Supporting Information

Three-Component Synthesis of Polysubstituted 6-Azaindolines and Its Tricyclic Derivatives

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Procedure for isocyanide synthesis (3a) et (3b)

To a solution of *N*-formylphenylalanine **6** (0.70 g, 3.65 mmol, 1.0 equiv.) and amine **7** (0.80 g, 3.65 mmol, 1.0 equiv.) in 7.0 mL of dry dichloromethane was added EDCI (4.02 mmol, 1.1 equiv.) at 0 °C and the reaction mixture was stirred for 6 h at room temperature. The reaction mixture was diluted with saturated ammonium chloride and extracted with dichloromethane. The organic layer was washed with brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash column chromatography on silica gel (eluent: Hept/EtOAc 1/2 then CH₂Cl₂/MeOH 10/1) to give the amide (**8a**).

Colorless oil, yield 70 %; IR (CHCl₃) ν 3418, 3027, 3004, 2952, 1720, 1685, 1641, 1496, 1438, 1330, 1283 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) two rotamers δ 2.08 (m, 1H), 2.20-2.36 (m, 1H), 2.97-3.15 (m, 2H), 3.27 (m, 1H), 3.45 (m, 1H), 3.64 (s, 3H), 4.16-4.36 (m, 1H), 4.70 (d, J = 14.6 Hz, 1H), 5.22 (m, 1H), 5.71 & 5.72 (dt, J = 15.6, 1.4 Hz, 1H), 6.64-6.85 (m, 1H), 6.90-7.29 (m, 10H), 8.10 (d, J = 6.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 30.1 & 31.2, 39.6 & 39.8, 45.1 & 45.4, 48.8 & 49.1, 49.2 & 51.2, 51.6, 122.8 & 123.5, 126.8 (2C), 127.1, 127.2, 127.7 & 128.2 (2C), 128.6 (2C), 129.4 & 129.5 (2C), 135.6 & 135.8, 135.9 & 136.0, 143.8 &

145.1, 160.3 & 160.4, 166.3 & 166.6, 171.5 & 171.6; MS (ESI, positive mode) m/z 417.1 $[M+Na]^+$.

A stirred solution of amide of *N*-formyl phenylalanine **8a** (0.83 g, 2.10 mmol, 1.0 equiv.) and triethylamine (1.46 mL, 10.49 mmol, 5.0 equiv.) in 10.0 mL of dry dichloromethane was cooled to - 40 °C. Phosphorus oxychloride (297.0 μ L, 3.15 mmol, 1.5 equiv.) was added dropwise and the reaction mixture was stirred for 3 h at - 40 °C. An aqueous saturated sodium carbonate solution was introduced dropwise so that the temperature of mixture was maintained at - 40 °C. The mixture was stirred for 0.5 h and raised to room temperature. The aqueous layer was separated and extracted with dichloromethane. The organic extracts were combined, washed with brine and dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: Hept/EtOAc 2/1) to provide the isocyanide (**3a**).

Orange oil, yield 83 %; IR ($CHCl_3$) ν 3066, 3003, 2952, 2141, 1721, 1666, 1496, 1437, 1330, 1283, 1179 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) two rotamers δ 2.21-2.49 (m, 2H), 3.13-3.58 (m, 4H), 3.74 (s, 3H), 4.32 (d, J = 17.6 Hz, 1H), 4.44-4.62 (m, 2H), 5.77 & 5.84 (dt, J = 15.6, 1.3 Hz, 1H), 6.70-6.90 (m, 1H), 6.98 -7.32 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.1 & 31.1, 39.2 & 39.3, 45.5 & 46.3, 49.3 & 51.6, 51.7, 53.4 & 55.2, 123.2 & 124.1, 126.0 (2C), 127.9 & 128.0, 128.2, 128.8 & 128.8 (2C), 128.9 (4C), 134.9 & 135.1, 136.0, 142.9 & 144.6, 159.5 & 159.8, 165.0 & 165.4, 166.1 & 166.5; MS (ESI, positive mode) m/z 399.0 $[M+Na]^+$; *Anal. calcd. for* $C_{23}H_{24}N_2O_3$: %C 73.38 %H 6.43 %N 7.44, *found*: %C 72.79 %H 6.47 %N 7.32.

To a solution of *N*-formylphenylglycine (820.0 mg, 4.57 mmol, 1.2 equiv.) and triethylamine (634.0 μ L, 4.57 mmol, 1.2 equiv.) in 20.0 mL of dry THF was slowly added ethyl chloroformate (435.0 μ L, 4.57 mmol, 1.2 equiv.) at - 30 $^{\circ}$ C and the reaction mixture was stirred for 30 min. A solution of 5-benzylamino-pentene (613.0 mg, 3.81 mmol, 1.0 equiv.) and triethylamine (530.0 μ L, 3.81 mmol, 1.0 equiv.) in dry THF (5.0 mL) were added. The reaction mixture was stirred for 5 h at room temperature. The reaction mixture was diluted with saturated ammonium chloride and extracted with dichloromethane. The organic layer was washed with brine and water, dried over anhydrous sodium sulfate and concentrated. The residue was purified by flash column chromatography on silica gel (eluent: Hept/EtOAc 8/1 then 2/1) to give the amide (**8b**).

Yellow oil, yield 53 %; IR (CHCl_3) ν 3400, 3068, 3003, 2883, 1682, 1643, 1495, 1451 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) two rotamers δ 1.83 & 2.20-2.27 (m, 2H), 3.10-3.17 & 3.14 & 3.30 (m, 2H), 4.23 & 4.56 (d, J = 16.6 Hz, 1H), 4.52 & 4.78 (d, J = 15.0 Hz, 1H), 4.94-5.03 (m, 2H), 5.57 & 5.69 (m, 1H), 5.93 & 6.00 (d, J = 7.5 Hz, 1H), 6.97-7.45 (m, 10H), 8.17 (d, J = 7.9 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.5 & 32.2, 45.5 & 46.1, 48.7 & 50.8, 52.8 & 52.9, 117.1 & 117.9, 126.8-129.1, 133.6 & 134.8, 135.3 & 136.6, 137.2 & 137.3, 159.8 & 159.9, 169.5; MS (ESI, positive mode) m/z 345.1 $[\text{M}+\text{Na}]^+$.

Same procedure as for **3a**.

White oil, yield 87 %; IR (CHCl_3) ν 3069, 3003, 2934, 2148, 1670, 1496, 1453 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) two rotamers δ 2.12 (m, 1H), 2.30 (m, 1H), 3.16-3.34 (m, 1H), 3.66 (m, 1H), 4.43 (m, 1H), 4.54 (d, J = 14.9 Hz, 1H), 4.74 (d, J = 14.9 Hz, 1H), 4.97-5.20 (m, 2H), 5.51-5.78 (m, 1H), 7.04 -7.47 (m, 10H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.7 & 32.2, 46.1 & 46.8, 48.9 & 51.2, 59.6, 117.4 & 118.3, 126.2-126.9, 132.6 & 133.3, 134.6 & 135.3, 136.3, 164.7 & 164.9; MS (ESI, positive mode) m/z 327.1 $[\text{M}+\text{Na}]^+$.

General procedure for the three-component synthesis of azaindolines (1) and its tricyclic derivatives (2)

A solution of amine (1.25 equiv.), aldehyde (1.25 equiv.) and α -isocyanoacetamide **3** (1.0 equiv.) in dry toluene (0.1 M) was stirred at room temperature for 1 h. The reaction mixture was heated to reflux and was monitored by TLC (typically 15 h). The reaction mixture was cooled to room temperature and toluene was removed under reduce pressure. The crude was purified by preparative TLC or flash column chromatography (silica gel, eluent Hept/AcOEt).

Yellow oil, yield 61 %; IR (CHCl₃) ν 2928, 2857, 1720, 1565, 1494, 1452, 1422, 1356, 1285, 1114 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.85 (t, J = 6.7 Hz, 3H), 1.23 (m, 8H), 1.70 (m, 1H), 2.08 (m, 1H), 2.38-2.53 (m, 4H), 2.90-3.19 (m, 2H), 3.32-3.39 (m, 2H), 3.60 (m, 4H), 3.87 (s, 3H), 3.90 (m, 1H), 4.15 (s, 2H), 4.31 (s, 2H), 7.07-7.33 (m, 10H); ¹³C NMR (75 MHz, MeOD) δ 14.5, 23.7, 28.1, 29.3, 30.3, 30.7, 33.0, 41.7, 51.4 (2C), 52.5, 54.5, 56.4, 67.6, 68.0 (2C), 126.3, 127.2, 128.2, 128.3 (2C), 129.4 (2C), 129.5 (2C), 129.6 (2C), 140.1, 141.1, 141.7, 142.2, 147.3, 148.9, 169.9; MS (IE) m/z 455.0 [M-C₄H₈NO]⁺; MS (ESI, positive mode) m/z 455.1 [M-C₄H₈NO]⁺, 542.2 [M+1]⁺, 564.2 [M+Na]⁺; HRMS m/z calcd. for: [M+1]⁺ 542.3383, m/z found: 542.3384.

Yellow oil, yield 70 %; IR (CHCl₃) ν 2933, 2855, 1719, 1566, 1494, 1452, 1357, 1261 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.84 (t, J = 6.7 Hz, 3H), 1.22-1.36 (m, 8H), 1.45 (m, 6H), 1.63 (m, 1H), 2.08 (m, 1H), 2.37 (m, 4H), 2.94 (m, 1H), 3.14 (m, 1H), 3.33 (m, 2H), 3.87 (s, 3H), 3.90 (m, 1H), 4.16 (s, 2H), 4.27 (d, J = 15.7 Hz, 1H), 4.35 (d, J = 15.7 Hz, 1H), 7.10-7.34 (m, 10H); ¹³C NMR (75 MHz, CDCl₃) δ 14.1, 22.7 (2C), 24.7, 25.8, 27.7, 28.2, 29.4, 29.7, 31.7 (2C), 41.0, 50.1, 71.7, 53.6, 55.8, 66.3, 124.6, 125.9, 127.1, 127.2 (2C), 128.3 (2C), 128.5, 128.6 (2C), 129.4 (2C), 138.9, 139.6, 140.0, 140.3, 145.4, 168.9; MS (ESI, positive mode) m/z 455.2 [M-C₄H₈NO]⁺, 540.3 [M+H]⁺; HRMS m/z calcd. for: [M+1]⁺ 540.3590, m/z found: 540.3579.

Yellow oil, yield 60 %; IR (CHCl₃) ν 2954, 2860, 1720, 1604, 1562, 1518, 1494, 1452, 1347, 1284, 1115 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.32-2.44 (m, 4H), 3.01 (m, 1H), 3.16 (m, 1H), 3.36-3.43 (m, 2H), 3.67 (m, 4H), 3.97 (s, 3H), 4.11 (s, 2H), 4.35 (s, 2H), 5.03 (s, 1H), 7.01 (m, 2H), 7.17-7.34 (m, 8H), 7.70 (d, J = 8.8 Hz, 2H), 8.10 (d, J = 8.8 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 27.8, 39.9, 50.8 (2C), 51.4, 52.6, 54.5, 66.2 (2C), 70.1, 122.0 (2C), 123.2, 125.3, 126.1 (2C), 126.4, 127.5 (2C), 127.7 (2C), 127.8 (2C), 129.5 (2C), 137.6, 138.4, 139.5, 140.8, 144.6, 145.1, 146.0, 147.0, 167.3; MS (ESI, positive mode) m/z 492.2 [M-C₄H₈NO]⁺, 579.3 [M+H]⁺; HRMS m/z calcd. for: [M+1]⁺ 579.2607, m/z found: 579.2631.

Yellow oil, yield 43 %; IR (CHCl₃) ν 3004, 2954, 2837, 1720, 1609, 1510, 1494, 1452, 1421, 1357, 1255, 1115 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.34-2.46 (m, 4H), 2.91-3.13 (m, 2H), 3.30-3.37 (m, 2H), 3.67 (m, 4H), 3.78 (s, 3H), 3.91 (s, 3H), 4.16 (s, 2H), 4.30 (s, 2H), 4.76 (s, 1H), 6.80 (d, J = 8.7, 2H), 7.05-7.33 (m, 10H), 7.44 (d, J = 8.7, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 28.4, 41.0, 52.0 (3C), 53.5, 55.2, 55.5, 67.0 (2C), 71.9, 113.1 (2C), 123.9, 126.0, 127.1 (2C), 127.2, 128.3 (2C), 128.6 (4C), 130.9 (2C), 131.5, 138.7, 139.7, 140.2, 141.4, 145.6, 147.7, 158.6, 168.5; MS (ESI, positive mode) m/z 477.3 [M-C₄H₈NO]⁺; HRMS m/z *calcd. for*: [M-C₄H₈NO]⁺ 477.2178, m/z *found*: 477.2158.

Yellow oil, yield 53 %; IR (CHCl₃) ν 3032, 3003, 2967, 1720, 1563, 1494, 1452, 1357, 1283, 1115 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.44-2.56 (m, 4H), 3.05-3.17 (m, 2H), 3.38-3.46 (m, 2H), 3.74-3.79 (m, 4H), 4.01 (s, 3H), 4.24 (s, 2H), 4.38 (s, 2H), 4.92 (s, 1H), 7.12-7.40 (m, 13H), 7.61 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 28.6, 41.1, 52.2 (3C), 53.6, 55.7, 67.1 (2C), 72.6, 124.1, 126.2, 127.2, 127.3, 127.9 (2C), 128.2 (2C), 128.6 (2C), 128.7 (2C), 129.0 (2C), 130.2 (2C), 138.8, 139.7, 139.8, 140.3, 141.6, 145.8, 147.4, 168.6; MS (ESI, positive mode) m/z 447.1 [M-C₄H₈NO]⁺, 534.3 [M+H]⁺, 556.3 [M+Na]⁺; HRMS m/z *calcd. for*: [M+1]⁺ 534.2757, m/z *found*: 534.2744.

Yellow oil, yield 37 %; IR (CHCl₃) ν 3003, 2954, 2859, 1720, 1567, 1494, 1452, 1422, 1358, 1281, 1115 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.29-2.44 (m, 4H), 2.90-3.14 (m, 2H), 2.35-3.41 (m, 2H), 3.64 (m, 4H), 3.92 (s, 3H), 4.07 (d, J = 15.8 Hz, 1H), 4.15 (d, J = 15.8 Hz, 1H), 4.25 (d, J = 15.4 Hz, 1H), 4.34 (d, J = 15.4 Hz, 1H), 4.81 (s, 1H), 7.02-7.44 (m, 13H), 7.72 (t, J = 1.7 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 29.7, 41.6, 53.0 (2C), 53.3, 54.7, 56.6, 68.2 (2C), 72.8, 123.1, 125.1, 127.2, 128.3 (2C), 128.4, 129.6 (2C), 129.7 (2C), 129.9 (3C), 130.5, 131.2, 133.7, 139.8, 140.7, 141.4, 142.8, 143.3, 147.0, 147.6, 169.4; MS (ESI, positive mode) m/z 525.1 [⁷⁹BrM-C₄H₈NO]⁺, 527.1 [⁸¹BrM-C₄H₈NO]⁺; HRMS m/z calcd. for: [⁷⁹BrM-C₄H₈NO]⁺ 525.1178, m/z found: 525.1150; m/z calcd. for: [⁸¹BrM-C₄H₈NO]⁺ 527.1157, m/z found: 527.1138.

Yellow oil, yield 54 %; IR (CHCl₃) ν 2929, 2855, 2233, 1715, 1563, 1495, 1453, 1367, 1261 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.88 (t, J = 6.5 Hz, 3H), 1.27 (m, 8H), 1.30 (t, J = 7.3 Hz, 3H), 1.77 (m, 1H), 2.09 (m, 1H), 2.18-2.33 (m, 2H), 2.61 (m, 1H), 2.86-3.02 (m, 3H), 3.20-3.41 (m, 2H), 3.45 (d, J = 14.4 Hz, 1H), 3.73 (d, J = 14.4 Hz, 1H), 3.75 (s, 3H), 4.17 (s, 2H), 4.20 (q, J = 7.3 Hz, 2H), 4.31 (d, J = 15.6 Hz, 1H), 4.34 (m, 1H), 4.41 (d, J = 15.6 Hz, 1H), 7.11-7.37 (m, 15H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 14.2, 19.1, 22.6, 26.9, 28.8,

29.1, 29.5, 31.8, 41.1, 48.7, 51.7, 53.5, 55.1, 55.8, 60.5, 61.6, 73.4, 88.6, 116.6, 123.9, 126.0, 126.5, 127.1, 127.2 (2C), 128.3 (2C), 128.4 (2C), 128.5 (2C), 128.6 (2C), 129.1 (2C), 138.7, 139.7, 140.6, 140.8, 145.5, 149.1, 153.8, 168.3; MS (ESI, positive mode) m/z 455.2 $[M-C_{14}H_{16}NO_2]^+$, 686.5 $[M+H]^+$; HRMS m/z *calcd. for*: $[M+1]^+$ 686.3958, m/z *found*: 686.3956.

Same procedure as before but with *o*-xylene as solvent.

Yellow oil, yield 52 %; IR (CHCl₃) ν 3038, 3005, 3014, 2971, 2859, 1521, 1453, 1427, 1347, 1116 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.49 (m, 4H), 2.99 (t, J = 8.6 Hz, 2H), 3.18-3.22 (m, 2H), 3.77 (m, 4H), 3.80 (d, J = 14.8 Hz, 1H), 3.97 (d, J = 14.8 Hz, 1H), 4.65 (s, 1H), 7.13-7.38 (m, 9H), 7.69 (d, J = 6.8 Hz, 2H), 7.76 (d, J = 8.8 Hz, 2H), 8.18 (d, J = 8.8 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 28.4, 52.3 (2C), 53.5, 55.7, 67.1 (2C), 76.9, 117.0, 123.8 (2C), 127.0, 127.6 (2C), 127.8, 128.0 (2C), 128.3 (2C), 128.3 (2C), 128.8 (2C), 138.1, 139.6, 140.5, 142.6, 146.0, 146.9, 149.6, 150.3; MS (ESI, positive mode) m/z 420.1 $[M-C_4H_8NO]^+$, 529.2 $[M+Na]^+$; HRMS m/z *calcd. for*: $[M+Na]^+$ 529.2216, m/z *found*: 529.2233.

Same procedure as before but with *o*-xylene as solvent.

Yellow oil, yield 67 %; IR (CHCl₃) ν 2930, 2859, 1453, 1429, 1262, 1114 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.86 (t, J = 6.7 Hz, 3H), 1.22-1.25 (m, 9H), 1.88 (m, 1H), 2.48-2.64 (m, 4H), 3.00 (t, J = 8.5 Hz, 2H), 3.31 (m, 2H), 3.54 (t, J = 7.0 Hz, 1H), 3.72 (m, 4H), 3.90 (d, J = 14.8 Hz, 1H), 3.97 (d, J = 14.8 Hz, 1H), 7.02 (s, 1H), 7.17-7.38 (m, 8H), 7.77 (d, J = 8.3 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 14.1, 22.6, 26.2, 28.5, 29.5, 31.5, 31.8, 50.7 (2C), 53.5, 56.1, 67.5 (2C), 70.7, 117.7, 126.9, 127.7 (2C), 127.8 (2C), 128.2, 128.3 (2C), 128.6 (2C), 138.4, 140.1, 140.3, 141.8, 145.6, 151.5; MS (ESI, positive mode) m/z 383.2 [M-C₄H₈NO]⁺, 470.3 [M+H]⁺; HRMS m/z calcd. for: [M+1]⁺ 470.3171, m/z found: 470.3161. Anal. calcd. for C₂₃H₂₄N₂O₃: % C 79.28 % H 8.95 % N 8.37 found: % C 78.96 % H 8.79 % N 8.12;

Yellow oil, yield 54 %; IR (CHCl₃) ν 2931, 2861, 1671, 1494, 1453, 1422, 1403, 1357 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.81 (t, J = 6.7 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H), 1.16-1.25 (m, 8H), 1.36 (sext, J = 7.2 Hz, 2H), 1.53-1.65 (m, 2H), 1.86 (m, 1H), 2.14 (m, 1H), 3.06 (m, 1H), 3.28-3.48 (m, 4H), 3.99 (m, 1H), 4.21 (s, 2H), 4.24 (d, J = 15.8 Hz, 1H), 4.32 (d, J = 15.8 Hz, 1H), 4.52 (m, 1H), 7.06-7.30 (m, 10H); ¹³C NMR (75 MHz, CDCl₃) δ 13.9, 14.2, 20.3, 22.4, 22.7, 26.8, 29.3, 29.8, 30.6, 31.8, 39.4, 41.2, 54.6, 56.1, 60.3, 121.5, 126.3, 127.3 (3C), 128.4 (2C), 128.6 (2C), 128.7 (2C), 138.3, 139.0, 139.7, 143.5, 148.3, 155.8, 167.7; MS (ESI, positive mode) m/z 496.4 [M+H]⁺; HRMS m/z calcd. for: [M+1]⁺ 496.3328, m/z found: 496.3318.

Yellow oil, yield 46 %; IR (CHCl₃) ν 2930, 2859, 1674, 1495, 1453, 1421, 1401, 1357 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.77 (t, J = 6.7 Hz, 3H), 1.06-1.20 (m, 8H), 1.80 (m, 1H), 2.06 (m, 1H), 3.27-3.44 (m, 4H), 4.10 (d, J = 15.0 Hz, 1H), 4.14 (s, 2H), 4.20 (d, J = 15.8 Hz, 1H), 4.28 (d, J = 15.8 Hz, 1H), 4.31 (dd, J = 5.0, 3.1 Hz, 1H), 5.23 (d, J = 15.0 Hz, 1H), 6.99-7.28 (m, 15H); ¹³C NMR (75 MHz, CDCl₃) δ 14.2, 22.3, 22.6, 26.9, 29.3, 29.5, 31.7, 41.2, 43.8, 54.6, 56.1, 60.2, 121.1, 126.3, 127.2, 127.3 (2C), 127.7, 128.3 (2C), 128.4 (2C), 128.6 (2C), 128.7 (2C), 128.8 (2C), 137.3, 138.5, 138.9, 139.6, 143.8, 148.3, 155.8, 167.8; MS (ESI, positive mode) m/z 530.4 [M+H]⁺, 552.3 [M+Na]⁺; HRMS m/z *calcd. for*: [M+1]⁺ 530.3171, m/z *found*: 530.3157.

Yellow oil, yield 63 %; IR (CHCl₃) ν 3006, 2929, 2859, 1683, 1598, 1495, 1453, 1388 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.77 (t, J = 6.7 Hz, 3H), 1.04-1.16 (m, 8H), 1.85 (m, 1H), 2.11 (m, 1H), 3.34-3.55 (m, 4H), 4.77 (s, 2H), 4.29 (d, J = 15.8 Hz, 1H), 4.37 (d, J = 15.8 Hz, 1H), 5.21 (dd, J = 5.4, 3.0 Hz, 1H), 7.19-7.36 (m, 11H), 7.44 (t, J = 7.6 Hz, 2H), 7.98 (d, J = 7.6 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 22.3, 22.5, 26.9, 29.1, 30.1, 31.6, 41.3, 54.6, 56.0, 62.0, 121.3, 123.4 (2C), 125.4, 126.4, 127.3 (2C), 127.4, 128.4 (2C), 128.6 (2C), 128.7 (2C), 129.1 (2C), 132.2, 138.9, 138.9, 139.5, 144.4, 148.6, 155.1, 166.6; MS (ESI, positive mode) m/z 516.3 [M+H]⁺, 538.3 [M+Na]⁺; HRMS m/z *calcd. for*: [M+1]⁺ 516.3015, m/z *found*: 516.3005.

Yellow oil, yield 41 %; IR (CHCl₃) ν 3017, 2930, 2855, 1683, 1598, 1495, 1451, 1391, 1358 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.41 (m, 1H), 0.91-1.21 (m, 4H), 1.51-1.73 (m, 4H), 1.92 (m, 2H), 3.35-3.55 (m, 4H), 4.28 (s, 2H), 4.31 (d, J = 15.7 Hz, 1H), 4.43 (d, J = 15.7 Hz, 1H), 5.03 (s, 1H), 7.17-7.56 (m, 15H); ¹³C NMR (75 MHz, CDCl₃) δ 26.0, 26.4, 26.6, 26.7, 26.9, 28.7, 39.9, 41.2, 54.6, 56.3, 66.8, 121.5, 124.3 (2C), 125.8, 126.5, 127.4 (2C), 127.5, 128.7, 128.7, 128.8 (4C), 129.2 (4C), 137.5, 138.8, 139.5, 149.4, 155.5, 167.8; MS (ESI, positive mode) m/z 514.4 [M+H]⁺; HRMS m/z *calcd. for*: [M+1]⁺ 514.2858, m/z *found*: 514.2857; m/z *calcd. for*: [M+Na]⁺ 536.2678, m/z *found*: 536.2688.

Yellow oil, yield 44 %; IR (CHCl₃) ν 3003, 2933, 2859, 1672, 1515, 1454, 1421, 1403, 1357, 1262 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.82 (t, J = 6.7 Hz, 3H), 1.17-1.24 (m, 8H), 1.85 (m, 1H), 2.11 (m, 1H), 2.91 (m, 2H), 3.30 (m, 3H), 3.44 (m, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 4.22 (s, 2H), 4.22 (m, 1H), 4.25 (d, J = 15.7 Hz, 1H), 4.34 (d, J = 15.7 Hz, 1H), 4.40 (m, 1H), 6.78 (m, 2H), 7.02 (d, J = 8.1 Hz, 1H), 7.14-7.32 (m, 10H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 22.3, 22.5, 26.6, 29.2, 29.7, 31.6, 34.3, 41.0, 41.4, 54.5, 55.9 (3C), 60.7, 111.3, 111.8,

120.6, 121.2, 126.2, 127.1 (2C), 127.2, 128.2 (2C), 128.5 (2C), 128.6 (2C), 131.3, 138.2, 138.8, 139.4, 143.4, 147.6, 148.1, 148.9, 155.5, 167.6; MS (ESI, positive mode) m/z : 604.4 $[M+H]^+$, 626.4 $[M+Na]^+$; HRMS m/z *calcd. for*: $[M+1]^+$ 604.3539, m/z *found*: 604.3535; m/z *calcd. for*: $[M+Na]^+$ 626.3359, m/z *found*: 626.3379.

Procedure for the synthesis of amino-oxazole (9a)

A solution of morpholine (1.2 equiv.), heptanal (1.2 equiv.) and α -isocyanoacetamide **3a** (1.0 equiv.) in dry MeOH (0.1 M) was stirred at room temperature for 2 h. The reaction mixture was heated to reflux and was monitored by TLC (typically 15 h). MeOH was removed under reduce pressure. The crude was purified by column (silica gel, eluent Hept/AcOEt 2/1).

Yellow oil, yield 88 %; IR (CHCl_3) ν 2928, 2858, 1719, 1494, 1453, 1265, 1115 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 0.90 (d, J = 6.7 Hz, 3H), 1.23-1.31 (m, 8H), 1.86 (m, 2H), 2.26 (m, 2H), 2.40-2.53 (m, 4H), 3.09 (t, J = 7.2 Hz, 2H), 3.57 (m, 1H), 3.69 (s, 2H), 3.69-3.76 (m, 4H), 3.72 (s, 3H), 4.09 (s, 2H), 5.78 (d, J = 15.7 Hz, 1H), 6.88 (dt, J = 15.7, 7.0 Hz, 1H), 7.06-7.29 (m, 10H); ^{13}C NMR (75 MHz, CDCl_3) δ 14.2, 22.7, 26.4, 29.1, 30.1, 31.0, 31.4, 31.8, 50.4 (2C), 51.5, 51.9, 59.0, 63.5, 67.4 (2C), 122.4, 126.1, 127.7, 128.4 (2C), 128.5, 128.5 (2C), 129.0 (2C), 129.6 (2C), 137.4, 139.3, 146.3, 150.4, 159.0, 166.8; MS (EI) m/z 473.0 $[M-\text{C}_4\text{H}_8\text{NO}]^+$, 474.0 $[M-\text{C}_6\text{H}_{13}]^+$, 560.1 $[M+H]^+$; MS (ESI, positive mode) m/z 473.2 $[M-\text{C}_4\text{H}_8\text{NO}]^+$, 582.2 $[M+Na]^+$.

Procedure for the synthesis of (13)

Product **1a** (50.0 mg, 0.092 mmol) was dissolved in EtOH (1.0 mL) and 10 % (mass) of Pd(OH)₂ was added. The mixture was stirred under H₂ atmosphere for 72 h at room temperature. After celite filtration, washing with EtOH and evaporation of the solvent in vacuo, the residue was purified by preparative TLC (silica gel, eluent AcOEt).

Yellow oil, yield 83 %; IR (CHCl₃) ν 2955, 2858, 1719, 1590, 1494, 1445, 1261, 1114 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.88 (dt J = 6.8 Hz, 3H), 1.19-1.35 (m, 8H), 1.75 (m, 1H), 2.15 (m, 1H), 2.40-2.60 (m, 4H), 2.98-3.22 (m, 2H), 3.52 (m, 2H), 3.64 (m, 4H), 3.90 (s, 3H), 3.95 (m, 1H), 4.06 (s, 2H), 7.23-7.30 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 13.1, 21.6, 26.2, 27.6, 28.7 (3C), 30.8, 40.0, 45.8, 49.0, 50.8, 65.4, 66.4 (2C), 123.6, 125.4, 127.6 (2C), 127.7 (2C), 137.3, 137.5, 140.1, 143.7, 147.8, 167.8; MS (ESI, positive mode) m/z 365.1 [M-C₄H₈NO]⁺, 542.2 [M+H]⁺, 474.2 [M+Na]⁺; HRMS m/z *calcd. for*: [M+Na]⁺ 474.2733, m/z *found*: 474.2691.