmol), $Pd(OAc)_2$ (5 mol %), $PhI(OAc)_2$ (3.5 equiv.), ROH: Toluene = 4: 1 (1 mL), 120 °C, 3~6 h. [b] Isolated yield.



Scheme 6 C-H acyloxylation and benzoxylation of α-phenylglycine. [a] Ac_2O (10 equiv.), $PhI(OAc)_2$ (4 equiv.) were used.

In conclusion, palladium-catalyzed picolinamide-assisted diselective *o*-C-H arylation, halogenation, alkylation, alkynylation, alkoxylation and acyloxylation of α-phenylglycine has been achieved in moderate to good yields. Moreover, the reaction can be scaled up to gram scale and the picolinamide group could be removed with Lewis acid. The optimized protocol provides a valuable tool for the synthesis of unnatural amino acids which can be further applied in pharmaceutical chemistry.

Experimental

General remarks

All reagents and metal catalysts were obtained from commercial sources without further purification. Massspectra were recorded with an TSQ Quantum-LC/MS/MS of Finnigan using Electrosprayionization (ESI) techniques. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AV-300 and AV-500 spectrometer operating at 300MHz/500MHz and 75MHz/125MHz, respectively, with chemical shift values being reported in ppm relative to chloroform (δ=7.26 ppm) for ^{1}H NMR, and chloroform (δ=77.16 ppm) for ^{13}C NMR.

General procedure for the *o*-C-H diarylation. To a 15 mL Schlenk tube, substrate **1a**(**1b**/**1c**/**1d**) (0.1 mmol), aryl iodides (0.5 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), Ag salt (0.25 mmol) and *t*-AmylOH (1 mL) were added under atmospheric air. The mixture was stirred for 12~24 h (for **1b**/**1c**/**1d**, was stirred for 24~36 h) at 130 ℃ followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product (**3a~3u**, **4a~4i**).

General procedure for the *o*-C-H dihalogenation. (For **chlorination**) To a 15 mL Schlenk tube, **1a** (27 mg, 0.1 mmol), NCS (53.4 mg, 0.4 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), AgF (38.1 mg, 0.3 mmol) and p-xylene (1 mL) were added under atmospheric air. The mixture was stirred for 36 h at 110 ℃ followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product **6a**. (For **bromination**) To a 15 mL Schlenk tube, **1a** (27 mg, 0.1 mmol), NBS (71.2 mg, 0.4 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and DCE (1 mL) were added under atmospheric air. The mixture was stirred for 24 h at 120 ℃ followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product **6b**. (For **iodization**) To

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a 15 mL Schlenk tube, substrate **1a** (27 mg, 0.1 mmol), NIS (90 mg, 0.4 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and toluene (1 mL) were added under atmospheric air. The mixture was stirred for 24 h at 110 °C followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product **6c**.

General procedure for the *o*-C-H mono-alkylation. To a 15 mL Schlenk tube, **1a** (27 mg, 0.1 mmol), RI (0.5 mmol), $NaHCO_3$ (16.8 mg, 0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), DCE (1 mL) were added under oxygen atmospheric . The mixture was stirred for 24 h at corresponding temperature followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product **7a~7c**.

General procedure for the *o*-C-H mono-alkynylation. To a 15 mL Schlenk tube, **1a/1c** (0.1 mmol), bromoalkyne (0.4 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), NaOAc (16.4 mg, 0.2 mmol) and dioxane (1 mL) were added under atmospheric air. The mixture was stirred for 48 h at 120 °C followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product **8a/8b**.

General procedure for the *o*-C-H dialkoxylation. To a 15 mL Schlenk tube, **1a**/**1b** (0.1 mmol), $PhI(OAc)_2$ (0.35 mmol, 112 mg), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), ROH and toluene (4:1, 1 mL) were added under atmospheric air. The mixture was stirred for 3 h (for **1b** was stirred for 3~6 h) at 120 °C followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product (**9a~9h**).

General procedure for the *o*-C-H diacyloxylation. To a 15 mL Schlenk tube, **1a** (27 mg, 0.1 mmol), $PhI(OR)_2$ (0.5 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), Ag_2CO_3 (27.6 mg, 0.1 mmol) and toluene (1 mL) were added under atmospheric air. (For acetoxylaion, $PhI(OAc)_2$ (0.4 mmol), Ac_2O (1mmol) were added.) The mixture was stirred for 12 h at 120 °C followed by cooling. The mixture was filtered through a celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: petroleum ether /EtOAc) to afford the desired arylated product **10a~10c**.

Compound 1a. White solid, mp 67-68 °C. This compound is known. (Reference: A. V. Malkov, L. Gouriou, G. C. Lloydjones, I. Starý, V. Langer, P. Spoor, V. Vinader and P. Kocovský, *Chem. Eur. J.*, 2006, **12**, 6910-6929.) ^{1}H NMR (300 MHz, CDCl3) δ 8.94 (d, J = 6.1 Hz, 1H), 8.59 (d, J = 4.1 Hz, 1H), 8.16 (d, J = 7.8 Hz, 1H), 7.83 (td, J = 7.7, 1.6 Hz, 1H), 7.58 – 7.29 (m, 6H), 5.78 (d, J = 7.6 Hz, 1H), 3.77 (s, 3H).

Compound 1b. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (d, *J* = 7.1 Hz, 1H), 8.57 (d, *J* = 4.6 Hz, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.98 – 7.67 (m, 1H), 7.42 (dd, *J* = 6.5, 4.9 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 5.69 (d, *J* = 7.5 Hz, 1H), 3.76 (s, 3H), 0.96 (s, 9H), 0.18 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.28, 163.70, 155.93, 149.29, 148.27, 137.25, 129.16, 128.64, 126.42, 122.27, 120.43, 56.05, 52.60, 25.61, 18.10, -4.46. HRMS (EI) calcd. for $C_{21}H_{28}N_2O_4Si$: 400.1818. Found: 400.1815.

Compound 1c. Light yellow solid, mp 126-127 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (dd, *J* = 46.5, 7.3 Hz, 1H), 8.57 (d, *J* = 4.3 Hz, 1H), 8.14 (t, *J* = 8.4 Hz, 1H), 7.83 (dtd, *J* = 9.4, 7.8, 1.7 Hz, 1H), 7.44 – 7.35 (m, 7H), 7.34 – 7.29 (m, 1H), 7.04 – 6.88 (m, 2H), 5.73 (dd, *J* = 25.9, 7.4 Hz, 1H), 5.05 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.37, 163.84, 159.06, 149.38, 148.34, 137.33, 136.82, 128.90, 128.75, 128.67, 128.09, 127.49, 126.47, 122.39, 115.36, 70.11, 56.11, 52.81. HRMS (EI) calcd. for $C_{22}H_{20}N_2O_4$: 376.1423. Found: 376.1420.

Compound 1d. Colorless oil. This compound is known. (Reference: R. R. Pulimamidi, R. Nomula, R. Pallepogu and H. Shaik, *Eur. J. Med. Chem.*, 2014, **79**, 117.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.7 Hz, 1H), 8.48 (d, *J* = 8.1 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.7, 1.5 Hz, 1H), 7.48 – 7.36 (m, 1H), 7.26 (t, *J* = 7.2 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.17 (d, *J* = 7.2 Hz, 2H), 5.15 – 4.94 (m, 1H), 3.70 (s, 3H), 3.23 (qd, *J* = 13.9, 6.2 Hz, 2H).

Compound 3a. Yellow oil, yield 82 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, *J* = 4.6 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 1.5 Hz, 1H), 7.47 – 7.31 (m, 12H), 7.26 (d, *J* = 7.5 Hz, 2H), 6.09 (d, *J* = 8.6 Hz, 1H), 3.59 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.31, 162.78, 149.34, 147.89, 143.00, 140.90, 136.94, 134.28, 133.24, 130.12, 129.54, 128.09, 127.58, 127.32, 125.99, 122.08, 52.80, 52.52. HRMS (ESI) calcd. for $C_{27}H_{22}N_2O_3$: 422.1630. Found 422.1632.

Compound 3b. White solid, yield 70 %, mp 139-140 °C. ^{1}H NMR (300 MHz, CDCl3) δ 8.49 (d, J = 4.1 Hz, 1H), 8.40 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J*= 7.7 Hz, 1H), 7.75 (t, *J*= 7.6 Hz, 1H), 7.44 –7.15 (m, 12H),6.12 (d, J = 8.7 Hz, 1H), 3.61 (s, 3H), 2.43 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.39, 162.72, 149.35, 147.79, 142.95, 138.02, 137.16, 137.03, 133.41, 130.14, 129.38, 128.83, 127.31, 126.00, 122.18, 52.81, 52.51, 21.29. HRMS (ESI) calcd. for $C_{29}H_{26}N_2O_3$: 450.1943. Found 450.1941.

Compound 3c. Yellow solid, yield 70 %, mp 135-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.42 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 6.8 Hz, 1H), 7.75 (s, 1H), 7.35 (t, *J* = 7.5 Hz, 6H), 7.24 (t, *J* = 7.5 Hz, 2H), 6.97 (d, *J* = 8.3 Hz, 4H), 6.14 (d, *J* = 8.5 Hz, 1H), 3.86 (s, 6H), 3.62 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.12, 162.50, 158.70, 149.04, 147.57, 142.35, 136.70, 133.51, 132.97, 130.33, 129.99, 126.99, 125.73, 121.81, 113.22, 54.91, 52.54, 52.23. HRMS (EI) calcd. for $C_{29}H_{26}N_2O_5$: 482.1842. Found: 482.1843.

Compound 3d. White solid, yield 72 %. mp 166-167 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 11.7, 6.3 Hz, 2H), 8.05 (d, *J* = 7.7 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 8H), 7.57 – 7.43 (m, 8H), 7.42 – 7.30 (m, 6H), 6.21 (d, *J* = 8.4 Hz, 1H), 3.67 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.42, 162.85, 149.26, 147.92, 142.68, 140.73, 140.31, 140.05, 136.99, 133.37, 130.31, 129.97, 128.77, 127.49, 127.34, 127.11, 126.84, 126.05, 122.06, 53.13, 52.69. HRMS (EI) calcd. for $C_{39}H_{30}N_2O_3$: 574.2256. Found: 574.2257.

Compound 3e. Yellow oil, yield 55 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.4 Hz, 1H), 8.36 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.76 (td, *J* = 7.7, 1.4 Hz, 1H), 7.48 – 7.29 (m, 6H), 7.23 (d, *J* = 7.6 Hz, 2H), 7.13 (t, *J* = 8.7 Hz, 4H), 6.03 (d, *J* = 8.4 Hz, 1H), 3.63 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.31, 162.47 (d, J_{CF} = 246.7 Hz), 162.90, 149.24, 148.10, 142.13, 137.18, 136.88, 133.74, 131.35(d, J_{CF} = 5.2 Hz), 130.58, 127.54, 126.29, 122.17, 115.17 (d, J_{CF} = 21.4 Hz), 52.95, 52.79. HRMS (EI) calcd. for $C_{27}H_{20}F_2N_2O_3$: 458.1442. Found: 458.1440.

Compound 3e'. Yellow oil, yield 16 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.85 (d, *J* = 6.2 Hz, 1H), 8.58 (d, *J* = 3.9 Hz, 1H), 8.11 (d, *J* = 7.7 Hz, 1H), 7.82 (t, *J* = 7.7 Hz, 1H), 7.57 – 7.35 (m, 6H), 7.29 (dd, *J* = 6.9, 4.0

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Hz, 1H), 7.14 (t, *J* = 8.7 Hz, 2H), 5.80 (d, *J* = 7.0 Hz, 1H), 3.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.24, 162.30 (d, J_{CF} = 246.1 Hz), 163.52, 149.16, 148.18, 141.51, 137.18, 136.12, 134.43, 131.13 (d, J_{CF} = 7.4 Hz), 130.79, 128.29 (d, J_{CF} = 8.2 Hz), 126.86, 126.34, 122.18, 117.58, 115.14 (d, J_{CF} = 21.5 Hz), 53.47, 52.67. HRMS (EI) calcd. for $C_{21}H_{17}FN_2O_3$: 364.1223. Found: 364.1227.

Compound 3f. Yellow oil, yield 80 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.6 Hz, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.76 (td, *J* = 7.7, 1.5 Hz, 1H), 7.50 – 7.29 (m, 10H), 7.21 (d, *J* = 7.6 Hz, 2H), 6.00 (d, *J* = 8.2 Hz, 1H), 3.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.06, 162.67, 148.94, 147.94, 141.81, 139.27, 137.17, 133.72, 133.19, 130.85, 130.37, 128.31, 127.52, 126.23, 122.05, 52.91, 52.74. HRMS (EI) calcd. for $C_{27}H_{20}Cl_2N_2O_3$: 490.0851. Found: 490.0851.

Compound 3g. white solid, yield 87 %, mp 149-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.0 Hz, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.77 (td, *J* = 7.7, 1.7 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 4H), 7.46 – 7.30 (m, 2H), 7.33 – 7.13 (m, 6H), 5.99 (d, *J* = 8.2 Hz, 1H), 3.65 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.04, 162.69, 148.95, 147.99, 141.78, 139.77, 137.10, 133.07, 131.25, 130.31, 127.52, 126.20, 121.94, 52.92, 52.74. HRMS (EI) calcd. for $C_{27}H_{20}Br_2N_2O_3$: 577.9841. Found: 577.9840.

Compound 3h. White solid, yield 66 %, mp 145-146 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, *J* = 4.3 Hz, 1H), 8.22 (d, *J* = 7.6 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.75 (ddd, *J* = 22.3, 14.2, 4.4 Hz, 5H), 7.52 (d, *J* = 7.9 Hz, 4H), 7.46 – 7.35 (m, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 5.93 (d, *J* = 7.8 Hz, 1H), 3.66 (d, *J* = 10.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.05, 162.88, 148.92, 148.09, 144.73, 141.77, 137.17, 132.99, 130.56, 129.97, 129.90 (q, J_{CF3} = 32.51 Hz), 127.76, 126.37, 125.20 (q, J_{CF3} = 3.31 Hz), 124.28 (q, J_{CF3} = 273.22 Hz), 121.96, 53.19, 52.97. HRMS (EI) calcd. for $C_{29}H_{20}F_6N_2O_3$: 558.1378. Found: 558.1375.

Compound 3i. White solid, yield 67 %, mp 125-126 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.2 Hz, 1H), 8.22 (d, *J* = 7.4 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.77 (ddd, *J* = 19.2, 12.6, 4.5 Hz, 5H), 7.56 – 7.40 (m, 6H), 7.24 (t, *J* = 7.6 Hz, 2H), 5.83 (d, *J* = 7.5 Hz, 1H), 3.68 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.60, 162.69, 148.58, 148.01, 145.54, 141.31, 137.28, 132.53, 131.88, 130.43, 130.33, 127.83, 126.49, 121.97, 118.64, 111.66, 52.99. HRMS (EI) calcd. for $C_{29}H_{20}N_4O_3$: 472.1535. Found: 472.1536.

Compound 3j. White solid, yield 70 %, mp 166-167 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.5 Hz, 1H), 8.28 (d, *J* = 8.1 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 4H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.73 (td, *J* = 7.7, 1.5 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 5H), 7.43 – 7.32 (m, 2H), 7.23 (d, *J* = 7.6 Hz, 1H), 5.96 (d, *J* = 8.2 Hz, 1H), 3.93 (s, 6H), 3.62 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.93, 166.80, 162.73, 148.91, 148.00, 145.57, 142.08, 137.03, 132.81, 130.17, 129.61, 129.40, 128.64, 127.52, 126.17, 121.95, 52.84, 52.74, 52.06. HRMS (EI) calcd. for $C_{31}H_{26}N_2O_7$: 538.1740. Found: 538.1742.

Compound 3j'. White solid, yield 20 %, mp 124-125 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (d, *J* = 6.7 Hz, 1H), 8.55 (d, *J* = 4.2 Hz, 1H), 8.11 (t, *J* = 9.4 Hz, 3H), 7.87 – 7.72 (m, 1H), 7.68 – 7.52 (m, 3H), 7.40 (dd, *J* = 7.8, 4.9 Hz, 3H), 7.35 – 7.22 (m, 1H), 5.79 (d, *J* = 7.0 Hz, 1H), 3.93 (d, *J* = 5.1 Hz, 3H), 3.68 (d, *J* = 5.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.09, 166.85, 163.45, 149.04, 148.13, 144.99, 141.47, 137.27, 134.19, 130.40, 129.54, 129.16, 128.59, 128.42, 126.95, 126.39, 122.22, 53.47, 52.71, 52.03. HRMS (EI) calcd. for $C_{23}H_{20}N_2O_5$: 404.1372. Found: 404.1378.

Compound 3k. Yellow solid, yield 72 %, mp 123-124 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.5 Hz, 1H), 8.46 (d, *J* = 8.7 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.77 (td, *J* = 7.7, 1.5 Hz, 1H), 7.38 (dd, *J* = 15.9, 8.2 Hz, 4H), 7.32 – 7.20 (m, 8H), 6.18 (t, *J* = 12.6 Hz, 1H), 3.61 (s, 3H), 2.43 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.47, 162.86, 149.65, 148.06, 143.24, 140.92, 137.82, 137.09, 133.28, 130.48, 130.08, 128.45, 128.13, 127.41, 126.67, 126.09, 122.35, 52.89, 52.57, 21.60. HRMS (EI) calcd. for $C_{29}H_{26}N_2O_3$: 450.1943. Found: 450.1941.

Compound 3l. Yellow oil, yield 70 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.1 Hz, 1H), 8.38 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.75 (td, *J* = 7.7, 1.2 Hz, 1H), 7.44 – 7.31 (m, 4H), 7.27 (d, *J* = 7.5 Hz, 2H), 6.97 (d, *J* = 7.8 Hz, 6H), 6.16 (d, *J* = 8.8 Hz, 1H), 3.79 (s, 6H), 3.61 (d, *J* = 8.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.55, 162.89, 159.34, 149.50, 148.01, 142.91, 142.30, 137.05, 133.16, 130.11, 129.29, 127.43, 126.08, 122.22, 121.90, 114.92, 113.81, 55.19, 52.93, 52.68. HRMS (EI) calcd. for $C_{29}H_{26}N_2O_5$: 482.1842. Found: 482.1853.

Compound 3m. White solid, yield 85 %, mp 135-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 – 8.46 (m, 1H), 8.41 (d, *J* = 8.3 Hz, 1H), 8.07 – 8.00 (m, 1H), 7.79 – 7.69 (m, 1H), 7.48 – 7.33 (m, 4H), 7.28 – 7.06 (m, 8H), 6.07 (d, *J* = 8.5 Hz, 1H), 3.67 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.14, 162.38 (d, J_{CF} = 247.5 Hz), 162.79, 149.06, 148.06, 142.82 (d, J_{CF} = 7.52 Hz), 141.71, 137.02, 133.17, 130.23, 129.69 (d, J_{CF} = 8.04 Hz), 127.50, 126.13, 125.30, 121.98, 116.85 (d, J_{CF} = 21.14 Hz), 114.64 (d, J_{CF} = 21.04 Hz), 52.71. HRMS (EI) calcd. for $C_{27}H_{20}F_2N_2O_3$: 458.1442. Found: 458.1449.

Compound 3n. Yellow oil. Yield 73 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 3.9 Hz, 1H), 8.38 (d, *J* = 8.1 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.76 (td, *J* = 7.7, 1.5 Hz, 1H), 7.44 – 7.35 (m, 8H), 7.31 (d, *J* = 5.9 Hz, 2H), 7.24 (d, *J* = 7.6 Hz, 2H), 6.00 (d, *J* = 8.3 Hz, 1H), 3.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.04, 162.74, 149.02, 148.19, 142.43, 141.60, 137.04, 134.04, 133.21, 130.30, 129.79, 129.37, 127.86, 127.70, 127.52, 126.10, 122.03, 52.79. HRMS (EI) calcd. for $C_{27}H_{20}Cl_2N_2O_3$: 490.0851. Found: 490.0857.

Compound 3o. Yellow solid, yield 73 %, mp 101-102 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.37 (d, *J* = 8.1 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.76 (td, *J* = 7.7, 1.5 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 4H), 7.42 – 7.27 (m, 6H), 7.24 (t, *J* = 6.4 Hz, 2H), 5.98 (d, *J* = 8.3 Hz, 1H), 3.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.01, 162.77, 149.00, 148.35, 142.70, 141.49, 137.04, 133.19, 132.61, 130.77, 130.35, 129.67, 128.17, 127.56, 126.15, 122.28, 122.00, 52.89, 52.78. HRMS (EI) calcd. for $C_{27}H_{20}Br_2N_2O_3$: 577.9841. Found: 577.9846.

Compound 3p. Yellow oil, yield 63 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, *J* = 4.0 Hz, 1H), 8.35 (d, *J* = 7.5 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.83 – 7.56 (m, 9H), 7.49 – 7.35 (m, 2H), 7.34 – 7.26 (m, 2H), 5.93 (d, *J* = 7.8 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.96, 162.99, 149.01, 148.23, 141.82, 141.59, 137.12, 133.41, 132.99, 130.71, 130.54 (q, J_{CF3} = 32.2 Hz), 128.81, 127.82, 126.56, 126.31, 124.69(d, J_{CF3} = 3.11 Hz), 124.18(q, J_{CF3} = 272.50 Hz), 122.06, 53.12, 52.81. (CF_3 peak is overlapping with other peaks.) HRMS (EI) calcd. for $C_{29}H_{20}F_6N_2O_3$: 558.1378. Found: 558.1384.

Compound 3p'. Yellow oil, yield 21 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.89 (d, *J* = 6.5 Hz, 1H), 8.59 (d, *J* = 4.6 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.89 – 7.75 (m, 3H), 7.71 – 7.56 (m, 3H), 7.48 – 7.38 (m, 3H), 7.35 – 7.29 (m, 1H), 5.73 (d, *J* = 7.0 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.18, 163.62, 149.23, 148.33, 141.12，141.08，137.31, 134.61, 132.86, 130.69, 130.61(q, J_{CF3} = 32.4 Hz), 128.83, 128.80，128.57, 127.23, 126.68(d, J_{CF3} = 3.28 Hz), 126.49, 126.86(q, J_{CF3} =

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272.08 Hz), 124.41(d, J_{CF3} = 3.10 Hz), 122.29, 53.69, 52.82. (CF_3 peak is overlapping with other peaks.) HRMS (EI) calcd. for $C_{22}H_{17}F_3N_2O_3$: 414.1191. Found: 414.1192.

Compound 3q. Yellow oil. yield 75 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.3 Hz, 1H), 8.34 (d, *J* = 7.9 Hz, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.79 (t, *J* = 7.4 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 2H), 7.40 (dd, *J* = 14.7, 7.4 Hz, 2H), 7.25 – 7.14 (m, 4H), 7.08 (d, *J* = 8.1 Hz, 2H), 5.97 (d, *J* = 8.0 Hz, 1H), 3.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.89, 162.67, 158.59 (d, J = 249 Hz), 148.69, 148.14, 141.98 (d, J = 6.91 Hz), 140.77, 137.25, 136.74, 133.20, 132.99, 130.41, 127.70, 126.36, 121.99, 117.94 (d, J = 22.58 Hz), 108.57 (d, J = 20.60 Hz), 52.93, 52.88. HRMS (EI) calcd. for $C_{27}H_{18}Br_2F_2N_2O_3$: 613.9652. Found: 613.9649.

Compound 3r. Yellow oil, yield 53 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.6 Hz, 1H), 8.38 (d, *J* = 8.8 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.74 (td, *J* = 7.7, 1.5 Hz, 1H), 7.36 (dd, *J* = 7.2, 5.0 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 4H), 6.95 (d, *J* = 8.8 Hz, 4H), 6.70 (s, 2H), 6.03 (d, *J* = 8.8 Hz, 1H), 3.85 (s, 6H), 3.58 (s, 3H), 0.95 (s, 9H), 0.19 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.77, 162.90, 159.11, 154.13, 149.58, 147.99, 144.14, 137.08, 133.36, 130.64, 127.04, 126.08, 122.25, 121.69, 113.62, 55.31, 52.54, 52.43, 25.65, 18.16, -4.34. HRMS (EI) calcd. for $C_{35}H_{40}N_2O_6Si$: 612.2656. Found: 612.2649.

Compound 3r'. Yellow oil, yield 36 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 6.7 Hz, 1H), 8.55 (d, *J* = 4.7 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.7, 1.2 Hz, 1H), 7.50 – 7.32 (m, 4H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.81 (dt, *J* = 13.4, 6.7 Hz, 1H), 6.76 (d, *J* = 2.5 Hz, 1H), 5.73 (d, *J* = 6.9 Hz, 1H), 3.84 (s, 3H), 3.68 (s, 3H), 0.97 (s, 9H), 0.20 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.82, 163.68, 159.10, 155.52, 149.43, 148.27, 143.82, 137.28, 132.52, 130.52, 128.28, 127.00, 126.39, 122.36, 122.30, 119.44, 113.81, 55.31, 53.25, 52.66, 25.66, 18.19, -4.32. HRMS (EI) calcd. for $C_{28}H_{34}N_2O_5Si$: 506.2237. Found: 506.2230.

Compound 3s. White solid, yield 50 %, mp 130-131 °C. ^{1}H NMR (500 MHz, CDCl3) δ 8.46 – 8.38 (m, 2H), 8.04 (d, J = 7.8 Hz, 1H), 7.74 (td, J = 7.7, 1.6 Hz, 1H), 7.66 (t, J = 7.9 Hz, 8H), 7.53 – 7.44 (m, 8H), 7.35 (ddd, J = 10.4, 7.5, 4.2 Hz, 3H), 6.80 (s, 2H), 6.10 (d, J = 8.6 Hz, 1H), 3.61 (s, 3H), 0.98 (s, 9H), 0.23 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.73, 162.88, 154.29, 149.54, 148.02, 144.19, 140.88, 140.44, 140.09, 137.06, 129.96, 128.83, 127.41, 127.22, 126.93, 126.56, 126.07, 122.18, 121.69, 52.67, 52.64, 25.66, 18.19, -4.30. HRMS (EI) calcd. for $C_{45}H_{44}N_2O_4Si$: 704.3070. Found: 704.3078.

Compound 3t. Yellow oil, yield 81 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (dd, *J* = 4.0, 0.6 Hz, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.75 (td, *J* = 7.7, 1.6 Hz, 1H), 7.43 – 7.28 (m, 10H), 7.01 – 6.93 (m, 4H), 6.88 (d, *J* = 1.4 Hz, 2H), 6.05 (d, *J* = 8.6 Hz, 1H), 5.04 (s, 2H), 3.85 (s, 6H), 3.61 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.76, 162.92, 159.18, 157.28, 149.56, 148.00, 144.24, 137.09, 136.79, 133.37, 130.64, 128.63, 128.08, 127.64, 126.90, 126.10, 122.25, 116.61, 113.67, 70.07, 55.33, 52.61, 52.56. HRMS (EI) calcd. for $C_{36}H_{32}N_2O_6$: 588.2260. Found: 588.2255.

Compound 3u. White solid, yield 68 %, mp 264-265 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 – 8.39 (m, 2H), 8.08 – 8.02 (m, 1H), 7.75 (td, *J* = 7.7, 1.7 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 8H), 7.52 (d, *J* = 8.3 Hz, 4H), 7.48 (dd, *J* = 10.6, 4.8 Hz, 4H), 7.45 – 7.42 (m, 2H), 7.38 (ddd, *J* = 7.4, 4.4, 1.9 Hz, 4H), 7.36 – 7.33 (m, 2H),6.97 (s, 2H) 6.11 (d, *J* = 8.4 Hz, 1H), 5.09 (s, 2H), 3.65 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.72, 162.91, 157.41, 149.50, 148.03, 144.26, 140.84, 140.51, 140.10, 137.07, 136.74, 129.94, 128.85, 128.65, 128.12, 127.64, 127.44, 127.22, 126.95, 126.39, 126.09, 122.17, 116.61, 70.15, 52.80, 52.72. HRMS (EI) calcd. for $C_{46}H_{36}N_2O_4$: 680.2675. Found: 680.2669.

Compound 4a. Colorless oil, yield 78 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 – 8.51 (m, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.80 – 7.74 (m, 2H), 7.46 – 7.35 (m, 11H), 7.26 (dd, *J* = 6.1, 1.8 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 2H), 4.44 (ddd, *J* = 10.8, 9.1, 4.3 Hz, 1H), 3.47 (dd, *J* = 14.2, 4.3 Hz, 1H), 3.42 (s, 3H), 3.15 (dd, *J* = 14.2, 10.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.84, 163.89, 149.36, 147.90, 143.72, 141.71, 137.14, 131.75, 129.76, 129.71, 128.41, 127.19, 126.52, 126.20, 122.28, 52.28, 52.07, 31.98. HRMS (EI) calcd. for $C_{28}H_{24}N_2O_3$: 436.1787. Found: 436.1793.

Compound 4b. Yellow oil, yield 70 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (ddd, *J* = 4.7, 1.5, 0.8 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.77 (td, *J* = 7.7, 1.7 Hz, 2H), 7.40 (ddd, *J* = 7.6, 4.7, 1.2 Hz, 1H), 7.24 (ddd, *J* = 9.2, 8.0, 6.4 Hz, 9H), 7.13 (d, *J* = 7.5 Hz, 2H), 4.43 (ddd, *J* = 10.9, 8.9, 4.2 Hz, 1H), 3.48 (dt, *J* = 11.6, 5.8 Hz, 1H), 3.43 (s, 3H), 3.17 (dd, *J* = 14.1, 10.9 Hz, 1H), 2.42 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.97, 163.94, 149.40, 147.87, 143.66, 138.82, 137.13, 136.73, 131.93, 129.72, 129.56, 129.11, 126.47, 126.18, 122.27, 52.32, 52.04, 31.80, 21.30. HRMS (EI) calcd. for $C_{30}H_{28}N_2O_3$: 464.2100. Found: 464.2106.

Compound 4c. Yellow oil, yield 86 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.7 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.76 (td, *J* = 7.7, 1.5 Hz, 2H), 7.41 – 7.37 (m, 1H), 7.30 (t, *J* = 5.7 Hz, 4H), 7.24 – 7.17 (m, 1H), 7.12 (d, *J* = 7.5 Hz, 2H), 6.97 (t, *J* = 5.7 Hz, 4H), 4.54 – 4.33 (m, 1H), 3.86 (s, 6H), 3.53 – 3.40 (m, 4H), 3.18 (dd, *J* = 14.1, 11.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.97, 163.96, 158.78, 149.34, 147.88, 143.34, 137.16, 134.16, 132.22, 130.77, 129.80, 126.49, 126.22, 122.27, 113.85, 55.35, 52.27, 52.11, 31.85. HRMS (EI) calcd. for $C_{30}H_{28}N_2O_5$: 496.1998. Found: 496.2003.

Compound 4d. Light yellow oil, yield 85 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 4.0, 0.7 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.77 (td, *J* = 7.7, 1.7 Hz, 1H), 7.71 – 7.65 (m, 8H), 7.51 – 7.46 (m, 8H), 7.41 – 7.36 (m, 3H), 7.31 (dd, *J* = 8.2, 6.8 Hz, 1H), 7.24 (t, *J* = 6.5 Hz, 2H), 4.56 (ddd, *J* = 10.8, 9.2, 3.9 Hz, 1H), 3.59 (dd, *J* = 14.2, 3.9 Hz, 1H), 3.41 (s, 3H), 3.27 (dd, *J* = 14.2, 10.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.89, 163.98, 149.33, 147.94, 143.41, 140.91, 140.74, 140.01, 137.18, 132.08, 130.20, 129.90, 128.88, 127.40, 127.19, 127.16, 126.70, 126.24, 122.29, 52.50, 52.15, 32.05. HRMS (EI) calcd. for $C_{40}H_{32}N_2O_3$: 588.2413. Found: 588.2419.

Compound 4e. Yellow solid, yield 58 %, mp 128-129 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.6 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.84 – 7.74 (m, 2H), 7.45 – 7.40 (m, 1H), 7.33 (dd, *J* = 8.2, 5.5 Hz, 4H), 7.28 – 7.22 (m, 1H), 7.16 – 7.08 (m, 6H), 4.47 (td, *J* = 10.8, 4.0 Hz, 1H), 3.47 (d, *J* = 0.4 Hz, 3H), 3.41 (dd, *J* = 14.2, 4.0 Hz, 1H), 3.10 (dd, *J* = 14.2, 11.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.72, 163.84, 162.19 (d, J_F = 246.17 Hz), 149.18, 147.95, 142.73, 137.53, 137.28, 132.04, 131.31 (d, J_F = 7.85 Hz), 130.02, 126.67, 126.37, 122.31, 115.36 (d, J_F = 21.23 Hz), 52.23, 52.14, 32.04. HRMS (EI) calcd. for $C_{28}H_{22}F_2N_2O_3$: 472.1598. Found: 472.1601.

Compound 4f. Yellow oil, yield 75 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 3.1 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.78 (dd, *J* = 14.8, 7.9 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 4H), 7.48 – 7.39 (m, 1H), 7.30 – 7.17 (m, 5H), 7.12 (d, *J* = 7.6 Hz, 2H), 4.46 (td, *J* = 10.7, 3.7 Hz, 1H), 3.47 (s, 3H), 3.40 (dd, *J* = 14.3, 3.7 Hz, 1H), 3.08 (dd, *J* = 14.2, 11.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.60, 163.87, 149.07, 148.01, 142.56, 140.42, 137.30, 131.74, 131.60, 131.39, 129.92, 126.82, 126.43, 122.31, 121.54, 52.31, 52.25, 32.00. HRMS (EI) calcd. for $C_{28}H_{22}Br_2N_2O_3$: 591.9997. Found: 591.9999.

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Compound 4g. Yellow solid, yield 52 %, mp 121-122 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.7 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.87 – 7.72 (m, 2H), 7.68 (d, *J* = 7.9 Hz, 4H), 7.49 (d, *J* = 7.7 Hz, 4H), 7.47 – 7.41 (m, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 2H), 4.45 (td, *J* = 10.3, 3.3 Hz, 1H), 3.42 (s, 3H), 3.38 (dd, *J* = 11.2, 4.9 Hz, 1H), 3.05 (dd, *J* = 14.3, 11.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.44, 163.82, 149.04, 148.03, 145.13, 142.48, 137.33, 131.80, 130.13, 129.55(q, J_{CF3} = 33.24 Hz), 126.99, 126.47, 125.43(q, J_{CF3} = 3.31 Hz), 124.30 (q, J_{CF3} = 271.55 Hz), 123.21, 122.29, 52.29, 52.19, 32.14. (CF_3 peak is overlapping with other peaks.) HRMS (EI) calcd. for $C_{30}H_{22}F_6N_2O_3$: 572.1535. Found: 572.1538.

Compound 4h. Yellow oil, yield 34 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.5 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 4H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.77 (ddd, *J* = 14.1, 10.1, 5.3 Hz, 2H), 7.43 (t, *J* = 6.6 Hz, 6H), 7.28 (dd, *J* = 13.3, 5.3 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 2H), 4.42 (td, *J* = 10.8, 3.8 Hz, 1H), 3.96 (s, 6H), 3.41 (s, 3H), 3.08 (dd, *J* = 14.1, 11.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.45, 167.05, 163.81, 149.05, 148.05, 146.30, 142.89, 137.28, 131.43, 129.93, 129.83, 129.79, 129.08, 126.86, 126.41, 122.28, 52.25, 52.19, 32.09. HRMS (EI) calcd. for $C_{32}H_{28}N_2O_7$: 552.1897. Found: 552.1900.

Compound 4h'. Yellow oil, yield 25 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.6 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 8.00 (t, *J* = 8.2 Hz, 3H), 7.79 (td, *J* = 7.7, 1.5 Hz, 1H), 7.41 (dd, *J* = 6.9, 4.9 Hz, 1H), 7.33 (dd, *J* = 12.9, 8.1 Hz, 3H), 7.29 (ddd, *J* = 14.1, 7.0, 1.4 Hz, 2H), 7.19 – 7.14 (m, 1H), 4.84 (td, *J* = 8.3, 5.6 Hz, 1H), 3.93 (s, 3H), 3.61 (s, 3H), 3.36 (dd, *J* = 14.2, 5.5 Hz, 1H), 3.13 (dd, *J* = 14.2, 8.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.77, 166.99, 163.86, 149.14, 148.15, 146.09, 141.79, 137.26, 133.64, 130.17, 129.89, 129.59, 128.85, 128.41, 128.13, 127.11, 126.41, 122.31, 53.39, 52.40, 52.19, 35.09. HRMS (EI) calcd. for $C_{24}H_{22}N_2O_5$: 418.1529. Found: 418.1533.

Compound 4i. Yellow oil, yield 65 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.5 Hz, 1H), 7.98 (t, *J* = 10.4 Hz, 1H), 7.79 (ddd, *J* = 11.8, 9.3, 5.4 Hz, 2H), 7.44 – 7.39 (m, 1H), 7.37 (d, *J* = 4.7 Hz, 6H), 7.27 (dd, *J* = 7.1, 2.9 Hz, 3H), 7.14 (d, *J* = 7.6 Hz, 2H), 4.49 (td, *J* = 11.0, 3.8 Hz, 1H), 3.49 (s, 3H), 3.37 (dd, *J* = 16.1, 8.9 Hz, 1H), 3.10 (dd, *J* = 14.2, 11.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.64, 163.88, 149.10, 148.36, 143.29, 142.41, 137.21, 134.32, 131.66, 130.05, 129.72, 129.67, 128.08, 127.49, 126.83, 126.28, 122.22, 52.31, 52.12, 32.20. HRMS (EI) calcd. for $C_{28}H_{22}Cl_2N_2O_3$: 504.1007. Found: 504.1010.

Compound 5. White solid, yield 84 %, mp 63-64 °C.^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.3 Hz, 4H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 8.4 Hz, 6H), 5.50 (d, *J* = 7.8 Hz, 1H), 4.70 (s, 1H), 3.55 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.41, 153.97, 141.72, 139.92, 133.54, 131.29, 131.14, 130.45, 127.42, 122.00, 79.63, 54.16, 52.66, 28.34. HRMS (EI) calcd. for $C_{26}H_{25}Br_2NO_4$: 573.0150. Found: 573.0153.

Compound 6a. Yellow oil, yield 77 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.27 (d, *J* = 8.4 Hz, 1H), 8.59 (dd, *J* = 4.7, 0.6 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1H), 7.34 (d, *J* = 7.7 Hz, 2H), 7.20 (dd, *J* = 8.6, 7.4 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.85, 163.95, 149.24, 148.45, 137.33, 135.80, 133.62, 129.93, 128.91, 126.51, 122.55, 53.30, 52.58. HRMS (EI) calcd. for $C_{15}H_{12}Cl_2N_2O_3$: 338.0225. Found: 338.0229.

Compound 6b. White solid, yield 99 %, mp 101-102 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.38 (d, *J* = 8.2 Hz, 1H), 8.60 (dd, *J* = 4.0, 0.7 Hz, 1H), 8.33 – 8.03 (m, 1H), 7.83 (td, *J* = 7.8, 1.6 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.43 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1H), 7.03 (t, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.62, 163.74, 149.08, 148.33, 137.20, 136.23, 132.86, 130.47, 126.38, 122.41, 56.99, 53.21. HRMS (EI) calcd. for $C_{15}H_{12}Br_2N_2O_3$: 425.9215. Found: 425.9213.

Compound 6c. Yellow solid, yield 70 %, mp 118-119 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.52 (d, *J* = 7.6 Hz, 1H), 8.61 (dt, *J* = 11.3, 5.7 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.95 – 7.77 (m, 3H), 7.47 – 7.39 (m, 1H), 6.76 – 6.53 (m, 2H), 3.81 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.67, 163.74, 149.18, 148.53, 141.11, 140.94, 137.35, 131.09, 126.54, 122.51, 64.98, 53.51. HRMS (EI) calcd. for $C_{15}H_{12}I_2N_2O_3$: 521.8937. Found: 521.8936.

Compound 7a. Colorless oil, yield 50 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, J = 7.2 Hz, 1H), 8.55 (d, J = 4.5 Hz, 1H), 8.16 (d, J = 7.7 Hz, 1H), 7.82 (dd, J = 10.3, 5.0 Hz, 1H), 7.46 – 7.35 (m, 2H), 7.26 (ddd, J = 16.9, 11.6, 7.1 Hz, 3H), 6.03 (d, J = 7.6 Hz, 1H), 3.75 (d, J = 1.5 Hz, 3H), 2.98 – 2.86 (m, 2H), 1.32 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.74, 163.86, 149.30, 148.33, 142.90, 137.34, 134.40, 129.43, 128.88, 126.94, 126.70, 126.49, 122.38, 52.79, 52.69, 25.90, 15.51. HRMS (EI) calcd. for $C_{17}H_{18}N_2O_3$: 298.1317. Found: 298.1321.

Compound 7b. Colorless oil, yield 45 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, J = 7.0 Hz, 1H), 8.55 (d, J = 4.4 Hz, 1H), 8.16 (d, J = 7.8 Hz, 1H), 7.82 (t, J = 7.2 Hz, 1H), 7.41 (dd, J = 7.0, 5.2 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.30 – 7.19 (m, 3H), 6.02 (d, J = 7.6 Hz, 1H), 3.75 (s, 3H), 2.83 (dd, J = 18.1, 8.2 Hz, 2H), 1.72 (dd, J = 15.0, 7.5 Hz, 2H), 1.02 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.75, 163.85, 149.31, 148.32, 141.48, 137.32, 134.53, 130.29, 128.65, 126.95, 126.74, 126.47, 122.38, 52.77, 35.03, 24.51, 14.23. HRMS (EI) calcd. for $C_{18}H_{20}N_2O_3$: 312.1474. Found: 312.1473.

Compound 7c. Colorless oil, yield 42 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, J = 7.0 Hz, 1H), 8.55 (d, J = 4.4 Hz, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.83 (td, J = 7.7, 1.4 Hz, 1H), 7.42 (dd, J = 7.0, 5.2 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.24 (dt, J = 14.5, 6.9 Hz, 3H), 6.01 (d, J = 7.6 Hz, 1H), 3.75 (s, 3H), 2.93 – 2.76 (m, 2H), 1.71 – 1.62 (m, 2H), 1.44 (dd, J = 14.8, 7.4 Hz, 2H), 0.94 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.76, 163.84, 149.32, 148.31, 141.73, 137.32, 134.46, 130.24, 128.68, 127.03, 126.68, 126.46, 122.39, 52.84, 52.77, 33.57, 32.68, 22.80, 14.04. HRMS (EI) calcd. for $C_{19}H_{22}N_2O_3$: 326.1630. Found: 326.1635.

Compound 8a. Yellow oil, yield 51 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (d, *J* = 7.5 Hz, 1H), 8.54 (d, *J* = 4.3 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.7, 1.6 Hz, 1H), 7.54 (dt, *J* = 4.1, 2.0 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.40 (ddd, *J* = 7.5, 4.8, 1.0 Hz, 1H), 7.33 (td, *J* = 7.6, 1.5 Hz, 1H), 7.28 (td, *J* = 7.5, 1.3 Hz, 1H), 6.16 (d, *J* = 7.7 Hz, 1H), 3.75 (s, 3H), 1.16 (dd, *J* = 8.3, 3.8 Hz, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.75, 163.82, 149.49, 148.17, 138.35, 137.20, 133.97, 128.96, 128.44, 128.28, 126.35, 123.07, 122.39, 103.94, 97.16, 55.60, 52.76, 18.68, 11.39. HRMS (EI) calcd. for $C_{26}H_{34}N_2O_3Si$: 450.2339. Found: 450.2333.

Compound 8b. Yellow oil, yield 55 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, *J* = 7.4 Hz, 1H), 8.53 (d, *J* = 4.7 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.7, 1.4 Hz, 1H), 7.43 – 7.36 (m, 6H), 7.33 (t, *J* = 7.0 Hz, 1H), 7.15 (d, *J* = 2.7 Hz, 1H), 6.94 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.09 (d, *J* = 7.5 Hz, 1H), 5.04 (s, 2H), 3.74 (s, 3H), 1.15 (dd, *J* = 8.5, 3.8 Hz, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.01, 163.79, 158.42, 149.57, 148.16, 137.18, 136.54, 130.92, 129.66, 128.70, 128.19, 127.61, 126.29, 124.16, 122.39, 119.95, 115.70, 103.76, 97.03, 70.26, 55.03, 52.75, 18.68, 11.38. HRMS (EI) calcd. for $C_{33}H_{40}N_2O_4Si$: 556.2757. Found: 556.2753.

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Compound 9a. White solid, yield 89 %, mp 131-132 °C. ^{1}H NMR (300 MHz, CDCl3) δ 8.99 (d, J = 9.0 Hz, 1H), 8.55 (d, J = 3.9 Hz, 1H), 8.20 (d, J = 7.8 Hz, 1H), 7.80 (td, J = 7.7, 1.6 Hz, 1H), 7.38 (ddd, J = 7.4, 4.8, 1.1 Hz, 1H), 7.26 (dd, J = 9.9, 6.8 Hz, 1H), 6.62 (dd, J = 13.3, 9.0 Hz, 3H), 3.89 (s, 6H), 3.69 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 171.75, 163.71, 158.10, 149.78, 148.10, 137.01, 129.70, 126.01, 122.35, 114.04, 104.25, 56.04, 52.37, 46.15. HRMS (EI) calcd. for $C_{17}H_8N_2O_5$: 330.1216. Found: 330.1220.

Compound 9b. White solid, yield 91 %, mp 104-105 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.18 (d, *J* = 9.5 Hz, 1H), 8.52 (d, *J* = 4.7 Hz, 1H), 8.20 (d, *J* = 7.7 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.43 – 7.32 (m, 1H), 7.20 (t, *J* = 8.3 Hz, 1H), 6.71 (d, *J* = 9.8 Hz, 1H), 6.55 (d, *J* = 8.3 Hz, 2H), 4.13 – 3.85 (m, 4H), 3.68 (s, 3H), 2.04 – 1.75 (m, 4H), 1.10 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.83, 163.56, 157.55, 149.94, 147.95, 136.97, 129.46, 125.91, 122.32, 114.26, 104.67, 70.22, 52.27, 46.19, 22.53, 10.51. HRMS (EI) calcd. for $C_{21}H_{26}N_2O_5$: 386.1842. Found: 386.1848.

Compound 9c. Yellow oil, yield 89 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.17 (d, *J* = 9.5 Hz, 1H), 8.53 (d, *J* = 4.4 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.43 – 7.34 (m, 1H), 7.20 (t, *J* = 8.3 Hz, 1H), 6.69 (d, *J* = 9.8 Hz, 1H), 6.56 (d, *J* = 8.3 Hz, 2H), 4.21 – 3.89 (m, 4H), 3.68 (s, 3H), 1.94 – 1.77 (m, 4H), 1.64 – 1.51 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.79, 163.58, 157.57, 149.98, 147.92, 136.97, 129.44, 125.90, 122.36, 114.24, 104.66, 68.34, 52.27, 46.23, 31.20, 19.08, 13.78. HRMS (EI) calcd. for $C_{23}H_{30}N_2O_5$: 414.2155. Found: 414.2159.

Compound 9d. Colorless oil, yield 82 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (d, *J* = 9.8 Hz, 1H), 8.63 – 8.34 (m, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.78 (td, *J* = 7.7, 1.7 Hz, 1H), 7.36 (ddd, *J* = 7.5, 4.7, 1.1 Hz, 1H), 7.19 (t, *J* = 8.3 Hz, 1H), 6.74 (d, *J* = 9.9 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 2H), 3.84 (dd, *J* = 8.7, 6.4 Hz, 2H), 3.77 (dd, *J* = 8.7, 6.3 Hz, 2H), 3.67 (s, 3H), 2.19 (dp, *J* = 13.2, 6.6 Hz, 2H), 1.09 (dd, *J* = 6.7, 3.3 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.95, 163.71, 157.73, 150.09, 148.01, 137.10, 129.58, 126.02, 122.49, 114.23, 104.63, 75.17, 52.44, 46.21, 28.43, 19.36. HRMS (EI) calcd. for $C_{23}H_{30}N_2O_5$: 414.2155. Found: 414.2158.

Compound 9e. Colorless oil, yield 93 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (d, *J* = 9.3 Hz, 1H), 8.54 (d, *J* = 4.4 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.4 Hz, 1H), 7.37 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.50 (d, *J* = 9.5 Hz, 1H), 6.06 (s, 2H), 3.82 (s, 6H), 3.67 (s, 3H), 0.97 (s, 9H), 0.21 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.18, 163.85, 158.81, 157.47, 150.03, 148.24, 137.16, 126.10, 122.59, 107.43, 96.88, 56.07, 52.53, 46.20, 25.70, 18.21, -4.25. HRMS (EI) calcd. for $C_{23}H_{32}N_2O_6Si$: 460.2030. Found: 460.2035.

Compound 9f. Yellow oil, yield 91 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (d, *J* = 9.8 Hz, 1H), 8.52 (d, *J* = 4.7 Hz, 1H), 8.18 (t, *J* = 8.7 Hz, 1H), 7.79 (td, *J* = 7.7, 1.5 Hz, 1H), 7.40 – 7.30 (m, 1H), 6.57 (d, *J* = 9.8 Hz, 1H), 6.03 (s, 2H), 4.01 – 3.83 (m, 4H), 3.66 (s, 3H), 1.94 – 1.76 (m, 4H), 1.08 (t, *J* = 7.4 Hz, 6H), 0.97 (d, *J* = 2.0 Hz, 9H), 0.20 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.21, 163.67, 158.17, 157.21, 150.17, 148.09, 137.11, 126.00, 122.51, 107.67, 97.31, 70.24, 52.40, 46.22, 25.72, 22.62, 18.21, 10.66, -4.25. HRMS (EI) calcd. for $C_{27}H_{40}N_2O_6Si$: 516.2656. Found: 516.2661.

Compound 9g. Yellow oil, yield 85 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (d, *J* = 9.8 Hz, 1H), 8.52 (d, *J* = 4.2 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.6 Hz, 1H), 7.37 (ddd, *J* = 7.5, 4.8, 1.0 Hz, 1H), 6.55 (d, *J* = 9.8 Hz, 1H), 6.03 (s, 2H), 4.13 – 3.81 (m, 4H), 3.65 (s, 3H), 1.94 – 1.70 (m, 4H), 1.57 (tq, *J* = 14.8, 7.3 Hz, 4H), 0.97 (s, 9H), 0.20 (s, 6H), 0.06 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.15, 163.63, 158.19, 157.18, 150.24, 148.05, 137.09, 125.97, 122.52, 107.70, 97.30, 68.36, 52.37, 46.25, 31.29, 25.72, 19.23, 18.21, 13.95, -4.25. HRMS (EI) calcd. for $C_{29}H_{44}N_2O_6Si$: 544.2969. Found: 544.2972.

Compound 9h. Yellow oil, yield 82 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (d, *J* = 9.8 Hz, 1H), 8.49 (d, *J* = 4.5 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.6 Hz, 1H), 7.36 (ddd, *J* = 7.5, 4.7, 1.0 Hz, 1H), 6.61 (d, *J* = 9.8 Hz, 1H), 6.01 (s, 2H), 3.72 (ddd, *J* = 33.6, 8.7, 6.4 Hz, 4H), 3.65 (s, 3H), 2.16 (dt, *J* = 13.2, 6.6 Hz, 2H), 1.08 (dd, *J* = 6.7, 3.7 Hz, 12H), 0.97 (s, 9H), 0.20 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.17, 163.64, 158.20, 157.19, 150.18, 148.00, 137.08, 125.97, 122.51, 107.51, 97.12, 75.01, 52.39, 46.10, 28.40, 25.72, 19.37, 18.20, -4.23. HRMS (EI) calcd. for $C_{29}H_{44}N_2O_6Si$: 544.2969. Found: 544.2973.

Compound 10a. Yellow oil, yield 69 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, *J* = 9.1 Hz, 1H), 8.58 (d, *J* = 4.2 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.7, 1.6 Hz, 1H), 7.55 – 7.29 (m, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.30 (d, *J* = 9.2 Hz, 1H), 3.70 (s, 3H), 2.40 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.62, 168.92, 163.80, 149.53, 149.28, 148.41, 137.25, 129.35, 126.45, 122.50, 122.45, 120.89, 52.93, 46.93, 20.96. HRMS (EI) calcd. for $C_{19}H_{18}N_2O_7$: 386.1114. Found: 386.1118.

Compound 10b. White solid, yield: 54 %, mp 105-106 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.28 (d, *J* = 8.8 Hz, 1H), 8.42 (d, *J* = 4.3 Hz, 1H), 8.37 – 8.28 (m, 4H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.67 (t, *J* = 7.3 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 4H), 7.51 – 7.44 (m, 1H), 7.38 (dd, *J* = 7.0, 5.3 Hz, 1H), 7.29 – 7.24 (m, 2H), 6.48 (d, *J* = 8.9 Hz, 1H), 3.58 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.01, 164.45, 163.60, 149.83, 149.31, 148.11, 137.27, 133.97, 130.55, 129.32, 128.98, 128.79, 126.39, 122.73, 122.42, 121.01, 52.97, 47.46. HRMS (EI) calcd. for $C_{29}H_{22}N_2O_7$: 510.1427. Found: 510.1430.

Compound 10c. White solid, yield 67 %, mp 114-115 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.20 (d, *J* = 8.8 Hz, 1H), 8.45 (d, *J* = 4.6 Hz, 1H), 8.27 (d, *J* = 8.6 Hz, 4H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 4H), 7.48 (t, *J* = 8.3 Hz, 1H), 7.42 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 6.43 – 6.37 (m, 1H), 3.58 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.96, 163.62, 163.55, 149.63, 149.20, 148.12, 140.61, 137.37, 131.91, 129.43, 129.20, 127.39, 126.52, 122.62, 122.48, 121.09, 53.05, 47.38. HRMS (EI) calcd. for $C_{29}H_{20}Cl_2N_2O_7$: 578.0648. Found: 578.0655.

Conflicts of interest

There are no conflicts to declare.

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