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EFFICIENT ONE-POT, THREE-STEP SYNTHESIS OF 1,2,3,5-TETRASUBSTITUTED PYRROLES VIA AZA-MICHAEL ADDITION OF METHYL 3-IMINOACRYLATES

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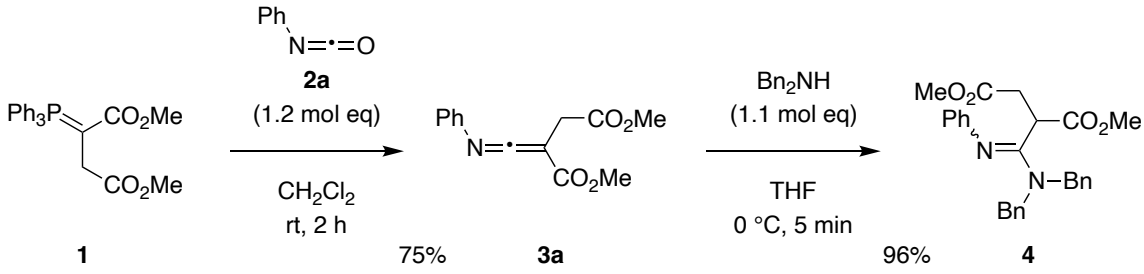
Abstract – An efficient one-pot, three-step procedure for the aza-Michael addition of methyl 3-iminoacrylates with secondary amines followed by intramolecular cyclization and silylation successfully afforded novel 1,2,3,5-tetrasubstituted pyrroles in high yields.

Pyrrole is one of the most important heterocycles because of its numerous biological activities and therapeutic potentials.[1–3] Hence, there are many reports on the synthesis of substituted pyrroles.[4–9] In particular, a one-pot procedure for the synthesis of substituted pyrroles and their derivatives is a useful and practical method.[10–15] We recently demonstrated novel synthetic approaches for disubstituted and trisubstituted thiophenes based on the thia-Michael addition of allenyl esters with thiols bearing electrophilic moieties.[16,17] In continuation of our efforts to synthesize polysubstituted heterocycles, we herein describe a novel one-pot synthesis of 1,2,3,5-tetrasubstituted pyrroles via the aza-Michael addition of methyl 3-iminoacrylates with secondary amines followed by intramolecular cyclization and silylation.

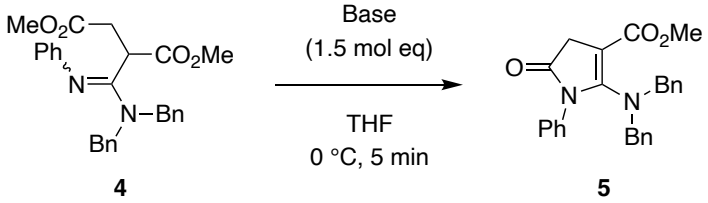
We started our investigation with the aza-Michael addition of dibenzylamine to methyl 3-iminoacrylate **3a** (Scheme 1). Methyl 3-iminoacrylate **3a** was prepared by a Wittig reaction between dimethyl (triphenylphosphoranylidene)succinate (**1**)[18,19] and phenyl isocyanate (**2a**) in CH_2Cl_2 at room temperature. The aza-Michael addition of methyl 3-iminoacrylate **3a** proceeded rapidly at 0 °C in THF, affording diastereomerically pure, racemic imine **4**. Unfortunately, the *E*/*Z* geometry of **4** has not been determined. Next, intramolecular cyclization of aza-Michael adduct **4** was investigated in the presence of bases (Table 1). Treatment of **4** with 1.5 equiv of sodium hydride in THF at 0 °C for 5 min resulted in the formation of 1,4,5-trisubstituted 1,3-dihydro-2*H*-pyrrol-2-one **5** in only 2% yield with the recovery of **4** (88%) (Entry 1). In the case of the reaction using *n*-butyllithium or isopropylmagnesium bromide as a base, the yield of **5** was increased to 17 and 46% (Entries 2 and 3). Each hexamethyldisilazide was found to be suitable for the intramolecular cyclization of aza-Michael adduct **4** (Entries 4–6), and sodium hexamethyldisilazide (NHMDS) provided 1,4,5-trisubstituted 1,3-dihydro-2*H*-pyrrol-2-one **5** in 86% yield (Entry 5). Finally,

the silylation of 1,4,5-trisubstituted 1,3-dihydro-2*H*-pyrrol-2-one **5** with 3 equiv of *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBDMSOTf) and 6 equiv of 2,6-lutidine in THF at 0 °C for 5 min furnished a novel 1,2,3,5-tetrasubstituted pyrrole **6** in 87% yield (Scheme 2).



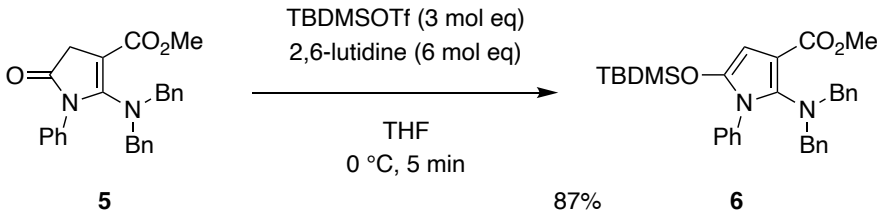
Scheme 1. Synthesis of aza-Michael adduct **4**

Table 1. Intramolecular cyclization of aza-Michael adduct **4** in the presence of bases



Entry	Base	Yield of **5** (%) [a]	Recovery of **4** (%) [a]
1	NaH	2	88
2	*n*-BuLi	17	ca. 54 [b]
3	*i*-PrMgBr	46	50
4	LHMDS	72	20
5	NHMDS	86	0
6	KHMDS	82	0

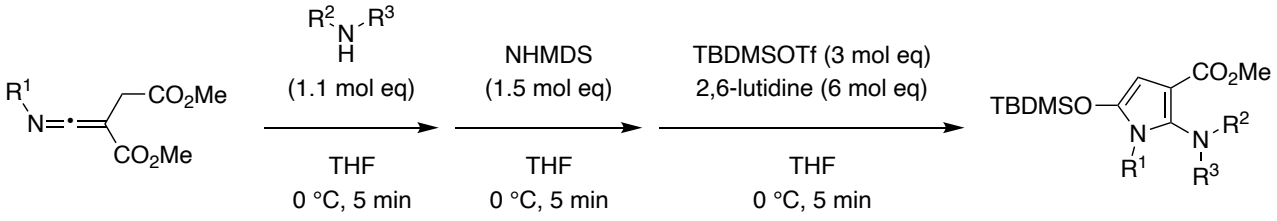
a) Isolated yields.
b) Small amounts of impurities were included.



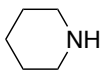
Scheme 2. Synthesis of 1,2,3,5-tetrasubstituted pyrrole **6** by silylation of 1,4,5-trisubstituted 1,3-dihydro-2*H*-pyrrol-2-one **5**

In pursuit of our objective of one-pot operation, we investigated the synthesis of 1,2,3,5-tetrasubstituted pyrroles **6**–**14** via the aza-Michael addition of methyl 3-iminoacrylates **3** with secondary amines again (Table 2). Remarkably, the reagents for intramolecular cyclization (NHMDS) and silylation (TBDMSOTf, 2,6-lutidine) were sequentially added to a mixture of methyl 3-iminoacrylate **3a** and dibenzylamine at 0 °C for 5 min intervals. The resulting mixture was stirred for an additional 5 min, resulting in the formation of 1,2,3,5-tetrasubstituted pyrrole **6** in a yield of 80% (Entry 1). The one-pot reaction of methyl 3-iminoacrylates **3b**–**d** and dibenzylamine was also found to afford 1,2,3,5-tetrasubstituted pyrroles **7**–**9** in 81–90% yields (Entries 2–4). In the reaction of **3b**,**d** bearing either the 4-$MeOC_6H_4$ group or the Bn group, aza-Michael addition required a higher reaction temperature and/or a longer reaction time, probably due to the reduced electrophilicity of methyl 3-iminoacrylates **3b** and **3d** (Entries 2 and 4). Methyl 3-iminoacrylates **3b**–**d** were synthesized in 35–80% yields by reacting phosphonium ylide **1** with the corresponding isocyanates **2b**–**d**.

Table 2. One-pot, three-step synthesis of 1,2,3,5-tetrasubstituted pyrroles **6**–**14**



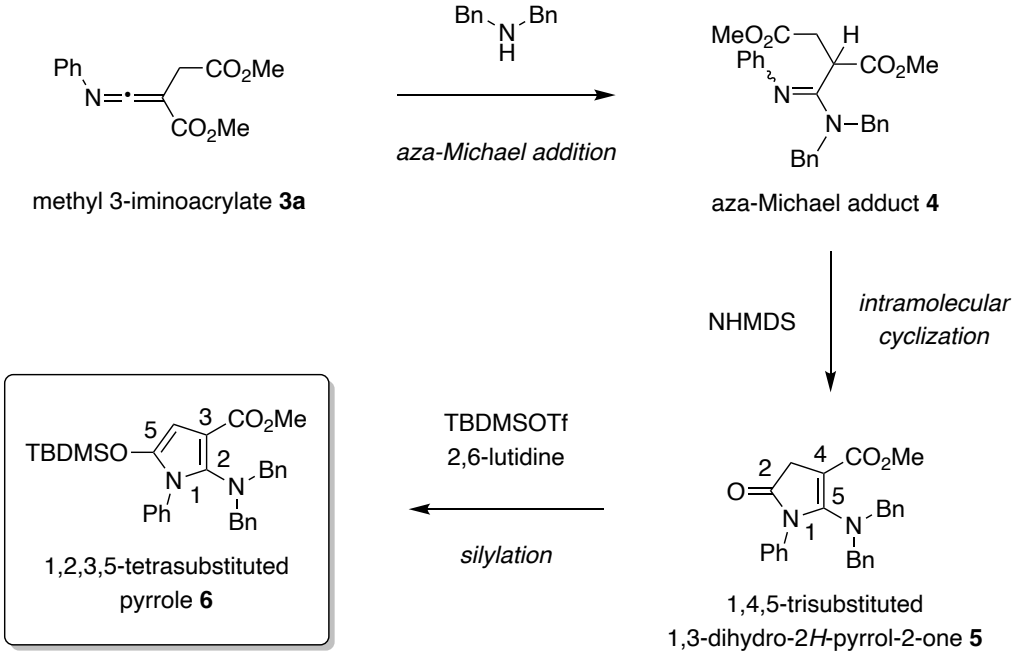
3 **6–14**

Entry	**3**	R^1	Secondary amine	R^2	R^3	Yield of **6–14** (%) [a]
1	**3a**	Ph	Bn_2NH	Bn	Bn	80 (**6**)
2	**3b**	4-$MeOC_6H_4$	Bn_2NH	Bn	Bn	85 (**7**) [b]
3	**3c**	4-FC_6H_4	Bn_2NH	Bn	Bn	81 (**8**)
4	**3d**	Bn	Bn_2NH	Bn	Bn	90 (**9**) [c]
5	**3a**	Ph	Me_2NH	Me	Me	89 (**10**)
6	**3a**	Ph	Et_2NH	Et	Et	89 (**11**)
7	**3a**	Ph		Bn	Me	89 (**12**)
8	**3a**	Ph		$(CH_2)_4$		66 (**13**)
9	**3a**	Ph		$(CH_2)_5$		82 (**14**)

a) Isolated yields.
b) Reaction conditions of aza-Michael addition: THF, 0 °C, 30 min.
c) Reaction conditions of aza-Michael addition: THF, rt, 3 h.

The reaction of methyl 3-iminoacrylate **3a** with dimethylamine, diethylamine, and benzylmethylamine provided 1,2,3,5-tetrasubstituted pyrroles **10**–**12** in 89% yield (Entries 5–7). In addition, 1,2,3,5-tetrasubstituted pyrroles **13** and **14** were also obtained in 66% and 82% yields, respectively, from the one-pot reaction of methyl 3-iminoacrylate **3a** with cyclic secondary amines such as pyrrolidine and piperidine (Entries 8 and 9). The structures of novel 1,2,3,5-tetrasubstituted pyrroles **6**–**14** were confirmed by spectroscopic methods including ^{1}H and ^{13}C NMR, IR, and HRMS.

Scheme 3 illustrates a reaction pathway for the synthesis of 1,2,3,5-tetrasubstituted pyrrole **6**, including both stepwise and one-pot approaches. Aza-Michael addition of dibenzylamine to methyl 3-iminoacrylate **3a** resulted in the formation of aza-Michael adduct **4**. Subsequently, intramolecular cyclization of **4** promoted by NHMDS afforded 1,4,5-trisubstituted 1,3-dihydro-2*H*-pyrrol-2-one **5**. Finally, the enolizable carbonyl oxygen of **5** was silylated with TBDMSOTf mediated by 2,6-lutidine, resulting in the formation of 1,2,3,5-tetrasubstituted pyrrole **6**. The reaction pathway can also account for the formation of 1,2,3,5-tetrasubstituted pyrroles **7**–**14** through a reaction similar to that of methyl 3-iminoacrylate **3** with secondary amines.



Scheme 3. Reaction pathway for the formation of 1,2,3,5-tetrasubstituted pyrrole **6**

In conclusion, we have succeeded in developing an efficient one-pot, three-step synthesis of novel 1,2,3,5-tetrasubstituted pyrroles **6**–**14** via the aza-Michael addition of methyl 3-iminoacrylates **3** with secondary amines followed by intramolecular cyclization and silylation. This method will be valuable for the rapid and practical synthesis of functionalized tetrasubstituted pyrroles.

EXPERIMENTAL

All melting points were determined using a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were obtained with a JASCO FT/IR-6200 IR Fourier transform spectrometer. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded with a JEOL JNM-ECZL500R. Chemical shifts are given in δ values (ppm) using TMS as an internal standard. HRMS (ESI) data were recorded with a Waters LCT Premier spectrometer. Elemental combustion analyses were performed with a J-SCIENCE LAB JM10. All reactions were monitored by TLC employing 0.25 mm silica gel plates (Merck 5715; 60 F_{254}). Column chromatography was carried out on silica gel [Silica Gel PSQ 60B (Fuji Silysia Chemical)]. Anhydrous CH_2Cl_2 and THF were used as purchased from Kanto Chemical. All other reagents were used as purchased.

Dimethyl 2-[(Phenylimino)methylene]succinate (3a)

To a solution of dimethyl 2-(triphenylphosphoranylidene)succinate (**1**)[18,19] (1.22 g, 3.00 mmol) in anhydrous CH_2Cl_2 (5 mL) was added phenyl isocyanate (**2a**) (390 μL, 3.60 mmol) at room temperature under argon. After stirring for 2 h, the reaction mixture was purified by column chromatography [Silica Gel PSQ 60B: *n*-hexane–AcOEt (5:1)] to afford **3a** (556 mg, 75%).

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.32 (s, 2H), 3.72 (s, 3H), 3.75 (s, 3H), 7.33–7.45 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.4, 52.0, 52.2, 60.1, 124.9, 128.8, 129.7, 137.1, 169.1, 171.3, 179.7; IR (neat) 2952, 2044, 1741, 1704, 1592, 1490, 1437, 1279, 1200, 1176, 1154, 1108 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{13}NO_4Na$: 270.0742; found: 270.0751.

Dimethyl 2-{[(4-Methoxyphenyl)imino]methylene}succinate (3b)

White powder (Et_2O–*n*-hexane); mp 46–47 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.30 (s, 2H), 3.72 (s, 3H), 3.73 (s, 3H), 3.83 (s, 3H), 6.90–6.94 (m, 2H), 7.33–7.38 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.6, 52.0, 52.3, 55.6, 59.8, 114.8, 126.7, 129.2, 160.0, 169.5, 171.6, 178.0; IR (KBr) 2952, 2845, 2043, 1732, 1688, 1583, 1509, 1442, 1290, 1248, 1215, 1178, 1113, 1020 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{15}NO_5Na$: 300.0848; found: 300.0843. Anal. Calcd for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.64; H, 5.55; N, 5.15%.

Dimethyl 2-{[(4-Fluorophenyl)imino]methylene}succinate (3c)

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.32 (s, 2H), 3.73 (s, 3H), 3.75 (s, 3H), 7.08–7.14 (m, 2H), 7.38–7.43 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.4, 52.2, 52.4, 60.5, 116.7 (d, $^{2}J_{C,F}$ = 23.0 Hz), 126.9 (d, $^{3}J_{C,F}$ = 8.8 Hz), 133.1 (d, $^{4}J_{C,F}$ = 3.2 Hz), 162.5 (d, $^{1}J_{C,F}$ = 249.5 Hz), 169.1, 171.4, 180.2 (d,

$^{6}J_{C,F}$ = 1.7 Hz); IR (neat) 2954, 2040, 1741, 1703, 1597, 1505, 1438, 1280, 1227, 1177, 1158, 1107 cm^{-1}; HRMS (ESI): *m*/*z* [M + Na]$^{+}$ calcd for $C_{13}H_{12}FNO_4Na$: 288.0648; found: 288.0639.

Dimethyl 2-[(Benzylimino)methylene]succinate (3d)

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.14 (s, 2H), 3.68 (s, 3H), 3.70 (s, 3H), 4.85 (s, 2H), 7.31–7.40 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.1, 51.8, 52.1, 54.9, 58.2, 127.8, 128.1, 128.7, 135.6, 169.9, 171.5, 176.4; IR (neat) 2952, 2060, 1741, 1699, 1438, 1281, 1197, 1173, 1118 cm^{-1}; HRMS (ESI): *m*/*z* [M + Na]$^{+}$ calcd for $C_{14}H_{15}NO_4Na$: 284.0899; found: 284.0884.

Dimethyl 2-(*N*,*N*-Dibenzyl-*N*'-phenylcarbamimidoyl)succinate (4)

To a solution of **3a** (41.9 mg, 0.170 mmol) in anhydrous THF (1.3 mL) was added dibenzylamine (35.7 μL, 0.186 mmol) at 0 °C under argon. After stirring for 5 min, the reaction mixture was treated with 1/15 mol/L phosphate buffer (pH 7.0, 10 mL) and then extracted with $CHCl_3$ (20 mL x 3). The extract was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The oily residue was purified by column chromatography [Silica Gel PSQ 60B: *n*-hexane–AcOEt (5:1)] to afford **4** (71.9 mg, 96%).

Colorless amorphous solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.52 (dd, *J* = 4.5, 16.8 Hz, 1H), 3.02 (dd, *J* = 9.2, 16.8 Hz, 1H), 3.50 (s, 3H), 3.58 (s, 3H), 4.49–4.55 (m, 3H), 4.60 (d, *J* = 16.2 Hz, 2H), 6.74–6.78 (m, 2H), 6.97–7.01 (m, 1H), 7.22–7.26 (m, 5H), 7.27–7.30 (m, 3H), 7.33–7.37 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.9, 41.2, 50.3, 52.0, 52.5, 121.7, 122.3, 127.2, 127.4, 128.5, 128.9, 137.6, 149.9, 154.4, 170.8; IR (KBr) 2952, 1737, 1613, 1592, 1437, 1222, 1170 cm^{-1}; HRMS (ESI): *m*/*z* [M + H]$^{+}$ calcd for $C_{27}H_{29}N_2O_4$: 445.2127; found: 445.2119.

Methyl 2-(Dibenzylamino)-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrrole-3-carboxylate (5)

To a solution of **4** (65.2 mg, 0.147 mmol) in anhydrous THF (1.1 mL) was added NHMDS (1 mol/L in THF, 220 μL, 0.220 mmol) at 0 °C under argon. After stirring for 5 min, the reaction mixture was treated with 1/15 mol/L phosphate buffer (pH 7.0, 40 mL) and then extracted with $CHCl_3$ (25 mL x 3). The extract was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The oily residue was purified by column chromatography [Silica Gel PSQ 60B: *n*-hexane–AcOEt (5:1)] to afford **5** (51.8 mg, 86%).

Colorless amorphous solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.56 (s, 2H), 3.76 (s, 3H), 4.06 (s, 4H), 6.99–7.03 (m, 2H), 7.12–7.15 (m, 4H), 7.28–7.35 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.4, 51.0, 54.9, 87.9, 127.7, 128.3, 128.5, 128.63, 128.65, 129.3, 135.1, 136.6, 158.5, 163.6, 174.9; IR (KBr) 2947, 1740, 1687, 1578, 1224, 1096 cm^{-1}; HRMS (ESI): *m*/*z* [M + Na]$^{+}$ calcd for $C_{26}H_{24}N_2O_3Na$: 435.1685; found: 435.1673.

Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-2-(dibenzylamino)-1-phenyl-1*H*-pyrrole-3-carboxylate (6)

To a solution of **5** (35.8 mg, 0.0868 mmol) in anhydrous THF (1 mL) were added TBDMSOTf (59.8 μL, 0.260 mmol) and 2,6-lutidine (60.6 μL, 0.521 mmol) at 0 °C under argon. After stirring for 5 min, the reaction mixture was treated with 1/15 mol/L phosphate buffer (pH 7.0, 20 mL) and then extracted with $CHCl_3$ (20 mL x 3). The extract was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The oily residue was purified by column chromatography [Silica Gel PSQ 60B: *n*-hexane–AcOEt (30:1)] to afford **6** (39.9 mg, 87%).

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ –0.02 (s, 6H), 0.63 (s, 9H), 3.90 (s, 3H), 4.16 (brs, 4H), 5.63 (s, 1H), 6.40–6.45 (m, 2H), 6.87–6.92 (m, 4H), 7.14–7.23 (m, 8H), 7.29–7.34 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.1, 17.6, 25.1, 51.0, 56.9, 88.3, 106.8, 126.8, 127.6, 127.9, 129.2, 129.4, 135.3, 138.0, 138.8, 139.1, 165.2; IR (neat) 2950, 2930, 2858, 1704, 1578, 1532, 1439, 1319, 1305, 1254, 1223, 1098, 1051 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{32}H_{38}N_2O_3SiNa$: 549.2549; found: 549.2539. Anal. Calcd for $C_{32}H_{38}N_2O_3Si$: C, 72.97; H, 7.27; N, 5.32. Found: C, 72.77; H, 7.48; N, 5.22%.

Typical procedure for the one-pot, three-step synthesis of 1,2,3,5-tetrasubstituted pyrroles 6–14

To a solution of **3a** (59.7 mg, 0.242 mmol) in anhydrous THF (1.8 mL) was added dibenzylamine (50.9 μL, 0.266 mmol) at 0 °C under argon. After stirring for 5 min, NHMDS (1 mol/L in THF, 362 μL, 0.362 mmol) was added, followed by an additional 5 min of stirring, TBDMSOTf (167 μL, 0.724 mmol) and 2,6-lutidine (169 μL, 1.45 mmol) were then added. After stirring for 5 min, the reaction mixture was treated with 1/15 mol/L phosphate buffer (pH 7.0, 10 mL) and then extracted with $CHCl_3$ (20 mL x 3). The extract was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The oily residue was purified by column chromatography [Silica Gel PSQ 60B: *n*-hexane–AcOEt (30:1)] to afford **6** (102 mg, 80%).

Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-2-(dibenzylamino)-1-(4-methoxyphenyl)-1*H*-pyrrole-3-carboxylate (7)

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ –0.02 (s, 6H), 0.65 (s, 9H), 3.84 (s, 3H), 3.90 (s, 3H), 4.15 (brs, 4H), 5.61 (s, 1H), 6.29–6.33 (m, 2H), 6.70–6.74 (m, 2H), 6.90–6.94 (m, 4H), 7.15–7.20 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.1, 17.7, 25.2, 51.0, 55.6, 56.9, 88.2, 106.6, 113.1, 126.8, 127.9, 128.3, 129.4, 130.1, 138.2, 139.0, 139.2, 159.0, 165.2; IR (neat) 2952, 2931, 2858, 1703, 1578, 1532, 1515, 1441, 1384, 1316, 1298, 1222, 1098, 1052 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{33}H_{40}N_2O_4SiNa$: 579.2655; found: 579.2696.

Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-2-(dibenzylamino)-1-(4-fluorophenyl)-1*H*-pyrrole-3-carboxylate (8)

Colorless plates (Et_2O–*n*-hexane); mp 131–132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ –0.01 (s, 6H), 0.64 (s, 9H), 3.91 (s, 3H), 4.17 (brs, 4H), 5.63 (s, 1H), 6.26–6.32 (m, 2H), 6.84–6.94 (m, 6H), 7.15–7.22 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.1, 17.6, 25.1, 51.0, 57.1, 88.4, 107.1, 114.7 (d, $^2J_{C,F}$ = 22.6 Hz), 126.9, 128.0, 129.3, 130.8 (d, $^3J_{C,F}$ = 8.7 Hz), 131.3 (d, $^4J_{C,F}$ = 3.3 Hz), 138.0, 138.8, 139.0, 161.9 (d, $^1J_{C,F}$ = 246.9 Hz), 165.2; IR (KBr) 2957, 2930, 2856, 1702, 1578, 1535, 1514, 1457, 1441, 1386, 1316, 1236, 1217, 1149, 1103, 1049 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{32}H_{37}FN_2O_3SiNa$: 567.2455; found: 567.2490. Anal. Calcd for $C_{32}H_{37}FN_2O_3Si$: C, 70.56; H, 6.85; N, 5.14. Found: C, 70.43; H, 6.93; N, 5.17%.

Methyl 1-Benzyl-5-[(*tert*-butyldimethylsilyl)oxy]-2-(dibenzylamino)-1*H*-pyrrole-3-carboxylate (9)

White powder (Et_2O–*n*-hexane); mp 91–92 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.72 (s, 9H), 3.87 (s, 3H), 4.16 (brd, 4H), 4.53 (s, 2H), 5.57 (s, 1H), 6.73–6.77 (m, 2H), 7.00–7.05 (m, 4H), 7.08–7.13 (m, 1H), 7.14–7.20 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.0, 17.8, 25.4, 43.5, 50.9, 57.4, 87.5, 106.3, 125.5, 126.5, 126.9, 128.0, 128.3, 129.5, 138.0, 138.1, 138.4, 139.1, 165.2; IR (KBr) 2929, 2859, 1704, 1578, 1528, 1461, 1443, 1388, 1258, 1233, 1216, 1175, 1093, 1074, 1028 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{33}H_{40}N_2O_3SiNa$: 563.2706; found: 563.2654. Anal. Calcd for $C_{33}H_{40}N_2O_3Si$: C, 73.29; H, 7.46; N, 5.18. Found: C, 73.13; H, 7.46; N, 5.21%.

Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-2-(dimethylamino)-1-phenyl-1*H*-pyrrole-3-carboxylate (10)

Colorless plates ($CHCl_3$–*n*-hexane); mp 84–85 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.72 (s, 9H), 2.65 (s, 6H), 3.81 (s, 3H), 5.53 (s, 1H), 7.19–7.22 (m, 2H), 7.32–7.37 (m, 1H), 7.39–7.43 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.1, 17.7, 25.2, 42.7, 50.8, 87.2, 103.5, 127.4, 128.2, 128.3, 135.9, 137.8, 141.2, 164.9; IR (KBr) 2947, 2859, 1710, 1578, 1545, 1444, 1325, 1227, 1207, 1079 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{30}N_2O_3SiNa$: 397.1923; found: 397.1939. Anal. Calcd for $C_{20}H_{30}N_2O_3Si$: C, 64.13; H, 8.07; N, 7.48. Found: C, 63.98; H, 8.01; N, 7.42%.

Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-2-(diethylamino)-1-phenyl-1*H*-pyrrole-3-carboxylate (11)

Colorless plates (*t*-BuOMe–*n*-hexane); mp 47–49 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.71 (s, 9H), 0.83 (t, *J* = 7.2 Hz, 6H), 2.99 (q, *J* = 7.2 Hz, 4H), 3.79 (s, 3H), 5.59 (s, 1H), 7.18–7.21 (m, 2H), 7.31–7.35 (m, 1H), 7.37–7.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.0, 13.7, 17.7, 25.2, 47.2, 50.7, 87.7, 105.4, 127.4, 128.1, 129.0, 135.9, 138.0, 139.4, 164.9; IR (KBr) 2969, 2933, 2862, 1711, 1538,

1223, 1187, 1091 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{34}N_2O_3SiNa$: 425.2236; found: 425.2197. Anal. Calcd for $C_{22}H_{34}N_2O_3Si$: C, 65.63; H, 8.51; N, 6.96. Found: C, 65.42; H, 8.52; N, 7.00%.

Methyl 2-[Benzyl(methyl)amino]-5-[(*tert*-butyldimethylsilyl)oxy]-1-phenyl-1*H*-pyrrole-3-carboxylate (12)

Pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.71 (s, 9H), 2.64 (s, 3H), 3.85 (s, 3H), 4.07 (s, 2H), 5.58 (s, 1H), 6.78–6.81 (m, 2H), 7.08–7.13 (m, 5H), 7.38–7.42 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.0, 17.7, 25.2, 40.2, 50.9, 59.4, 87.6, 105.3, 126.6, 127.6, 127.9, 128.3, 128.5, 128.8, 135.8, 137.9, 139.1, 140.6, 165.0; IR (neat) 2949, 2930, 2887, 1707, 1578, 1543, 1440, 1254, 1226, 1074 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{26}H_{34}N_2O_3SiNa$: 473.2236; found: 473.2267.

Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-1-phenyl-2-(pyrrolidin-1-yl)-1*H*-pyrrole-3-carboxylate (13)

Colorless plates (*t*-BuOMe–*n*-hexane); mp 60–61 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.74 (s, 9H), 1.73–1.77 (m, 4H), 3.05–3.09 (m, 4H), 3.79 (s, 3H), 5.55 (s, 1H), 7.20–7.22 (m, 2H), 7.30–7.35 (m, 1H), 7.37–7.41 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.0, 17.8, 25.3, 26.1, 50.7, 51.4, 87.2, 103.1, 127.3, 128.0, 128.2, 136.0, 138.0, 138.7, 164.8; IR (KBr) 2932, 2858, 1704, 1577, 1536, 1438, 1416, 1323, 1252, 1225, 1094 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{32}N_2O_3SiNa$: 423.2080; found: 423.2065.

Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-1-phenyl-2-(piperidin-1-yl)-1*H*-pyrrole-3-carboxylate (14)

Colorless plates (Et_2O–*n*-hexane); mp 68–69 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.72 (s, 9H), 1.24–1.30 (m, 4H), 1.34–1.41 (m, 2H), 2.94–2.99 (m, 4H), 3.80 (s, 3H), 5.52 (s, 1H), 7.18–7.21 (m, 2H), 7.32–7.36 (m, 1H), 7.38–7.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –5.0, 17.7, 24.0, 25.2, 26.1, 50.7, 51.0, 87.1, 103.6, 127.3, 128.1, 128.6, 135.8, 137.9, 141.0, 165.0; IR (KBr) 2936, 2857, 1709, 1533, 1439, 1328, 1219, 1094 cm^{-1}; HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{34}N_2O_3SiNa$: 437.2236; found: 437.2194.

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