Palladium-Catalyzed Oxalyl Amide Assisted Direct ortho-Alkynylation of Arylalkylamines Derivatives at δ and ε Positions

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1. **Reagents:** Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Column chromatography purifications were performed using 300–400 mesh silica gel.

2. **Instruments:** NMR spectra were recorded on Varian Inova–400 MHz, Inova–300 MHz, Bruker DRX–400 or Bruker DRX–500 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, br = broad singlet, m = multiplet. HRMS analyses were carried out using a Bruker micrOTOF–Q instrument or a TOF–MS instrument.

3. **Preparation of Oxalamide Substrates**

3.1 Preparation of N, N–Diisopropyloxamoyl Chloride S1

A solution of Diisopropylamine (7.01 mL, 50 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (50 mL) was added dropwise to a solution of oxalyl chloride (6.44 ml, 75 mmol, 1.5 equiv) in CH$_2$Cl$_2$ (100 mL) at 0 °C, after stirring for 5 min, triethylamine (7.30 mL, 52.5 mmol, 1.05 equiv) was added dropwise. The solution was warmed to room temperature and stirred for 6 hours. The excess of oxalyl chloride and the solvent were removed under reduced pressure and CH$_2$Cl$_2$ (30 mL) was added and evaporated. This operation was performed twice to give $1f$ as a pale yellow solid. The crude product was used in the next step without any purification.

3.2 General procedures for the preparation of oxalamide substrates 1a-1r (except 1i, 1k, 1l, 1q), 4a-4h, 4j

A solution of amine (20 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (40 mL) was added dropwise to a solution of N,N–Diisopropyloxamoyl chloride S1 (25 mmol, 1.25 equiv) in CH$_2$Cl$_2$ (50 mL) at 0 °C, after stirring for 5 min, triethylamine (2.92 ml, 21 mmol, 1.05 equiv) was added dropwise and then the mixture was stirred for 6 hours at room temperature before quenched by water (50 mL). The organic layer was separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (20 mL × 2). The combined organic phase was washed with brine (30 mL), and then dried over anhydrous Na$_2$SO$_4$. Evaporation and column chromatography on silica gel afforded corresponding amide substrates as white solid or colourless liquid with >90% yield.

3.3 Preparation of 1i

The first step using 4–(2–aminoethyl)phenol (2.74 g, 20 mmol, 1.0 equiv) as starting material followed the general oxalamide coupling procedure, affording a white solid. The solid was dissolved in DCM
(30 mL) and treated with AcCl (1.56 mL, 22 mmol, 1.1 equiv) and Et$_3$N (5.56 mL, 40 mmol, 2.0 equiv) at room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layer was washed with water and brine, dried over anhydrous Na$_2$SO$_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the product 1i 4.21 g, 63%.

3.4 Preparation of 1k\[^4\]

![Chemical structure of 1k](image)

To a solution of homophenylalanine (3.30 g, 20 mmol, 1.0 equiv) in MeOH (30 mL), at 0°C, was added SOCl$_2$ (4.35 mL, 60 mmol, 3.0 equiv) dropwise. The resulting mixture was allowed to stir from 0°C to room temperature overnight. The solvent was removed under reduced pressure to afford a white solid, which was used directly for the next step. The second step followed the general oxalamide coupling procedure, to give the product 1k 5.21 g, 78%.

3.5 Preparation of 1l

![Chemical structure of 1l](image)

To a solution of homophenylalanine (3.30 g, 20 mmol, 1.0 equiv) in MeOH (30 mL), at 0°C, was added SOCl$_2$ (4.35 mL, 60 mmol, 3.0 equiv) dropwise. The resulting mixture was allowed to stir from 0°C to room temperature overnight. The solvent was removed under reduced pressure to afford a white solid, which was used directly for the next step. The second step followed the procedure of 1i to give the product 1l 5.65 g, 72%.

3.6 Preparation of 1q\[^5\]

![Chemical structure of 1q](image)

To a solution of tryptophan (2 g, 10 mmol, 1.0 equiv) in MeOH (20 mL), at 0 °C, was added SOCl$_2$ (2.1 mL, 30 mmol, 3.0 equiv) dropwise. The resulting mixture was allowed to stir from 0 °C to room temperature overnight. The solvent was removed under reduced pressure to afford a white solid, which was used directly for the next step. The second step followed the procedure of 1a. Then TsCl (15 mmol, 1.5 equiv), NaOH (0.8 g, 20 mmol, 2.0 equiv), TEBAC (3.4 g, 15 mmol, 1.5 equiv) were added, the resulting mixture was allowed to stir at room temperature overnight. Water was added and the mixture was extracted with DCM. The combined organic layer was washed with water and brine, dried over...
anhydrous Na$_2$SO$_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the product 1q 3.90 g, 74%.

3.7 Preparation of 1q

SOCl$_2$ (4.35 mL, 60 mmol, 3.0 equiv) was added dropwise to a solution of amino acid (20 mmol, 1.0 equiv) in MeOH (30 mL) at 0 °C. The resulting mixture was allowed to stir from 0 °C to rt overnight. The solvent was removed under reduced pressure to give white solid, which was used directly for next step. A solution of white solid (20 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (40 mL) was added dropwise to a solution of N,N–Diisopropyloxamoyl chloride S1 (25 mmol, 1.25 equiv) in CH$_2$Cl$_2$ (50 mL) at 0 °C, after stirring for 5 min, triethylamine (2.92 mL, 21 mmol, 1.05 equiv) was added dropwise and then the mixture was stirred for 6 hours at room temperature before quenched by water (50 mL). The organic layer was separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (20 mL × 2). The combined organic phase was washed with brine (30 mL), and then dried over anhydrous Na$_2$SO$_4$. Evaporation and column chromatography on silica gel afforded corresponding amide substrates as white solid or colourless oil with >70% yield.

A mixture of S2 (545 mg, 2 mmol), ArI (3 mmol, 1.5 equiv), Pd(OAc)$_2$ (22 mg, 5 mol %), Ag$_2$CO$_3$ (552 mg, 1.0 equiv), PivOH (61 mg, 0.3 equiv) and 6 mL mesitylene in a 25 mL glass vial was heated at 90 °C with vigorous stirring for 24 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:20 to 1:2) to give product 4i 643 mg, 85%.

$^{1}$H NMR (400 MHz, CDCl$_3$) δ 7.20 (t, $J$ = 7.6 Hz, 1H), 7.14–7.13 (m, 2H), 6.90–6.84 (m, 2H), 4.62–4.59 (m, 1H), 3.82 (s, 3H), 3.53–3.43 (m, 3H), 2.86 (t, $J$ = 6.7 Hz, 2H), 1.39 (d, $J$ = 6.7 Hz, 6H), 1.18 (d, $J$ = 6.5 Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.41, 157.56, 130.64, 128.00, 127.12, 120.69, 110.36, 55.30, 49.64, 46.45, 39.65, 30.13, 20.92, 20.11. This compound was known.$^{[5]}$
\( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.15–7.14 (m, 5H), 4.68–4.62 (m, 1H), 3.53–3.48 (m, 3H), 2.88–2.84 (m, 2H), 2.34 (s, 3H), 1.41 (d, \( J = 6.8 \) Hz, 6H); \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.41, 163.28, 136.77, 136.46, 130.55, 129.36, 126.78, 126.24, 49.75, 46.58, 39.47, 32.98, 20.96, 20.15, 19.45. This compound was known.\(^{[5]}\)

\( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.20–7.18 (m, 2H), 7.10–7.06 (m, 1H), 7.05–7.00 (m, 1H), 6.93 (br s, 1H), 4.67–4.60 (m, 1H), 3.58–3.53 (m, 2H), 3.51–3.46 (m, 1H), 2.90 (t, \( J = 7.1 \) Hz, 2H), 1.40 (d, \( J = 6.8 \) Hz, 6H), 1.22 (t, \( J = 11.6 \) Hz, 6H); \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.49, 163.27, 161.40 (d, \( J_{C−F} = 244 \) Hz), 131.18 (d, \( J_{C−F} = 5.0 \) Hz), 128.47 (d, \( J_{C−F} = 8.0 \) Hz), 125.63 (d, \( J_{C−F} = 16.0 \) Hz), 124.30 (d, \( J_{C−F} = 4.0 \) Hz), 115.48 (d, \( J_{C−F} = 22.0 \) Hz), 49.76, 46.55, 39.38, 29.02 (d, \( J_{C−F} = 2.0 \) Hz), 20.93, 20.15. This compound was known.\(^{[5]}\)

\( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.50 (d, \( J = 7.9 \) Hz, 1H), 7.29 (br s, 1H), 7.26–7.20 (m, 2H), 7.07–7.03 (m, 1H), 4.55–4.52 (m, 1H), 3.57–3.52 (m, 2H), 3.49–3.42 (m, 1H), 2.98 (t, \( J = 7.2 \) Hz, 2H), 1.37 (d, \( J = 6.8 \) Hz, 6H), 1.17 (d, \( J = 6.7 \) Hz, 6H); \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.49, 163.40, 138.04, 132.95, 130.97, 128.32, 127.65, 124.63, 49.73, 46.44, 38.96, 35.65, 20.87, 20.09. This compound was known.\(^{[5]}\)

\( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.51–7.46 (m, 2H), 7.43 (t, \( J = 6.7 \) Hz, 2H), 7.17 (br s, 1H), 4.63–4.57 (m, 1H), 3.60–3.55 (m, 2H), 3.53–3.46 (m, 1H), 2.93 (t, \( J = 7.2 \) Hz, 2H), 1.40 (d, \( J = 6.8 \) Hz, 6H), 1.19 (d, \( J = 6.7 \) Hz, 6H); \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.58, 163.42, 139.68, 132.32, 130.98 (q, \( J_{C−F} = \)
32 Hz), 129.14, 125.60 (q, $J_{C-F} = 4$ Hz), 124.22 (q, $J_{C-F} = 270$ Hz), 123.55 (q, $J_{C-F} = 4$ Hz), 49.89, 46.58, 40.24, 35.33, 20.86, 20.12. This compound was known.\[5\]

\[1\] H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.32–7.27 (m, 2H), 7.23–7.20 (m, 3H), 7.11 (br s, 1H), 4.60–4.53 (m, 1H), 3.58–3.53 (m, 2H), 3.52–3.45 (m, 1H), 2.86 (t, $J = 7.2$ Hz, 2H), 1.40 (d, $J = 6.8$ Hz, 6H), 1.19 (d, $J = 6.7$ Hz, 6H); \[13\] C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.45, 163.41, 138.68, 128.85, 128.70, 126.62, 49.78, 46.52, 40.53, 35.55, 20.92, 20.16. This compound was known.\[5\]

\[2\] H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.18–8.16 (m, 2H), 7.40–7.38 (m, 2H), 7.14 (br s, 1H), 4.63–4.57 (m, 1H), 3.61–3.55 (m, 2H), 3.53–3.46 (m, 1H), 2.97 (t, $J = 7.1$ Hz, 2H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.19 (d, $J = 6.7$ Hz, 6H); \[13\] C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.52, 163.16, 146.94, 146.53, 129.80, 123.92, 49.87, 46.64, 39.96, 35.47, 20.91, 20.13. This compound was known.\[5\]

\[3\] H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.12 (d, $J = 8.6$ Hz, 4H), 6.95 (br s, 1H), 4.65–4.58 (m, 1H), 3.55–3.45 (m, 3H), 2.81 (t, $J = 7.2$ Hz, 2H), 2.31 (s, 3H), 1.40 (d, $J = 6.8$ Hz, 6H), 1.19 (d, $J = 6.7$ Hz, 6H); \[13\] C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.38, 163.26, 163.18, 135.53, 129.44, 128.74, 49.75, 46.58, 40.68, 35.14, 21.14, 20.96, 20.18. This compound was known.\[5\]

\[4\] H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.21 (d, $J = 8.4$ Hz, 3H), 6.99 (d, $J = 8.4$ Hz, 2H), 4.52–4.47 (m, 1H), 3.54–3.49 (m, 2H), 3.48–3.43 (m, 1H), 2.82 (t, $J = 7.2$ Hz, 2H), 2.26 (s, 3H), 1.38 (d, $J = 6.8$ Hz, 6H), 1.17 (d, $J = 6.6$ Hz, 6H); \[13\] C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.58, 163.54, 163.52, 149.34, 136.26, 129.77, 121.69, 49.82, 46.42, 40.38, 34.88, 21.17, 20.85, 20.11. This compound was known.\[5\]
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.30 (t, $J = 7.6$ Hz, 2H), 7.23–7.19 (m, 3H), 6.94 (br s, 1H), 4.42–4.37 (m, 1H), 3.54–3.39 (m, 3H), 3.03–2.94 (m, 1H), 1.38–1.35 (m, 6H), 1.28 (d, $J = 7.0$ Hz, 3H), 1.16–1.12 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.54, 143.93, 128.72, 127.28, 126.77, 49.83, 46.40, 45.86, 39.78, 20.88, 20.16, 20.14, 19.45. This compound was known.$^{[5]}$

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.30–7.16 (m, 6H), 4.87–4.84 (m, 1H), 4.39–4.34 (m, 1H), 3.72 (s, 3H), 3.49–3.46 (m, 1H), 3.22–3.07 (m, 2H), 1.42–1.40 (m, 6H), 1.18–1.16 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.32, 162.95, 135.74, 129.34, 128.69, 127.21, 53.24, 52.52, 49.81, 46.50, 38.03, 20.90, 20.81, 20.10. This compound was known.$^{[5]}$

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.17 (d, $J = 8.5$ Hz, 3H), 7.11 (br s, 1H), 7.04–7.00 (m, 2H), 4.86–4.81 (m, 1H), 4.47–4.41 (m, 1H), 3.71 (s, 3H), 3.53–3.45 (m, 1H), 3.17 (dd, $J = 14.0$, 5.8 Hz, 1H), 3.08 (dd, $J = 14.0$, 6.7 Hz, 1H), 2.27 (s, 4H), 1.41 (dd, $J = 6.8$, 2.7 Hz, 7H), 1.18 (d, $J = 6.6$ Hz, 7H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.17, 169.47, 162.94, 162.53, 149.95, 133.37, 130.41, 121.86, 53.25, 52.60, 49.83, 46.63, 37.55, 21.25, 20.94, 20.90, 20.17; HRMS (ESI-TOF) m/z [M–H$^+$] Calcd for C$_{20}$H$_{27}$N$_2$O$_6$: 391.1869; Found: 391.1865.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.03 (br s, 1H), 6.81–6.78 (m, 1H), 6.74 (dd, $J = 5.9$, 1.8 Hz, 2H), 4.61–4.54 (m, 1H), 3.85 (d, $J = 9.5$ Hz, 6H), 3.54–3.44 (m, 3H), 2.78 (t, $J = 7.1$ Hz, 2H), 1.38 (d, $J = 6.8$ Hz, 6H), 1.18 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.41, 163.29, 149.09, 147.80, 131.16, 120.77, 112.02, 111.45, 56.00, 55.94, 49.76, 46.54, 40.60, 35.16, 20.91, 20.14. This compound was known.$^{[4]}$
1H NMR (400 MHz, CDCl$_3$) δ 7.37 (br s, 1H), 7.28 (s, 1H), 7.22–7.17 (m, 2H), 4.57–4.52 (m, 1H), 3.57–3.52 (m, 2H), 3.51–3.46 (m, 1H), 2.97 (t, $J = 7.1$ Hz, 2H), 1.40 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.52, 163.26, 134.99, 134.92, 133.12, 131.82, 129.45, 127.29, 49.81, 46.55, 38.71, 32.76, 20.90, 20.12. This compound was known. [5]

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.31 (br s, 1H), 7.04 (d, $J = 7.6$ Hz, 1H), 7.00–6.90 (m, 2H), 4.64 (m, 1H), 3.60–3.35 (m, 3H), 2.92–2.71 (m, 2H), 2.29 (d, $J = 4.9$ Hz, 6H), 1.41 (d, $J = 6.8$ Hz, 6H), 1.22 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.55, 163.46, 136.54, 135.46, 133.16, 130.30, 130.05, 127.30, 53.51, 49.73, 46.40, 39.48, 32.85, 20.89, 20.82, 20.05, 18.83. This compound was known. [5]

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.29 (br s, 1H), 7.13 (d, $J = 4.9$ Hz, 1H), 6.93 – 6.90 (m, 1H), 6.85 (s, 1H), 4.59 – 4.52 (m, 1H), 3.55 (dd, $J = 13.1$, 6.6 Hz, 2H), 3.51 – 3.44 (m, 1H), 3.06 (t, $J = 6.8$ Hz, 2H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.19 (d, $J = 6.6$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.50, 163.42, 140.98, 127.09, 125.47, 123.95, 49.81, 46.47, 40.69, 29.63, 20.88, 20.13; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{14}$H$_{22}$N$_2$O$_2$SNa: 305.1300; found: 305.1299.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.95 (d, $J = 8.2$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.48 (d, $J = 7.7$ Hz, 1H), 7.43 (s, 1H), 7.33–7.27 (m, 2H), 7.25–7.19 (m, 3H), 4.87 (m, $J = 8.0$, 6.1 Hz, 1H), 4.56 (m, $J = 13.3$, 6.7 Hz, 1H), 3.62 (s, 3H), 3.50 (m, $J = 13.6$, 6.8 Hz, 1H), 3.24 (t, $J = 6.4$ Hz, 2H), 2.33 (s, 3H), 1.42 (dd, $J = 6.8$, 3.1 Hz, 6H), 1.19 (t, $J = 6.4$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.19, 162.95, 162.27, 145.01, 135.23, 135.16, 130.67, 130.02, 127.01, 125.04, 124.71, 123.39, 119.45, 116.85, 113.83, 52.68, 52.27, 49.84, 46.73, 27.73, 21.71, 20.94, 20.92, 20.17; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{27}$H$_{33}$N$_3$O$_6$S: 550.1988; Found: 550.1997.
H NMR (400 MHz, CDCl$_3$) $\delta$ 6.84 (br s, 1H), 5.49 (s, 1H), 4.70 (m, 1H), 3.48 (m, 2H), 2.15 (d, $J = 6.8$ Hz, 2H), 1.96 (m, 4H), 1.65–1.58 (m, 2H), 1.41 (d, $J = 6.8$ Hz, 6H), 1.21 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.32, 163.27, 134.38, 123.73, 49.77, 46.60, 37.52, 37.36, 25.36, 22.94, 21.01, 20.22; HRMS (ESI-TOF) m/z $[\text{M+Na}]^+$ Calcd for C$_{15}$H$_{26}$N$_2$O$_2$: 289.1892; Found: 289.1901.

H NMR (400 MHz, CDCl$_3$) $\delta$ 7.08 (br s, 1H), 6.73 (d, $J = 7.9$ Hz, 1H), 6.69 (d, $J = 1.4$ Hz, 1H), 6.65 (dd, $J = 7.9$, 1.6 Hz, 1H), 5.91 (s, 2H), 4.62–4.55 (m, 1H), 3.51–3.44 (m, 3H), 2.75 (t, $J = 7.1$ Hz, 2H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.19 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.41, 163.33, 147.87, 146.30, 132.39, 121.77, 109.18, 108.46, 100.99, 49.79, 46.54, 40.73, 35.24, 20.92, 20.15. This compound was known.$^4$

H NMR (400 MHz, CDCl$_3$) $\delta$ 7.22–7.18 (m, 1H), 7.10 (br s, 1H), 6.80 (d, $J = 7.7$ Hz, 1H), 6.77–6.75 (m, 2H), 4.58–4.52 (m, 1H), 3.78 (s, 3H), 3.56–3.51 (m, 2H), 3.49–3.44 (m, 1H), 2.82 (t, $J = 7.2$ Hz, 2H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.18 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.46, 159.87, 140.22, 129.68, 121.15, 114.36, 112.18, 55.25, 49.80, 46.50, 40.39, 35.57, 20.90, 20.14. This compound was known.$^5$
H NMR (400 MHz, CDCl₃) δ 7.23 (d, J = 7.6 Hz, 1H), 7.21–7.17 (m, 3H), 7.10 (d, J = 7.0 Hz, 1H), 4.53–4.46 (m, 1H), 4.36–4.30 (m, 2H), 4.28 (t, J = 7.2 Hz, 1H), 1.18 (d, J = 6.7 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 163.55, 163.45, 140.75, 134.40, 129.94, 128.99, 127.07, 126.83, 49.90, 46.54, 40.21, 35.16, 20.91, 20.15. This compound was known.[5]

H NMR (400 MHz, CDCl₃) δ 7.45 (br s, 1H), 7.38 (s, 1H), 7.35–7.34 (m, 1H), 7.16 (d, J = 4.6 Hz, 2H), 4.46–4.41 (m, 1H), 3.57–3.52 (m, 2H), 3.50–3.44 (m, 1H), 2.84 (t, J = 7.2 Hz, 2H), 1.39 (d, J = 6.8 Hz, 6H), 1.19 (d, J = 6.7 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 163.65, 163.61, 141.08, 131.85, 130.15, 129.66, 127.49, 122.58, 49.93, 46.40, 40.11, 35.03, 20.85, 20.11. This compound was known.[5]

H NMR (400 MHz, CDCl₃) δ 7.48 (br s, 1H), 6.98–6.87 (m, 4H), 4.67–4.61 (m, 1H), 4.13–4.10 (m, 2H), 3.86 (s, 3H), 3.70–3.66 (m, 2H), 3.53–3.46 (m, 1H), 1.42 (d, J = 6.6 Hz, 6H), 1.21 (d, J = 6.4 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 184.72, 171.32, 162.95, 135.74, 129.34, 128.69, 127.21, 53.24, 52.52, 49.81, 46.50, 38.03, 20.90, 20.81, 20.10. This compound was known.[5]

H NMR (400 MHz, CDCl₃) δ 7.32 (br s, 1H), 7.11 – 7.01 (m, 2H), 7.09–7.02 (m, 2H), 4.68–4.64 (m, 1H), 4.14 (t, J = 5.2 Hz, 2H), 3.74–3.70 (m, 2H), 3.53–3.47 (m, 1H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 163.66, 162.91, 152.92 (d, J_C–F = 244 Hz), 146.65 (d, J_C–F = 10 Hz), 124.50 (d, J_C–F = 4 Hz), 121.98 (d, J_C–F = 7 Hz), 116.49 (d, J_C–F = 18 Hz), 115.56, 68.04, 49.85, 46.67, 38.89, 20.95, 20.16. This compound was known.[5]
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.35 (dd, $J = 8.2$, 1.6 Hz, 1H), 7.30 (br s, 1H), 7.22–7.18 (m, 1H), 6.93–6.89 (m, 2H), 4.69–4.66 (m, 1H), 4.13 (t, $J = 5.2$ Hz, 2H), 3.77–3.73 (m, 2H), 3.52–3.49 (m, 1H), 1.42 (d, $J = 6.8$ Hz, 6H), 1.22 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.63, 162.87, 154.07, 130.51, 127.92, 123.35, 122.22, 114.04, 67.80, 49.81, 46.69, 38.81, 20.98, 20.17. This compound was known.\[5\]

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.38 (br s, 1H), 7.14 (t, $J = 6.7$ Hz, 2H), 6.87 (t, $J = 7.4$ Hz, 1H), 6.79 (d, $J = 8.4$ Hz, 1H), 4.78–4.74 (m, 1H), 4.07 (t, $J = 5.2$ Hz, 2H), 3.74–3.70 (m, 2H), 3.53–3.49 (m, 1H), 2.23 (s, 3H), 1.42 (d, $J = 6.8$ Hz, 6H), 1.22 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.39, 162.78, 156.58, 130.90, 126.93, 120.98, 111.08, 66.39, 49.73, 46.71, 39.07, 20.97, 20.15, 16.37. This compound was known.\[5\]

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.51 (br s, 1H), 7.17 (t, $J = 8.1$ Hz, 1H), 6.92 (d, $J = 7.9$ Hz, 1H), 6.86 (s, 1H), 6.76 (d, $J = 8.1$ Hz, 1H), 4.69–4.62 (m, 1H), 4.03 (t, $J = 5.2$ Hz, 2H), 3.69–3.65 (m, 2H), 3.52–3.45 (m, 1H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.20 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.50, 162.94, 159.17, 134.94, 130.36, 121.37, 115.01, 112.95, 66.47, 49.81, 46.62, 38.72, 20.90, 20.11. This compound was known.\[5\]

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.43 (br s, 1H), 7.14 (t, $J = 7.8$ Hz, 1H), 6.76 (d, $J = 7.5$ Hz, 1H), 6.71 (s, 1H), 6.68 (d, $J = 8.2$ Hz, 1H), 4.71–4.67 (m, 1H), 4.04 (t, $J = 5.2$ Hz, 2H), 3.68 (dd, $J = 10.9$, 5.5 Hz, 2H), 3.53–3.46 (m, 1H), 2.31 (s, 3H), 1.41 (d, $J = 6.8$ Hz, 6H), 1.21 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.50, 162.99, 158.46, 139.61, 129.30, 122.03, 115.43, 111.38, 66.10, 49.74, 46.59, 38.90, 21.56, 20.90, 20.12; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{17}$H$_{25}$N$_2$O$_3$Na: 329.1841; found: 329.1838.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31–7.23 (m, 8H), 7.18 (t, $J = 6.9$ Hz, 2H), 6.96 (br s, 1H), 4.80–4.74 (m, 1H), 3.99 (t, $J = 7.9$ Hz, 1H), 3.54–3.48 (m, 1H), 3.26–3.21 (m, 2H), 2.36–2.30 (m, 2H), 1.42 (d, $J = 6.8$ Hz, 6H), 1.22 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.28, 163.16, 144.06, 128.70, 127.83, 126.51, 49.71, 48.89, 46.61, 38.22, 34.83, 20.97, 20.17. This compound was known.\[5\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32–7.28 (m, 2H), 7.22–7.19 (m, 3H), 7.12 (br s, 1H), 4.79–4.73 (m, 1H), 3.55–3.50 (m, 1H), 3.36–3.31 (m, 2H), 2.71–2.67 (m, 2H), 1.94–1.87 (m, 2H), 1.44 (d, $J = 6.8$ Hz, 6H), 1.25 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.36, 163.26, 141.32, 128.57, 128.49, 126.13, 49.77, 46.67, 39.03, 33.28, 30.92, 30.92, 20.98, 20.19. This compound was known.\[5\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.33 (d, $J = 7.9$ Hz, 1H), 7.08 (d, $J = 8.4$ Hz, 2H), 6.81 (d, $J = 8.5$ Hz, 2H), 4.68–4.62 (m, 1H), 4.59–4.54 (m, 1H), 3.74 (d, $J = 20.0$ Hz, 6H), 3.55–3.48 (m, 1H), 2.63 (t, $J = 7.9$ Hz, 2H), 2.23–2.14 (m, 1H), 2.07–1.98 (m, 1H), 1.43 (d, $J = 6.8$ Hz, 6H), 1.23 (dd, $J = 6.4$, 4.1 Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 172.02, 163.15, 162.61, 158.15, 132.48, 129.47, 114.01, 55.34, 52.56, 51.98, 49.79, 46.68, 34.01, 30.82, 20.97, 20.94, 20.22, 20.14; HRMS (ESI-TOF) m/z [M+H$^+$] Calcd for C$_{20}$H$_{31}$N$_2$O$_5$: 379.2233; Found: 379.2230.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.26 (t, $J = 7.4$ Hz, 2H), 7.17 (dd, $J = 10.4$, 4.5 Hz, 3H), 4.68 (br s, 1H), 3.53 – 3.46 (m, 1H), 3.29 (dd, $J = 13.1$, 6.8 Hz, 2H), 2.63 (t, $J = 7.5$ Hz, 2H), 1.71 – 1.63 (m, 2H), 1.62 – 1.54 (m, 2H), 1.41 (d, $J = 6.8$ Hz, 6H), 1.21 (d, $J = 6.7$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.38, 142.11, 128.47, 128.39, 125.87, 49.75, 46.54, 39.18, 35.51, 28.87, 28.73, 20.91, 20.15; HRMS (ESI-TOF) m/z [M+H$^+$] Calcd for C$_{18}$H$_{29}$N$_2$O$_5$: 305.2229; Found: 305.2231.
4. Optimization of Reaction Conditions

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<th>entry</th>
<th>Pd(OAc)$_2$ (mol %)</th>
<th>base</th>
<th>additive (equiv)</th>
<th>Yield (%)</th>
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<td>AgOAc (2)</td>
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<tr>
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<td>5</td>
<td>LiOA</td>
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<td>4</td>
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<tr>
<td>4</td>
<td>5</td>
<td>KOAc</td>
<td>–</td>
<td>62</td>
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<tr>
<td>5</td>
<td>5</td>
<td>CsOA</td>
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<td>93</td>
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<tr>
<td>6</td>
<td>5</td>
<td>Na$_2$CO$_3$</td>
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<td>K$_2$CO$_3$</td>
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<td>5</td>
<td>KHCO$_3$</td>
<td>–</td>
<td>56</td>
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<tr>
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<tr>
<td>10</td>
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<td>K$_2$CO$_3$</td>
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<td>11</td>
<td>5</td>
<td>CsOA</td>
<td>PivOH (0.3)</td>
<td>51</td>
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<tr>
<td>12</td>
<td>–</td>
<td>CsOA</td>
<td>–</td>
<td>NR</td>
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</table>

*Reaction conditions: 1a (0.1 mmol), 2 (0.12 mmol), Pd(OAc)$_2$ (5 mol %), base (2 equiv), toluene (0.5 mL), 100 °C, air, 24 h. Yield was based on LC using acetophenone as the internal standard. \(^4\)Isolated yield at 0.2 mmol scale.

5. *ortho*-Alkylation of β-Arylethamine Derivatives

A mixture of 1 (0.2 mmol, 1.0 equiv), 2 (0.24 mmol, 1.2 equiv), Pd(OAc)$_2$ (1.1 mg, 0.05 equiv), CsOAc (76.8 mg, 2 equiv), toluene (0.5 mL) in a 15 mL glass vial (sealed with PTFE cap) was heated at 80 °C for 24 hours. The reaction mixture was cooled to rt, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the alkylation product.

\[
\text{OMe} \quad \text{H} \quad \text{N(RP)$_2$} \quad \text{3a}
\]

\(^1\)H NMR (400 MHz, CDCl$_3$) δ 7.14 (br s, 1H), 7.11 (d, \(J = 7.8\) Hz, 1H), 7.10 – 7.07 (m, 1H), 6.83 (d, \(J = 7.6\) Hz, 1H), 4.64 – 4.57 (m, 1H), 3.83 (s, 3H), 3.53 (dd, \(J = 12.2, 6.2\) Hz, 2H), 3.48 – 3.42 (m, 1H), 3.15 (t, \(J = 6.6\) Hz, 2H), 1.39 (d, \(J = 6.8\) Hz, 6H), 1.15 (d, \(J = 6.7\) Hz, 6H), 1.12 (s, 18H), 1.10 – 1.04 (m, 3H); \(^{13}\)C NMR (101 MHz, CDCl$_3$) δ 163.26, 163.14, 157.56, 129.75, 127.42, 125.30, 124.75, 110.88, 105.09, 94.78, 55.63, 49.45, 46.43, 39.60, 27.41, 20.92, 20.08, 18.77, 11.39; HRMS (ESI-TOF) m/z [M+Na]$^+$ Caled for C$_{23}$H$_{40}$N$_2$O$_3$SiNa: 509.3175; found: 509.3177.
\[ \text{Me} \]

\[ \text{HN} \]

\[ \text{ON}(\text{IPr})_2 \]

\[ \text{O} \]

\[ \text{TIPS} \]

\[ 3b \]

\[^1\text{H} \text{NMR} (400 \text{ MHz, CDCl}_3) \delta 7.34 (d, J = 7.1 \text{ Hz}, 1 \text{H}), 7.12 (d, J = 7.2 \text{ Hz}, 1 \text{H}), 7.06 (t, J = 7.6 \text{ Hz}, 1 \text{H}), 6.92 (\text{br s, 1H}), 4.68 - 4.62 (m, 1 \text{H}), 3.55 (dd, J = 14.4, 6.6 \text{ Hz}, 2 \text{H}), 3.52 - 3.45 (m, 1 \text{H}), 3.14 (t, J = 7.4 \text{ Hz}, 2 \text{H}), 2.38 (s, 3 \text{H}), 1.41 (d, J = 6.8 \text{ Hz}, 6 \text{H}), 1.20 (d, J = 6.7 \text{ Hz}, 6 \text{H}), 1.13 (s, 18 \text{H}), 1.12 - 1.06 (m, 3 \text{H}); \]

\[^{13}\text{C} \text{NMR} (101 \text{ MHz, CDCl}_3) \delta 163.34, 163.02, 138.99, 137.16, 131.04, 130.94, 126.39, 123.81, 106.03, 94.24, 49.59, 46.59, 38.97, 31.20, 20.99, 20.14, 19.93, 18.83, 11.46; \]

HRMS (ESI-TOF) m/z [M+Na]^+ Calcd for C_{28}H_{46}N_2O_2SiNa: 493.3226; found: 493.3217.

\[ \text{F} \]

\[ \text{HN} \]

\[ \text{ON}(\text{IPr})_2 \]

\[ \text{O} \]

\[ \text{TIPS} \]

\[ 3c \]

\[^1\text{H} \text{NMR} (400 \text{ MHz, CDCl}_3) \delta 7.29 (d, J = 7.1 \text{ Hz}, 1 \text{H}), 7.17 - 7.12 (m, 1 \text{H}), 7.01 (t, J = 8.6 \text{ Hz}, 1 \text{H}), 6.90 (\text{br s, 1H}), 4.64 - 4.57 (m, 1 \text{H}), 3.63 - 3.58 (m, 2 \text{H}), 3.51 - 3.44 (m, 1 \text{H}), 3.13 (t, J = 6.8 \text{ Hz}, 6 \text{H}), 1.40 (d, J = 6.8 \text{ Hz}, 6 \text{H}), 1.19 (d, J = 6.7 \text{ Hz}, 6 \text{H}), 1.13 (d, J = 2.8 \text{ Hz}, 18 \text{H}), 1.10 (dd, J = 9.8, 4.9 \text{ Hz}, 3 \text{H}); \]

\[^{13}\text{C} \text{NMR} (101 \text{ MHz, CDCl}_3) \delta 163.34, 163.08, 161.30 (d, J_{C-F}= 244 \text{ Hz}), 128.86, 128.06 (d, J_{C-F}= 17 \text{ Hz}), 127.86 (d, J_{C-F}= 9 \text{ Hz}), 125.61 (d, J_{C-F}= 5 \text{ Hz}), 115.85 (d, J_{C-F}= 23 \text{ Hz}), 103.87 (d, J_{C-F}= 4 \text{ Hz}), 96.13, 49.60, 46.49, 38.88, 27.23, 20.90, 20.11, 18.75, 11.35; \]

\[^{19}\text{F} \text{NMR} (376 \text{ MHz, CDCl}_3) \delta -116.66; \]

HRMS (ESI-TOF) m/z [M+Na]^+ Calcd for C_{27}H_{43}FN_2O_2SiNa: 497.2976; found: 497.2972.

\[ \text{Br} \]

\[ \text{HN} \]

\[ \text{ON}(\text{IPr})_2 \]

\[ \text{O} \]

\[ \text{TIPS} \]

\[ 3d \]

\[^1\text{H} \text{NMR} (400 \text{ MHz, CDCl}_3) \delta 7.49 (d, J = 8.0 \text{ Hz}, 1 \text{H}), 7.43 (dd, J = 7.4, 3.4 \text{ Hz}, 1 \text{H}), 7.02 (d, J = 7.7 \text{ Hz}, 1 \text{H}), 6.97 (\text{br s, 1H}), 4.70 - 4.64 (m, 1 \text{H}), 3.62 (dd, J = 13.4, 6.9 \text{ Hz}, 2 \text{H}), 3.50 - 3.44 (m, 1 \text{H}), 3.29 (dd, J = 9.1, 5.1 \text{ Hz}, 2 \text{H}), 1.39 (d, J = 6.8 \text{ Hz}, 6 \text{H}), 1.18 (d, J = 6.7 \text{ Hz}, 6 \text{H}), 1.16 - 1.11 (m, 18 \text{H}), 1.08 (dd, J = 11.0, 3.5 \text{ Hz}, 3 \text{H}); \]

\[^{13}\text{C} \text{NMR} (101 \text{ MHz, CDCl}_3) \delta 163.09, 162.86, 161.30 (d, J_{C-F}= 244 \text{ Hz}), 128.86, 128.06 (d, J_{C-F}= 17 \text{ Hz}), 127.86 (d, J_{C-F}= 9 \text{ Hz}), 125.6 (d, J_{C-F}= 5 \text{ Hz}), 115.85 (d, J_{C-F}= 23 Hz), 103.87 (d, J_{C-F}= 4 \text{ Hz}), 96.13, 49.60, 46.49, 38.88, 27.23, 20.90, 20.11, 18.75, 11.37; \]

HRMS (ESI-TOF) m/z [M+Na]^+ Calcd for C_{27}H_{43}BrN_2O_2SiNa: 557.2175; found: 557.2161.

\[ \text{F}_3\text{C} \]

\[ \text{HN} \]

\[ \text{ON}(\text{IPr})_2 \]

\[ \text{O} \]

\[ \text{TIPS} \]

\[ 3e \]

\[^1\text{H} \text{NMR} (400 \text{ MHz, CDCl}_3) \delta 7.57 (d, J = 8.0 \text{ Hz}, 1 \text{H}), 7.46 (s, 1 \text{H}), 7.42 (d, J = 8.0 \text{ Hz}, 1 \text{H}), 7.11 (\text{br s, 1H}), 4.67 - 4.60 (m, 1 \text{H}), 3.64 - 3.59 (m, 2 \text{H}), 3.51 - 3.44 (m, 1 \text{H}), 3.11 (dd, J = 8.9, 5.1 \text{ Hz}, 2 \text{H}),

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1.38 (d, J = 6.8 Hz, 6H), 1.18 (d, J = 6.7 Hz, 6H), 1.13 (t, J = 3.7 Hz, 18H), 1.09 (dd, J = 11.0, 3.4 Hz, 3H); 13C NMR (101 MHz, CDCl3) δ 163.37, 162.93, 141.69, 133.44, 130.26 (q, J C-F= 32 Hz), 127.60, 126.19 (d, J C-F= 3 Hz), 123.91 (q, J C-F= 271 Hz), 123.41 (d, J C-F= 3 Hz), 103.74, 98.22, 49.70, 46.61, 39.28, 34.30, 20.86, 20.06, 18.74, 11.34; 19F NMR (376 MHz, CDCl3) δ -62.75; HRMS (ESI-TOF) m/z [M+Na]+ Calcd for C28H43F3N2O2SiNa: 547.2944; found: 547.2948.

1H NMR (400 MHz, CDCl3) δ 7.48 (d, J = 7.3 Hz, 1H), 7.26 (dd, J = 7.6, 6.0 Hz, 1H), 7.22 (d, J = 6.1 Hz, 1H), 7.20 – 7.16 (m, 1H), 6.82 (br s, 1H), 4.63 – 4.57 (m, 1H), 3.64 – 3.59 (m, 2H), 3.52 – 3.45 (m, 1H), 3.06 (t, J = 6.9 Hz, 2H), 1.40 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.7 Hz, 6H), 1.13 (s, 18H), 1.07 (dd, J = 13.0, 7.9 Hz, 3H); 13C NMR (101 MHz, CDCl3) δ 163.42, 163.21, 140.81, 133.22, 129.54, 128.80, 126.65, 123.32, 105.21, 95.04, 49.76, 46.58, 39.56, 34.40, 20.98, 20.16, 18.83, 11.43; HRMS (ESI-TOF) m/z [M+Na]+ Calcd for C27H44N2O2SiNa: 479.3070; found: 479.3063.

1H NMR (400 MHz, CDCl3) δ 7.43 (d, J = 7.7 Hz, 2H), 7.12 (t, J = 7.7 Hz, 1H), 6.88 (br s, 1H), 4.61 – 4.53 (m, 1H), 3.65 (dd, J = 12.8, 7.1 Hz, 2H), 3.48 – 3.42 (m, 1H), 3.34 (dd, J = 9.3, 5.0 Hz, 2H), 1.38 (d, J = 6.8 Hz, 6H), 1.16 (s, 6H), 1.12 (d, J = 2.5 Hz, 36H), 1.11 – 1.06 (m, 6H); 13C NMR (101 MHz, CDCl3) δ 162.94, 162.86, 142.74, 133.17, 126.45, 124.09, 104.77, 95.48, 49.45, 46.52, 39.30, 32.61, 20.99, 20.17, 18.83, 11.43; HRMS (ESI-TOF) m/z [M+Na]+ Calcd for C38H64N2O2SiNa: 659.4404; found: 659.4410.

1H NMR (400 MHz, CDCl3) δ 8.28 (d, J = 2.4 Hz, 1H), 8.08 (dd, J = 8.4, 2.4 Hz, 1H), 7.40 (d, J = 8.5 Hz, 1H), 7.02 (br s, 1H), 4.63 – 4.56 (m, 1H), 3.65 – 3.60 (m, 2H), 3.52 – 3.45 (m, 1H), 3.15 (dd, J = 8.7, 4.8 Hz, 2H), 1.38 (d, J = 6.8 Hz, 6H), 1.19 (d, J = 6.7 Hz, 6H), 1.16 – 1.12 (m, 18H), 1.12 – 1.06 (m, 3H); 13C NMR (101 MHz, CDCl3) δ 163.42, 162.82, 148.16, 146.67, 130.53, 127.81, 124.86, 123.23, 102.62, 98.61, 49.71, 46.65, 38.97, 34.53, 20.94, 20.12, 18.77, 11.33; HRMS (ESI-TOF) m/z [M+Na]+ Calcd for C39H66N2O3SiNa: 524.2921; found: 524.2914.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.22 (s, 2H), 6.95 (br s, 1H), 4.62 – 4.55 (m, 1H), 3.67 (dd, $J = 13.1$, 6.9 Hz, 2H), 3.47 (dd, $J = 13.6$, 6.8 Hz, 1H), 3.43 – 3.38 (m, 2H), 1.16 (s, 6H), 1.15 – 1.12 (m, 36H), 1.12 – 1.06 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.82, 162.36, 149.62, 146.24, 127.10, 125.70, 102.46, 99.04, 49.43, 46.68, 38.65, 33.23, 20.96, 20.13, 18.81, 11.35; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{38}$H$_{63}$N$_3$O$_4$Si$_2$Na: 704.4255; found: 704.4239.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.29 (s, 1H), 7.11 (d, $J = 7.8$ Hz, 1H), 7.08 – 7.05 (m, 1H), 6.80 (br s, 1H), 4.63 – 4.56 (m, 1H), 3.61 – 3.56 (m, 2H), 3.51 – 3.44 (m, 1H), 3.01 (t, $J = 6.9$ Hz, 2H), 2.28 (s, 3H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.19 (d, $J = 6.7$ Hz, 6H), 1.13 (s, 18H), 1.07 (dd, $J = 10.2$, 5.3 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.38, 163.20, 137.78, 136.25, 133.62, 129.69, 129.44, 123.07, 105.46, 94.48, 49.70, 46.55, 39.66, 33.92, 20.96, 20.85, 20.16, 18.82, 11.44; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{28}$H$_{46}$N$_2$O$_2$SiNa: 493.3226; found: 493.3226.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.26 (s, 2H), 6.87 (br s, 1H), 4.60 – 4.54 (m, 1H), 3.63 (dd, $J = 12.7$, 7.0 Hz, 2H), 3.49 – 3.42 (m, 1H), 3.30 (dd, $J = 9.2$, 5.0 Hz, 2H), 2.27 (s, 3H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.16 (d, $J = 6.7$ Hz, 6H), 1.13 (d, $J = 1.9$ Hz, 36H), 1.11 – 1.06 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.95, 162.89, 139.85, 136.16, 133.84, 123.88, 105.01, 94.92, 49.46, 46.53, 39.42, 32.13, 20.99, 20.64, 20.18, 18.84, 11.44; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{39}$H$_{60}$N$_2$O$_2$Si$_2$Na: 673.4561; found: 673.4559.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.23 (d, $J = 8.3$ Hz, 1H), 7.20 (d, $J = 2.5$ Hz, 1H), 6.99 (dd, $J = 8.3$, 2.5 Hz, 1H), 6.82 (br s, 1H), 4.63 – 4.57 (m, 1H), 3.61 – 3.56 (m, 2H), 3.51 – 3.44 (m, 1H), 3.03 (dd, $J =...
8.7, 5.0 Hz, 2H), 2.27 (s, 3H), 1.39 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.7 Hz, 6H), 1.15 – 1.11 (m, 18H), 1.11 – 1.04 (m, 3H); 13C NMR (101 MHz, CDCl₃) δ 169.46, 163.46, 163.11, 149.07, 138.51, 130.53, 125.93, 124.51, 122.23, 104.18, 96.13, 49.73, 46.56, 39.47, 33.90, 21.16, 20.96, 20.16, 18.79, 11.38; HRMS (ESI-TOF) m/z [M+Na]+ Calcd for C₂₉H₄₆N₂O₄SiNa: 537.3125; found: 537.3133.

H NMR (400 MHz, CDCl₃) δ 7.17 (d, J = 1.6 Hz, 2H), 6.87 (br s, 1H), 4.65 – 4.54 (m, 1H), 3.63 (dd, J = 13.0, 7.0 Hz, 2H), 3.49 – 3.42 (m, 1H), 3.30 (dd, J = 9.3, 5.1 Hz, 2H), 2.27 (s, 3H), 1.39 (d, J = 6.8 Hz, 6H), 1.16 (d, J = 3.0 Hz, 36H), 1.07 (dd, J = 10.9, 3.5 Hz, 6H); 13C NMR (101 MHz, CDCl₃) δ 169.22, 162.93, 162.80, 148.56, 140.54, 126.23, 125.25, 103.88, 96.57, 49.50, 46.54, 39.18, 32.28, 21.12, 20.96, 20.17, 18.82, 11.39; HRMS (ESI-TOF) m/z [M+Na]+ Calcd for C₄₂H₆₈N₂O₆Si₂Na: 775.4514; found: 775.4530.

H NMR (400 MHz, CDCl₃) δ 7.48 (dd, J = 7.7, 0.9 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.25 (dd, J = 7.6, 1.4 Hz, 1H), 7.15 (td, J = 7.6, 1.6 Hz, 1H), 6.60 (br s, 1H), 4.41 – 4.35 (m, 1H), 3.72 – 3.59 (m, 2H), 3.57 – 3.50 (m, 1H), 3.47 – 3.40 (m, 1H), 1.50 (dd, J = 7.1, 2.7 Hz, 3H), 1.36 (d, J = 6.8 Hz, 6H), 1.15 (s, 6H), 1.12 (d, J = 2.9 Hz, 36H), 1.09 – 0.99 (m, 6H); 13C NMR (101 MHz, CDCl₃) δ 163.49, 163.41, 145.49, 133.46, 128.97, 126.40, 125.84, 123.26, 105.25, 95.45, 49.75, 46.43, 44.30, 37.35, 20.92, 20.86, 20.18, 20.13, 18.80, 18.64, 11.45; HRMS (ESI-TOF) m/z [M+Na]+ Calcd for C₃₉H₆₆N₂O₂Si₂Na: 673.4526; found: 673.4521.
\[ \text{1H NMR (400 MHz, CDCl}_3\text{)} \delta 7.49 (d, J = 7.5 \text{ Hz, } 1\text{H}), 7.27 (d, J = 2.6 \text{ Hz, } 1\text{H}), 7.26 (br s, 1\text{H}), 7.24 – 7.20 (m, 1\text{H}), 7.18 (dd, J = 7.7, 3.6 \text{ Hz, } 1\text{H}), 1.41 – 1.37 (m, 6\text{H}), 1.14 (d, J = 2.7 \text{ Hz, } 18\text{H}), 1.12 (s, 6\text{H}), 1.11 – 1.08 (m, 3\text{H}); \text{13C NMR (101 MHz, CDCl}_3\text{)} \delta 171.48, 162.88, 162.47, 138.26, 133.18, 129.58, 128.68, 126.98, 123.85, 105.01, 95.55, 52.96, 52.51, 49.58, 46.51, 36.74, 20.98, 20.81, 20.17, 20.06, 18.80, 18.79, 11.41; \text{HRMS (ESI-TOF) m/z [M+Na]^+ Calcd for C}_{29}H_{46}N_2O_4SiNa: 537.3125; found: 537.3130.} \]
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\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{)} & \delta 7.18 (d, J = 1.9 Hz, 2H), 7.11 (d, J = 8.3 Hz, 1H), 5.12 – 5.05 (m, 1H), 4.03 – 3.97 (m, 1H), 3.74 (d, J = 2.5 Hz, 3H), 3.63 – 3.57 (m, 1H), 3.47 – 3.37 (m, 2H), 2.27 (s, 3H), 1.38 – 1.33 (m, 6H), 1.18 – 1.15 (m, 3H), 1.15 – 1.12 (m, 3H), 1.11 (d, J = 4.3 Hz, 3H), 1.10 – 1.07 (m, 6H); \\
\text{C NMR (101 MHz, CDCl}_3\text{)} & \delta 171.30, 169.05, 163.20, 162.77, 148.88, 138.11, 126.22, 125.75, 103.68, 97.44, 52.48, 51.97, 49.64, 46.32, 35.03, 21.13, 20.94, 20.71, 20.23, 20.00, 18.83, 18.82, 11.38; \text{HRMS (ESI-TOF) m/z [M+Na]}^+ \text{Calcd for } C_{42}H_{68}N_2O_6Si_2Na: 775.4514; \text{found: 775.4530.}
\end{align*}
\]

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\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{)} & \delta 6.92 (s, 1H), 6.82 (br s, 1H), 6.74 (s, 1H), 4.68 – 4.61 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.59 – 3.54 (m, 2H), 3.51 – 3.44 (m, 1H), 3.00 (t, J = 6.8 Hz, 2H), 1.39 (d, J = 6.8 Hz, 6H), 1.19 (d, J = 6.7 Hz, 6H), 1.13 (s, 18H), 1.12 – 1.06 (m, 3H); \\
\text{C NMR (101 MHz, CDCl}_3\text{)} & \delta 163.42, 163.04, 149.64, 147.39, 134.46, 115.26, 114.93, 112.61, 105.41, 93.03, 56.14, 56.11, 49.65, 46.59, 39.72, 34.12, 20.98, 20.15, 18.86, 11.49; \text{HRMS (ESI-TOF) m/z [M+Na]}^+ \text{Calcd for } C_{29}H_{48}N_2O_4SiNa: 539.3281; \text{found: 539.3272.}
\end{align*}
\]

\[
\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{)} & \delta 6.96 (s, 1H), 6.90 (br s, 1H), 4.68 – 4.61 (m, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.60 (dd, J = 12.7, 7.0 Hz, 2H), 3.49 – 3.43 (m, 1H), 3.25 (dd, J = 9.4, 4.9 Hz, 2H), 1.39 (d, J = 6.8 Hz, 6H), 1.16 (d, J = 6.7 Hz, 6H), 1.14 (s, 18H), 1.12 (d, J = 2.4 Hz, 18H), 1.10 – 0.99 (m, 6H); \\
\text{C NMR (101 MHz, CDCl}_3\text{)} & \delta 162.92, 162.79, 151.97, 151.12, 136.48, 119.24, 119.20, 116.67, 104.80, 100.40, 100.36, 94.27, 61.07, 56.22, 49.47, 46.56, 39.44, 32.08, 31.08, 21.02, 20.19, 18.87, 18.83, 11.47; \text{HRMS (ESI-TOF) m/z [M+Na]}^+ \text{Calcd for } C_{40}H_{68}N_2O_6SiNa: 719.4615; \text{found: 719.4611.}
\end{align*}
\]
\[ \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.35 (d, \( J = 2.0 \text{ Hz, 1H} \)), 7.31 (br s, 1H), 7.04 (s, 1H), 4.64 – 4.57 (m, 1H), 3.60 – 3.55 (m, 2H), 3.49 – 3.42 (m, 1H), 3.20 (dd, \( J = 8.9, 5.0 \text{ Hz, 2H} \)), 1.37 (d, \( J = 6.8 \text{ Hz, 6H} \)), 1.16 (d, \( J = 6.7 \text{ Hz, 6H} \)), 1.10 (d, \( J = 3.7 \text{ Hz, 18H} \)), 1.09 – 1.04 (m, 3H); \[ \text{^13C NMR (101 MHz, CDCl}_3 \] \( \delta \) 163.30, 162.99, 139.01, 139.00, 134.11, 130.37, 127.63, 123.68, 104.51, 99.08, 49.58, 46.60, 39.00, 31.44, 21.34, 20.99, 20.14, 19.67, 18.85, 11.46; HRMS (ESI-TOF) m/z [M+Na]^+ Calcd for C\(_{27}\)H\(_{42}\)Cl\(_2\)N\(_2\)O\(_2\): 547.2290; found: 547.2280.

\[ \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.03 – 6.98 (m, 2H), 6.92 (br s, 1H), 4.75 – 4.66 (m, 1H), 3.58 – 3.52 (m, 2H), 3.48 (dd, \( J = 13.6, 6.8 \text{ Hz, 1H} \)), 3.18 – 3.12 (m, 2H), 2.42 (s, 3H), 2.34 (s, 3H), 1.41 (d, \( J = 6.8 \text{ Hz, 6H} \)), 1.20 (d, \( J = 6.7 \text{ Hz, 6H} \)), 1.14 (d, \( J = 1.8 \text{ Hz, 18H} \)), 1.13 – 1.07 (m, 3H); \[ \text{^13C NMR (101 MHz, CDCl}_3 \] \( \delta \) 163.04, 162.70, 137.17, 135.47, 132.49, 131.26, 129.53, 126.55, 102.97, 97.76, 49.44, 46.49, 38.23, 31.30, 20.81, 20.00, 18.65, 11.22; HRMS (ESI-TOF) m/z [M+Na]^+ Calcd for C\(_{29}\)H\(_{48}\)N\(_2\)O\(_2\): 507.3383; found: 507.3375.

\[ \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.05 (d, \( J = 5.2 \text{ Hz, 1H} \)), 7.01 (d, \( J = 5.2 \text{ Hz, 1H} \)), 6.94 (br s, 1H), 4.70 – 4.63 (m, 1H), 3.63 – 3.58 (m, 2H), 3.53 – 3.46 (m, 1H), 3.17 (t, \( J = 6.8 \text{ Hz, 2H} \)), 1.41 (d, \( J = 6.8 \text{ Hz, 6H} \)), 1.21 (d, \( J = 6.7 \text{ Hz, 6H} \)), 1.11 (s, 18H), 1.08 – 1.04 (m, 3H); \[ \text{^13C NMR (101 MHz, CDCl}_3 \] \( \delta \) 163.39, 162.94, 144.90, 130.29, 122.83, 121.16, 100.89, 93.79, 49.73, 46.67, 39.94, 28.97, 21.01, 20.19, 18.83, 11.41; HRMS (ESI-TOF) m/z [M+Na]^+ Calcd for C\(_{25}\)H\(_{42}\)N\(_2\)O\(_2\): 485.2634; found: 485.2643.
20.18, 20.13, 18.81, 11.54; HRMS (ESI-TOF) m/z [M+Na]⁺ Calcd for C₃₆H₅₁N₃O₄SiNa: 672.3267; found: 672.3271.

1H NMR (400 MHz, CDCl₃) δ 6.77 (br s, 1H), 4.67 – 4.60 (m, 1H), 3.48 (dd, J = 13.6, 6.8 Hz, 1H), 3.41 (dd, J = 13.2, 6.9 Hz, 2H), 2.54 (t, J = 7.0 Hz, 2H), 2.16 (s, 2H), 2.10 (s, 2H), 1.61 – 1.54 (m, 4H), 1.39 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.7 Hz, 6H), 1.05 (s, 18H), 1.04 – 0.93 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ =163.44, 163.25, 142.79, 117.81, 107.45, 92.48, 49.74, 46.53, 37.77, 35.80, 30.18, 29.35, 22.50, 22.35, 21.00, 20.17, 18.81, 11.41; HRMS (ESI-TOF) m/z [M+Na]⁺ Calcd for C₂₇H₄₈N₂O₂SiNa: 483.3383; found: 483.3379.

1H NMR (400 MHz, CDCl₃) δ 6.88 (br s, 1H), 6.86 (s, 1H), 6.02 (s, 2H), 4.68 – 4.60 (m, 1H), 3.60 (d, J = 5.7 Hz, 2H), 3.50 – 3.43 (m, 1H), 3.25 (s, 2H), 1.39 (d, J = 6.8 Hz, 6H), 1.17 (d, J = 6.7 Hz, 6H), 1.12 (d, J = 3.0 Hz, 18H), 1.11 (d, J = 1.8 Hz, 18H), 1.08 (dd, J = 6.3, 4.6 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ =162.94, 162.82, 150.37, 145.98, 137.35, 116.63, 112.25, 105.92, 105.03, 102.10, 100.30, 98.23, 93.53, 49.49, 46.56, 39.48, 32.06, 21.01, 20.19, 18.85, 18.82, 11.46, 11.39; HRMS (ESI-TOF) m/z [M+Na]⁺ Calcd for C₃₉H₆₄N₂O₄Si₂Na: 703.4302; found: 703.4312.

1H NMR (400 MHz, CDCl₃) δ 6.93 (br s, 1H), 6.00 (s, 1H), 4.78 – 4.71 (m, 1H), 3.55 (dd, J = 12.8, 6.5 Hz, 2H), 3.48 (dd, J = 13.6, 6.8 Hz, 1H), 2.68 (t, J = 6.7 Hz, 2H), 1.40 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.7 Hz, 6H), 1.06 (d, J = 1.2 Hz, 36H), 1.05 – 0.99 (m, 6H); ¹³C NMR (101 MHz, CDCl₃) δ =163.06, 162.81, 133.13, 118.62, 106.61, 102.92, 102.79, 97.36, 49.57, 46.61, 37.75, 33.25, 20.97, 20.16, 18.73, 11.32, 11.30; HRMS (ESI-TOF) m/z [M+Na]⁺ Calcd for C₃₉H₆₄N₂O₂Si₂Na: 703.4302; found: 703.4312.
H NMR (400 MHz, CDCl$_3$) δ 7.39 (d, $J = 8.5$ Hz, 1H), 6.88 (br s, 1H), 6.75 (d, $J = 2.3$ Hz, 1H), 6.69 (dd, $J = 8.5$, 2.3 Hz, 1H), 4.63 – 4.56 (m, 1H), 3.78 (s, 3H), 3.62 – 3.54 (m, 2H), 3.50 – 3.43 (m, 1H), 3.02 (t, $J = 6.8$ Hz, 2H), 1.38 (d, $J = 6.8$ Hz, 6H), 1.18 (d, $J = 6.7$ Hz, 6H), 1.12 (d, $J = 7.6$ Hz, 18H), 1.09 – 1.04 (m, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.42, 163.14, 159.81, 142.60, 134.43, 115.43, 114.79, 112.59, 105.31, 92.98, 55.37, 49.66, 46.49, 39.44, 34.56, 20.90, 20.11, 18.78, 11.43; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{28}$H$_{46}$N$_2$O$_3$SiNa: 509.3175; found: 509.3168.

H NMR (400 MHz, CDCl$_3$) δ 7.40 (d, $J = 8.6$ Hz, 1H), 6.86 (br s, 1H), 6.69 (d, $J = 8.7$ Hz, 1H), 4.64 – 4.54 (m, 1H), 3.84 (s, 3H), 3.64 (dd, $J = 12.7$, 7.1 Hz, 2H), 3.49 – 3.42 (m, 1H), 3.32 (dd, $J = 9.3$, 5.1 Hz, 2H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.15 (d, $J = 6.7$ Hz, 6H), 1.13 (d, $J = 1.7$ Hz, 18H), 1.10 – 0.94 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 162.98, 162.93, 161.36, 144.70, 134.03, 116.13, 113.61, 109.07, 104.96, 100.50, 100.45, 93.28, 56.08, 49.49, 46.51, 39.31, 32.71, 21.00, 20.20, 18.87, 18.84, 11.49; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{39}$H$_{66}$N$_2$O$_3$Si$_2$Na: 689.4510; found: 689.4503.

H NMR (400 MHz, CDCl$_3$) δ 7.38 (dd, $J = 8.2$, 3.2 Hz, 1H), 7.20 (d, $J = 1.9$ Hz, 1H), 7.14 (dd, $J = 9.3$, 5.1 Hz, 2H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.15 (d, $J = 6.7$ Hz, 6H), 1.13 (d, $J = 2.2$ Hz, 18H), 1.10 – 0.94 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.40, 163.02, 142.86, 134.39, 134.37, 134.20, 129.52, 126.83, 121.81, 104.05, 96.20, 49.75, 46.52, 39.27, 34.17, 20.92, 20.12, 18.75, 11.34; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{27}$H$_{43}$ClN$_2$O$_2$SiNa: 513.2680; found: 513.2669.

H NMR (400 MHz, CDCl$_3$) δ 7.37 (d, $J = 1.4$ Hz, 1H), 7.32 (d, $J = 8.1$ Hz, 1H), 7.30 (d, $J = 1.7$ Hz, 1H), 6.96 (br s, 1H), 4.66 – 4.59 (m, 1H), 3.61 – 3.56 (m, 2H), 3.52 – 3.45 (m, 1H), 3.02 (dd, $J = 8.8$, 5.2 Hz, 2H), 1.39 (d, $J = 6.8$ Hz, 6H), 1.20 (d, $J = 6.7$ Hz, 6H), 1.11 (d, $J = 2.5$ Hz, 18H), 1.07 (dd, $J = 9.4$, 5.1 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.40, 163.02, 142.86, 134.39, 132.42, 129.80, 122.69, 122.29, 104.11, 96.50, 49.74, 46.58, 39.33, 34.17, 20.98, 20.15, 18.77, 11.36; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{26}$H$_{43}$BrN$_2$O$_2$SiNa: 557.2175; found: 557.2158.
6. ortho-Alkynylation of γ-Arylpropamine Derivatives

A mixture of 4 (0.2 mmol, 1.0 equiv), 2 (0.4 mmol, 2 equiv), Pd(OAc)$_2$ (1.1 mg, 0.05 equiv), AgOAc (66.8 mg, 2 equiv), KOAc (58.9 mg, 2 equiv), toluene (1 mL) in a 25 mL glass vial (purged with Ar, sealed with PTFE cap) was heated at 120 °C for 36 hours. The reaction mixture was cooled to rt, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the alkynylation product.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 (br s, 1H), 7.03 (dd, $J$ = 7.8, 1.7 Hz, 1H), 6.98 (t, $J$ = 7.9 Hz, 1H), 6.88 (dd, $J$ = 8.0, 1.6 Hz, 1H), 4.64 – 4.57 (m, 1H), 4.27 – 4.22 (m, 2H), 3.89 (s, 3H), 3.60 – 3.55 (m, 2H), 3.51 (dd, $J$ = 13.6, 6.8 Hz, 1H), 1.44 (d, $J$ = 6.8 Hz, 6H), 1.22 (d, $J$ = 6.7 Hz, 6H), 1.12 (d, $J$ = 1.6 Hz, 18H), 1.08 (dd, $J$ = 8.0, 5.6 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.77, 163.42, 152.58, 149.19, 125.74, 124.39, 118.72, 112.74, 102.59, 95.90, 72.08, 56.05, 49.75, 46.43, 39.60, 20.98, 20.16, 18.76, 11.41; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{28}$H$_{46}$N$_2$O$_4$SiNa: 525.3125; found: 525.3124.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.29 (br s, 1H), 7.20 (d, $J$ = 7.7 Hz, 1H), 7.05 (dd, $J$ = 13.8, 5.0 Hz, 1H), 6.97 – 6.92 (m, 1H), 4.68 – 4.62 (m, 1H), 4.29 (t, $J$ = 5.0 Hz, 2H), 3.65 (dd, $J$ = 10.7, 5.4 Hz, 2H), 3.54 – 3.47 (m, 1H), 1.42 (d, $J$ = 6.8 Hz, 6H), 1.22 (d, $J$ = 6.7 Hz, 6H), 1.12 (d, $J$ = 2.3 Hz, 18H), 1.07 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.65, 162.95, 155.41 (d, $J_{C-F} = 245$ Hz), 147.65 (d, $J_{C-F} = 12$ Hz), 129.50 (d, $J_{C-F} = 3$ Hz), 123.97 (d, $J_{C-F} = 8$ Hz), 119.36, 117.29 (d, $J_{C-F} = 19$ Hz), 101.68 (d, $J_{C-F} = 4$ Hz), 97.02, 72.48 (d, $J_{C-F} = 3$ Hz), 49.77, 46.59, 39.55, 20.94, 20.15, 18.76, 11.38; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -130.58; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{27}$H$_{43}$FN$_2$O$_3$SiNa: 513.2925; found: 513.2927.
**5c**

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\text{OTIPS} \quad \text{ClO}(i\text{Pr})_2O_5
\]

\(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.40\) (br s, 1H), 7.36 – 7.31 (m, 2H), 6.98 (t, \(J = 7.9\) Hz, 1H), 4.72 – 4.65 (m, 1H), 4.31 (t, \(J = 5.1\) Hz, 2H), 3.68 (dd, \(J = 10.5, 5.5\) Hz, 2H), 3.54 – 3.47 (m, 1H), 1.43 (d, \(J = 6.8\) Hz, 6H), 1.22 (d, \(J = 6.7\) Hz, 6H), 1.12 (d, \(J = 2.7\) Hz, 18H), 1.11 – 1.06 (m, 3H); \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \(\delta = 163.59, 162.91, 155.69, 133.02, 130.72, 124.69, 119.35, 101.94, 97.38, 72.06, 49.73, 46.61, 39.63, 21.01, 20.16, 18.78, 11.40; HRMS (ESI-TOF) m/z [M+Na\(^+\)] Calcd for C\(_{27}\)H\(_{43}\)ClN\(_2\)O\(_3\)SiNa: 529.2629; found: 529.2625.

**5d**

\[
\text{Me} \quad \text{OTIPS} \quad \text{N}(i\text{Pr})_2
\]

\(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.35\) (br s, 1H), 7.29 (dd, \(J = 7.6, 1.3\) Hz, 1H), 7.12 (dd, \(J = 7.5, 0.8\) Hz, 1H), 6.93 (t, \(J = 7.6\) Hz, 1H), 4.79 – 4.72 (m, 1H), 4.24 (t, \(J = 5.2\) Hz, 2H), 3.68 (dd, \(J = 10.9, 5.5\) Hz, 2H), 3.55 – 3.48 (m, 1H), 2.26 (s, 3H), 1.43 (d, \(J = 6.8\) Hz, 6H), 1.23 (d, \(J = 6.7\) Hz, 6H), 1.12 (s, 18H), 1.11 – 1.05 (m, 3H); \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \(\delta = 163.45, 162.77, 158.04, 132.44, 131.71, 131.25, 123.74, 116.92, 103.68, 95.37, 71.00, 49.68, 46.68, 39.88, 21.00, 20.15, 18.81, 16.41, 11.46; HRMS (ESI-TOF) m/z [M+Na\(^+\)] Calcd for C\(_{28}\)H\(_{43}\)N\(_2\)O\(_3\)SiNa: 509.3175; found: 509.3176.

**5e**

\[
\text{Me} \quad \text{OTIPS} \quad \text{N}(i\text{Pr})_2
\]

\(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.35\) (d, \(J = 8.2\) Hz, 1H), 7.21 (br s, 1H), 6.89 (dd, \(J = 8.2, 1.9\) Hz, 1H), 6.81 (d, \(J = 1.8\) Hz, 1H), 4.73 – 4.67 (m, 1H), 4.10 (t, \(J = 5.2\) Hz, 2H), 3.72 (dd, \(J = 11.0, 5.5\) Hz, 2H), 3.54 – 3.47 (m, 1H), 2.32 (s, 3H), 1.41 (d, \(J = 6.8\) Hz, 6H), 1.21 (d, \(J = 6.7\) Hz, 6H), 1.13 (s, 18H), 1.09 (dd, \(J = 9.3, 3.8\) Hz, 3H); \(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \(\delta = 163.57, 162.44, 159.99, 135.20, 134.59, 121.25, 112.70, 111.96, 101.84, 96.36, 67.44, 49.71, 46.73, 38.86, 21.00, 20.14, 18.84, 11.41; HRMS (ESI-TOF) m/z [M+Na\(^+\)] Calcd for C\(_{27}\)H\(_{43}\)ClN\(_2\)O\(_3\)SiNa: 529.2629; found: 529.2619.

**5f**

\[
\text{Me} \quad \text{OTIPS} \quad \text{N}(i\text{Pr})_2
\]

\(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta = 7.31\) (d, \(J = 7.7\) Hz, 1H), 7.18 (br s, 1H), 6.74 – 6.69 (m, 1H), 6.63 (s, 1H), 4.69 – 4.62 (m, 1H), 4.11 (t, \(J = 5.2\) Hz, 2H), 3.72 (dd, \(J = 10.9, 5.5\) Hz, 2H), 3.53 – 3.46 (m, 1H), 2.32 (s, 3H), 1.41 (d, \(J = 6.8\) Hz, 6H), 1.21 (d, \(J = 6.7\) Hz, 6H), 1.13 (s, 18H), 1.09 (dd, \(J = 7.1, 4.5\) Hz,
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.46 (d, $J = 7.6$ Hz, 1H), 7.25 – 7.21 (m, 1H), 7.18 (d, $J = 6.6$ Hz, 1H), 7.14 (dd, $J = 11.7$, 4.4 Hz, 1H), 6.97 (br s, 1H), 4.81 – 4.70 (m, 1H), 3.54 – 3.47 (m, 1H), 3.31 (d, $J = 6.8$ Hz, 2H), 2.91 – 2.81 (m, 2H), 1.92 (s, 2H), 1.42 (d, $J = 6.8$ Hz, 6H), 1.22 (d, $J = 6.8$ Hz, 6H), 1.13 (s, 18H), 1.08 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.24, 163.14, 143.55, 133.19, 128.96, 128.68, 126.12, 123.01, 105.51, 94.54, 49.74, 46.70, 39.19, 32.32, 30.02, 21.00, 20.19, 18.83, 11.45; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{28}$H$_{46}$N$_2$O$_3$SiNa: 509.3175; found: 509.3172.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.42 (d, $J = 7.7$ Hz, 1H), 7.09 (t, $J = 7.7$ Hz, 1H), 6.76 (br s, 1H), 4.79 – 4.72 (m, 1H), 3.35 – 3.46 (m, 1H), 3.35 (dd, $J = 15.3$, 6.0 Hz, 1H), 3.18 – 3.08 (m, 1H), 1.98 – 1.88 (m, 1H), 1.41 (d, $J = 6.8$ Hz, 3H), 1.21 (d, $J = 6.7$ Hz, 3H), 1.13 (d, $J = 2.4$ Hz, 18H), 1.09 (d, $J = 2.4$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 162.90, 145.75, 133.29, 125.97, 123.60, 105.08, 94.97, 49.59, 46.64, 39.60, 31.12, 29.70, 21.01, 20.21, 18.84, 11.44; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{39}$H$_{66}$N$_2$O$_2$Si$_2$Na: 673.4561; found:673.4563.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.47 (d, $J = 7.6$ Hz, 1H), 7.33 (d, $J = 7.4$ Hz, 2H), 7.27 (d, $J = 7.2$ Hz, 2H), 7.25 (s, 1H), 7.23 (d, $J = 6.5$ Hz, 1H), 7.16 (dd, $J = 11.0$, 3.6 Hz, 1H), 7.14 – 7.10 (m, 1H), 6.97 (br s, 1H), 4.80 – 4.68 (m, 2H), 3.52 – 3.45 (m, 1H), 3.33 – 3.17 (m, 2H), 2.41 – 2.29 (m, 2H), 1.40 (d, $J = 6.8$ Hz, 6H), 1.21 (d, $J = 6.6$ Hz, 6H), 1.16 (s, 18H), 1.11 (d, $J = 10.2$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.09, 162.89, 145.09, 143.05, 133.54, 129.03, 128.60, 127.92, 126.50, 126.22, 123.17, 105.87, 94.57, 49.57, 46.66, 46.14, 38.60, 34.94, 20.98, 20.14, 18.87, 11.49; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{34}$H$_{50}$N$_2$O$_2$SiNa: 569.3539; found:569.3532.
$^1$H NMR (400 MHz, CDCl$_3$) δ =7.22 (d, $J = 8.2$ Hz, 1H), 7.10 (d, $J = 8.5$ Hz, 1H), 6.98 (d, $J = 2.7$ Hz, 1H), 6.80 (d, $J = 8.5$, 2.8 Hz, 1H), 4.72 – 4.66 (m, 1H), 4.54 – 4.48 (m, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 3.55 – 3.48 (m, 1H), 3.59 – 3.48 (m, 1H), 2.88 – 2.79 (m, 1H), 2.35 – 2.27 (m, 1H), 2.06 – 1.97 (m, 1H), 1.44 (d, $J = 6.8$ Hz, 6H), 1.23 (d, $J = 6.6$ Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ =172.12, 163.17, 162.45, 157.82, 134.88, 130.26, 123.80, 117.99, 115.11, 105.30, 94.67, 55.50, 52.47, 52.00, 49.73, 46.73, 32.81, 30.18, 21.00, 20.98, 20.22, 20.16, 18.83, 11.43; HRMS (ESI-TOF) m/z [M+Na]$^+$ Calcd for C$_{31}$H$_{50}$N$_2$O$_5$SiNa: 581.3387; found:581.3381.

7. Gram Scale Reaction

Scheme 1S Gram Scale Reaction.

A mixture of 1a (1.226 g, 4 mmol, 1.0 equiv), 2 (1.568 g, 6 mmol, 1.5 equiv), Pd(OAc)$_2$ (11 mg, 0.025 equiv), CsOAc (1.536 g, 2 equiv) and toluene (10 mL) in a 50 mL glass vial (sealed with PTFE cap) was heated at 100 °C for 48 hours. The reaction mixture was cooled to rt, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give 3a as yellow solid in 82% yield.
8. Removal of the TIPS\textsuperscript{[6]}

**Scheme 2S** Removal of the TIPS.

3a (0.146 g, 0.3 mmol) was dissolved in dry THF (10 mL). After cooling to 0 °C TBAF (400 µL, 0.4 mmol, 1M solution in THF) were added and the reaction mixture stirred for 1h. Then some drops of water and CH\textsubscript{2}Cl\textsubscript{2} (20 mL) were added. The organic layer was washed three times with water and dried over MgSO\textsubscript{4}. After evaporation of the solvent the residue was purified by column chromatography on silica gel afforded 6a as pale yellow solid in 98% yield.

\[\text{OMeHNO}\]

1H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.16 (br s, 1H), 7.10 – 7.05 (m, 1H), 7.04 – 7.00 (m, 1H), 4.52 – 4.46 (m, 1H), 3.77 (s, 3H), 3.48 (dd, \(J = 12.5, 6.7\) Hz, 2H), 3.44 – 3.37 (m, 1H), 3.22 (s, 1H), 3.07 (t, \(J = 6.8\) Hz, 2H), 1.34 (d, \(J = 6.8\) Hz, 6H), 1.10 (d, \(J = 6.7\) Hz, 6H); \(^{13}\)C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 163.34, 163.31, 157.43, 129.90, 127.35, 124.93, 123.24, 111.10, 81.88, 81.02, 55.45, 49.41, 46.20, 39.06, 27.39, 20.74, 19.94; HRMS (ESI-TOF) m/z [M+H]\textsuperscript{+} Calcd for C\textsubscript{19}H\textsubscript{27}N\textsubscript{2}O\textsubscript{3}: 331.2022; found: 331.2017.

9. Removal of the Directing Group\textsuperscript{[7]}

**Scheme 3S** Removal of the Directing Group.

A mixture of 3a (0.146 g, 0.3 mmol, 1.0 equiv) in THF (2 mL) was stirred for 10 min at -10 °C, NaH (60 %) (0.06 g, 2.5 mmol, 5.0 equiv) was slowly added, and then stirred for another 1 hour. NsCl (0.1 g, 7.5 mmol, 1.5 equiv) was added slowly for thirty minutes. The mixture was stirred over night at room temperature and heated at 60 °C for another 12 hours. The reaction mixture was cooled to rt, quenched with water (20 mL), extracted with CH\textsubscript{2}Cl\textsubscript{2} (10 mL \(\times\) 2). The combined organic phase was washed with brine (20 mL), dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}. Evaporation and column chromatography on silica gel afforded 7a as pale yellow solid in 73% yield.
1H NMR (400 MHz, CDCl₃) δ 8.11 (d, J = 8.9 Hz, 2H), 7.71 (d, J = 8.9 Hz, 2H), 7.09 (t, J = 8.0 Hz, 1H), 6.95 (dd, J = 7.7, 0.9 Hz, 1H), 5.02 (br s, 1H), 3.79 (s, 3H), 3.41 – 3.30 (m, 2H), 3.07 – 2.98 (m, 2H), 1.14 (d, J = 2.6 Hz, 18H), 1.06 (d, J = 6.2 Hz, 3H); 13C NMR (101 MHz, CDCl₃) δ 157.22, 145.43, 128.32, 127.93, 127.87, 125.60, 124.83, 124.03, 111.02, 104.84, 95.92, 55.90, 43.30, 27.32, 18.83, 11.42; HRMS (ESI-TOF) m/z [M+H]+ Calcd for C₂₆H₃₇N₂O₅SSi: 517.2192; found: 517.2187.

10. Synthesis of 3,4-Dihydroisoquinoline 8a

Scheme 4S Synthesis of 3,4-Dihydroisoquinoline 8a.

A mixture of 3a (0.146 g, 0.3 mmol, 1.0 equiv) and NaOH (0.06 g, 1.5 mmol, 5.0 equiv) in EtOH (2 mL) was stirred at 80 °C for 12 hours. The reaction mixture was cooled to rt, then some drops of water and CH₂Cl₂ (20 mL) were added. The organic layer was washed three times with water and dried over MgSO₄. After evaporation of the solvent the residue was purified by column chromatography on silica gel afforded 8a as pale yellow solid in 65% yield.

1H NMR (400 MHz, CDCl₃) δ 7.33 (t, J = 8.0 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 7.07 (d, J = 8.2 Hz, 1H), 3.87 (s, 3H), 3.76 – 3.71 (m, 2H), 2.85 – 2.80 (m, 2H), 2.61 (s, 3H); 13C NMR (101 MHz, CDCl₃) δ 156.08, 128.91, 127.89, 125.89, 119.18, 114.92, 55.89, 44.29, 29.84, 22.22, 18.71; HRMS (ESI-TOF) m/z [M+H]+ Calcd for C₁₁H₁₄NO: 176.1075; found: 176.1070.

11. Optimization of Protecting Group
Table 2S Optimization of Protecting Group

<table>
<thead>
<tr>
<th>PG = O</th>
<th>O</th>
<th>Ac</th>
<th>TI</th>
</tr>
</thead>
<tbody>
<tr>
<td>21%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

A variety of protecting group for γ-Arylpropamine had been tested: However none could give synthetic acceptable yield. It worth to note that the picolinamide assisted alkynylation gave a mixture of γ and ε-alkynylated products analyzed by proton NMR.

12. Alkynylation of different substituted bromoalkyne

Table 3S Alkynylation of different substituted bromoalkyne

We had tested the alkyl and aryl alkynyl bromide under standard condition. The alkyl alkynyl bromide (2a) gave the desired products in 46% isolated yield. Unfortunately, the aryl alkynyl bromide (2b) failed to give any alkynylated product, only starting material recovered.

\[ ^1H \text{NMR (400 MHz, CDCl}_3 \delta \]: 7.11 (d, J = 7.9 Hz, 1H), 7.08 (br s, 1H), 6.99 (dd, J = 7.7, 0.8 Hz, 1H), 6.78 (d, J = 7.9 Hz, 1H), 4.58 – 4.51 (m, 1H), 3.82 (s, 3H), 3.55 – 3.50 (m, 2H), 3.45 (dd, J = 13.6, 6.8 Hz, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.32 (s, 9H), 1.14 (d, J = 6.7 Hz, 6H); \[ ^{13}C \text{NMR (101 MHz, CDCl}_3 \delta \]: 163.47, 163.41, 157.52, 129.20, 127.31, 125.27, 124.52, 110.05, 102.79, 55.60, 49.55, 46.43, 39.62, 31.11, 28.28, 27.24, 20.95, 20.17; HRMS (ESI-TOF) m/z [M+H]^+: Calcd for C\textsubscript{22}H\textsubscript{35}N\textsubscript{2}O\textsubscript{3}: 387.2648; found: 387.2645.
13. Alkynylation of δ-Arylbutamine Derivatives

Scheme 5S Alkynylation of δ-Arylbutamine Derivatives.

We had tested the delta-amide (4j) under standard condition. However it failed to give any delta-position alkynylated product. In fact a mixture of γ and δ-alkynylated product was observed which was analyzed by proton NMR.

14. References

15. NMR spectra
$$\text{AcO} \begin{array}{c} \text{H} \\ \text{N} \left( \text{Pr} \right)_{2} \end{array}$$
$\text{Me}$

$\text{HN}$

$\text{O}$

$\text{N(Pr)}_2$

$\mathbf{1j}$
$4c$
\[
\text{O} \text{HNN} \text{(iPr)}_2 \text{NO}_2
\]
BBrNO(IPr)2OTIPS

3d
\[
\text{S71}
\]

\[
\text{HNON} \quad (iPr)_2
\]

\[
\text{TIPS}
\]

\[
3f_{\text{mono}}
\]
\[
\text{Cl} \quad \text{O} \quad \text{N(N(Pr)}_2 \quad \text{O}
\]

5c
Me
O
N
O
N\((\text{Pr})_2\)
TIPS
5d