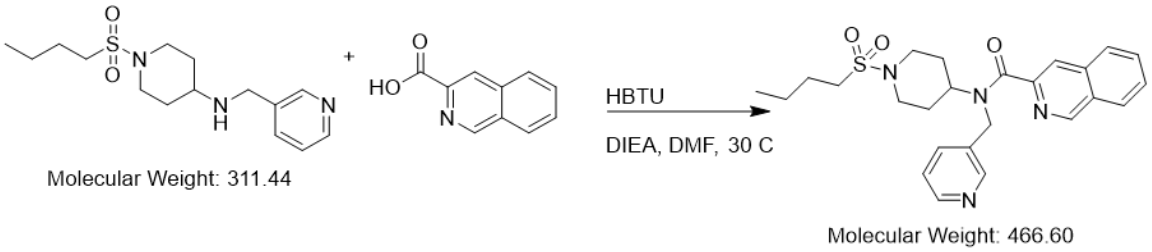
Kristen Begley Chemistry Section

KLB_NB01_012



Molecular Weight: 311.44

Molecular Weight: 466.60

To a mixture of KLB_NB01_011 (0.150 g, 0.48 mmol, 1. Equiv.), HBTU (0.220 g, 0.58 mmol, 1.2 equiv.), and DIEA (0.125 mL, 0.72 mmol, 1.5 equiv.) in DMF (3.0 mL) was added isoquinoline carboxylic acid (0.083 g, 0.48 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with methanol and dichloromethane.

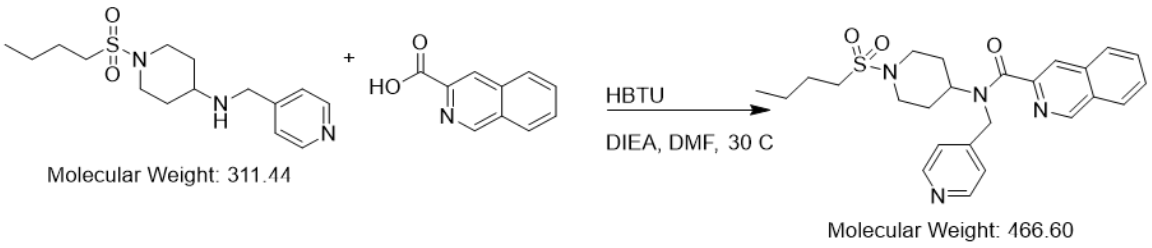
Yellow oil/solid (57.48 mg, 26%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ ^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.23 (s, 0.55H), 9.10 (s, 0.45H), 8.73 – 8.37 (m, 2H), 8.20 – 7.61 (m, 6H), 7.26 (m, 1H), 4.83 (d, *J* = 35.0 Hz, 2H), 4.66 (m, 0.45H), 4.19 (m, 0.55H), 3.84 (dd, *J* = 56.9, 12.3 Hz, 2H), 2.94 – 2.77 (m, 3H), 2.55 (t, *J* = 12.2 Hz, 1H), 2.04 – 1.64 (m, 6H), 1.48 – 1.33 (m, 2H), 1.01 – 0.82 (m, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 170.2, 170.0, 151.4, 151.2, 148.8, 148.7, 148.6, 148.1, 148.0, 136.1, 136.0, 135.1, 135.0, 134.4, 131.3, 131.2, 129.0, 128.8, 127.7, 127.6, 123.6, 123.3, 122.0, 121.8, 56.9, 53.5, 49.7, 47.1, 45.9, 45.6, 43.3, 31.3, 29.9, 25.2, 25.1, 21.8, 21.8, 13.7.

LC/MS (ESI) 467.53 *m/z* $[M+H]^+$

KLB_NB01_013



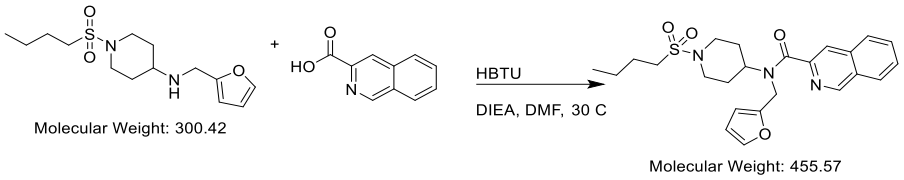
To a mixture of KLB_NB01_009 (0.150 g, 0.48 mmol, 1. Equiv.), HBTU (0.220 g, 0.48 mmol, 1.2 equiv.), and DIEA (0.125 mL, 0.72 mmol, 1.5 equiv.) in DMF (3.0 mL) was added isoquinoline carboxylic acid (0.083 g, 0.48 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with methanol and dichloromethane.

Yellow oil, (42.76 mg, 20%) There was a loss of product during purification.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.25 (s, 0.6H), 9.06 (s, 0.4H), 8.52 (dd, *J* = 46.5, 4.2 Hz, 2H), 8.20 – 7.61 (m, 5H), 7.26 (dd, *J* = 46.2, 4.9 Hz, 2H), 4.88 (s, 1H), 4.77 (m, 1.4H), 4.24 (t, *J* = 12.4 Hz, 0.6H), 3.85 (dd, *J* = 39.4, 12.1 Hz, 2H), 2.98 – 2.72 (m, 3H), 2.57 (t, *J* = 12.2 Hz, 1H), 2.14 – 1.63 (m, 6H), 1.42 (m, 2H), 0.93 (m, 3H).

LC/MS (ESI) 467.45 *m/z* $[M+H]^+$

KLB_NB01_017



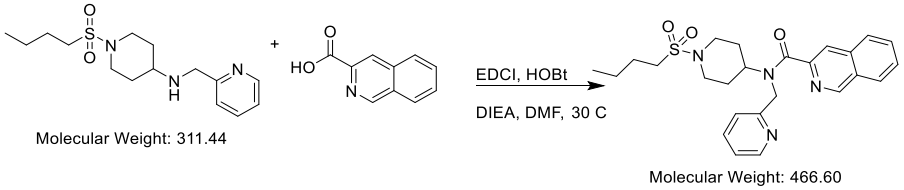
To a mixture of KLB_NB01_016 (0.276 g, 0.92 mmol, 1. Equiv.), HBTU (0.419 g, 1.10 mmol, 1.2 equiv.), and DIEA (0.240 mL, 1.38 mmol, 1.5 equiv.) in DMF (6.0 mL) was added isoquinoline carboxylic acid (0.159 g, 0.92 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with methanol and dichloromethane then again with ethyl acetate and hexanes.

Yellow oily solid, 223.96 mg, 53 %

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.21 (s, 1H), 8.16 – 7.61 (m, 5H), 7.29 (m, 1H), 6.38 (d, *J* = 30.0 Hz, 1H), 6.03 (d, *J* = 97.5 Hz, 1H), 4.75 (m, 2H), 4.63 (t, *J* = 11.5 Hz, 0.6H), 4.08 (m, 0.4H), 3.99 – 3.72 (m, 2H), 2.87 (m, 3H), 2.55 (m, 1H), 2.04 – 1.64 (m, 6H), 1.53 – 1.32 (m, 2H), 1.05 – 0.84 (m, 3H).

LC/MS (ESI) 456.58 *m/z* $[M+H]^+$

KLB_NB01_019



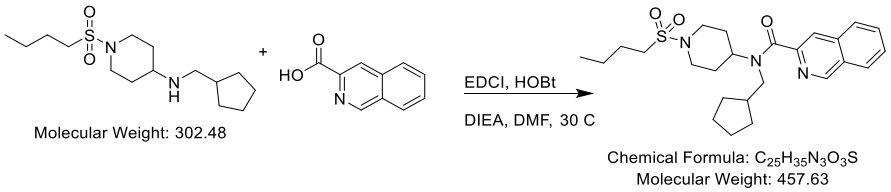
To a mixture of KLB_NB01_018 (0.200 g, 0.64 mmol, 1 Equiv.), EDCI (0.147 g, 0.77 mmol, 1.2 equiv.), HOBt (0.118 g, 0.77 mmol, 1.2 equiv.), and DIEA (0.167 mL, 0.96

mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.111 g, 0.64 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate.

Yellow oil/solid (152.85 mg, 51%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 (d, *J* = 55.0 Hz, 1H), 8.50 (dd, *J* = 41.9, 4.8 Hz, 1H), 8.12 (d, *J* = 21.2 Hz, 1H), 8.00 (dd, *J* = 43.9, 8.1 Hz, 2H), 7.68 (m, 4H), 7.42 (dd, *J* = 55.8, 7.8 Hz, 1H), 7.14 (dt, *J* = 34.8, 6.3 Hz, 1H), 4.91 (s, 2H), 4.71 (t, *J* = 12.0 Hz, 0.55H), 4.18 - 4.10 (m, 0.45H), 3.81 (dd, *J* = 41.1, 12.3 Hz, 2H), 2.85 (dt, *J* = 34.7, 8.2 Hz, 3H), 2.55 (t, *J* = 12.2 Hz, 1H), 2.01 – 1.65 (m, 6H), 1.42 (dq, *J* = 22.7, 7.5 Hz, 2H), 0.93 (dt, *J* = 18.3, 7.3 Hz, 3H).

KLB_NB01_034



Molecular Weight: 302.48

Chemical Formula: $C_{25}H_{35}N_3O_3S$
Molecular Weight: 457.63

To a mixture of KLB_NB01_033 (0.151 g, 0.50 mmol, 1 Equiv.), EDCI (0.115 g, 0.60 mmol, 1.2 equiv.), HOBt (0.092 g, 0.60 mmol, 1.2 equiv.), and DIEA (0.131 mL, 0.75 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.087 g, 0.50 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate.

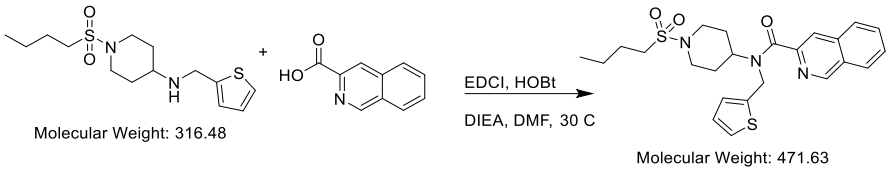
Yellow oil (122.49 mg, 54%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.20 (s, 1H), 8.05 – 7.86 (m, 3H), 7.72 (dddd, *J* = 28.2, 8.1, 6.9, 1.2 Hz, 2H), 4.37 (s, 1H), 3.90 (d, *J* = 51.7 Hz, 3H), 3.51 (dd, *J* = 18.2, 12.5 Hz, 2H), 3.19 – 2.78 (m, 4H), 2.46 (d, *J* = 46.5 Hz, 1H), 2.19 – 1.62 (m, 11H), 1.51 – 1.20 (m, 6H), 0.93 (dd, *J* = 14.0, 7.0 Hz, 5H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 170.3, 170.0, 151.2, 149.1, 136.0, 131.0, 128.6, 128.4, 127.6, 127.3, 121.1, 120.9, 66.1, 56.5, 54.1, 50.5, 49.6, 49.4, 46.7, 46.0, 45.7, 42.8, 40.5, 40..2, 33.8, 31.1, 31.1, 30.1, 29.7, 25.1, 25.0, 24.8, 24.6, 21.8, 13.6.

LC/MS (ESI) 458.65 *m/z* $[M+H]^{+}$

KLB_NB01_042



Molecular Weight: 316.48

Molecular Weight: 471.63

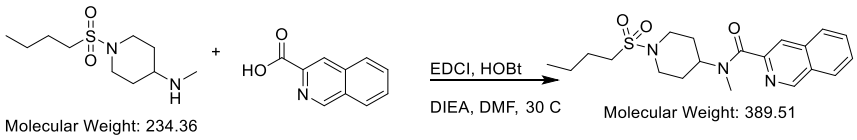
To a mixture of KLB_NB01_041 (0.158 g, 0.50 mmol, 1 Equiv.), EDCI (0.115 g, 0.60 mmol, 1.2 equiv.), HOBt (0.092 g, 0.60 mmol, 1.2 equiv.), and DIEA (0.131 mL, 0.75 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.087 g, 0.50 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate. MPLC was performed again with ethyl acetate: hexanes (50-100%).

Yellow/white solid (131.25 mg, 56%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.21 (s, 1H), 8.20 – 7.96 (m, 2H), 7.90 (dd, *J* = 23.9, 8.2 Hz, 1H), 7.84 – 7.64 (m, 2H), 7.23 – 7.07 (m, 1H), 6.99 – 6.85 (m, 1H), 6.79-6.77 (m, 1H), 4.94 (d, *J* = 34.4 Hz, 2H), 4.91-4.89 (m, 0.5H), 4.04-4.03 (m, 0.5H), 3.93 – 3.68 (m, 2H), 2.93 – 2.68 (m, 3H), 2.54 (t, *J* = 11.5 Hz, 1H), 2.02 – 1.89 (m, 4H), 1.85 – 1.68 (m, 2H), 1.51 – 1.37 (m, 2H), 1.01 – 0.83 (m, 3H).

LC/MS (ESI) *m/z* $[M+H]^+$ 472.49

KLB_NB01_040



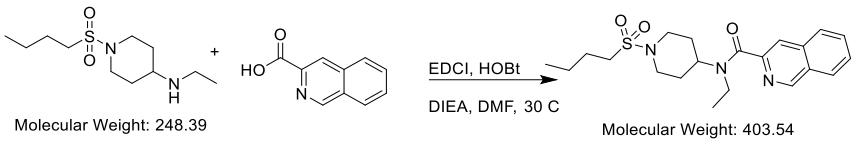
To a mixture of KLB_NB01_038 (0.117 g, 0.50 mmol, 1 Equiv.), EDCI (0.115 g, 0.60 mmol, 1.2 equiv.), HOBt (0.092 g, 0.60 mmol, 1.2 equiv.), and DIEA (0.131 mL, 0.75 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.087 g, 0.50 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate.

White/light yellow solid (189.82 mg, 97%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.24 (s, 0.6H), 9.20 (s, 0.4H), 8.11 – 7.98 (m, 2H), 7.91 (m, 1H), 7.73 (dt, *J* = 34.0, 7.3 Hz, 2H), 4.81 – 4.70 (m, 1H), 4.04 – 3.81 (m, 2H), 3.10 – 2.53 (m, 7H), 2.04 – 1.67 (m, 6H), 1.44 (ddd, *J* = 29.9, 15.2, 7.4 Hz, 2H), 0.94 (dt, *J* = 30.6, 7.3 Hz, 3H).

LC/MS (ESI) 390.27 *m/z* $[M+H]^+$

KLB_NB01_051



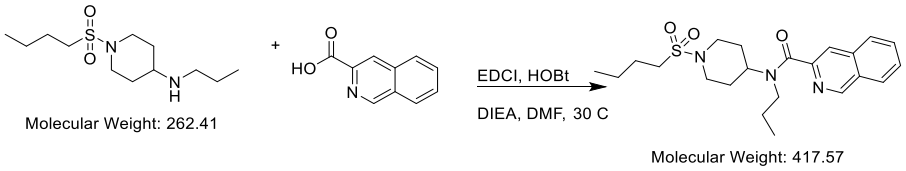
To a mixture of KLB_NB01_050 (0.124 g, 0.50 mmol, 1 Equiv.), EDCI (0.115 g, 0.60 mmol, 1.2 equiv.), HOBt (0.092 g, 0.60 mmol, 1.2 equiv.), and DIEA (0.131 mL, 0.75 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.087 g, 0.50 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate:hexanes (50-100%).

Yellow oil (70 mg, 35%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.21 (s, 1H), 8.06 – 7.93 (m, 2H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.3 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 4.68-4.63 (m, 0.5H), 4.01 – 3.80 (m, 2.5H), 3.57 – 3.44 (m, 2H), 3.01 – 2.79 (m, 3H), 2.60 – 2.50 (m, 1H), 2.05 – 1.90 (m, 4H), 1.87 – 1.69 (m, 2H), 1.50 – 1.30 (m, 4H), 1.08 – 0.90 (m, 4H).

LC/MS (ESI) *m/z* $[M+H]^+$ 404.11

KLB_NB01_028



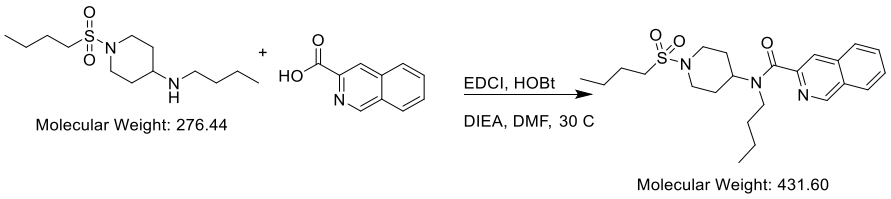
To a mixture of KLB_NB01_026 (0.157 g, 0.60 mmol, 1 Equiv.), EDCI (0.138 g, 0.72 mmol, 1.2 equiv.), HOBt (0.110 g, 0.72 mmol, 1.2 equiv.), and DIEA (0.157 mL, 0.90 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.104 g, 0.64 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate: hexanes first followed by methanol: dichloremethane.

Yellow oil (145.07 mg, 58%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.21 (d, *J* = 7.7 Hz, 1H), 8.07 – 7.94 (m, 2H), 7.90 (m, 1H), 7.72 (dt, *J* = 35.4, 7.6 Hz, 2H), 4.62-4.58 (m, 0.5H), 4.05 – 3.78 (m, 2.5H), 3.35 (m, 2H), 3.01 – 2.87 (m, 2H), 2.82 (t, *J* = 8.0 Hz, 1H), 2.54 (t, *J* = 12.1 Hz, 1H), 2.03 – 1.69 (m, 7H), 1.54 – 1.34 (m, 3H), 1.03 – 0.60 (m, 6H).

LC/MS (ESI) 418.47 *m/z* $[M+H]^+$

KLB_NB01_031



To a mixture of KLB_NB01_030 (0.138 g, 0.50 mmol, 1 Equiv.), EDCI (0.115 g, 0.60 mmol, 1.2 equiv.), HOBt (0.092 g, 0.60 mmol, 1.2 equiv.), and DIEA (0.131 mL, 0.75 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.087 g, 0.50 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water,

extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate.

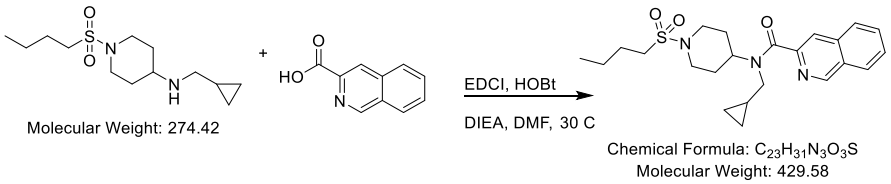
Yellow oil (116.81 mg, 54%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.20 (d, *J* = 7.8 Hz, 1H), 8.06 – 7.95 (m, 2H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.72 (dt, *J* = 35.4, 7.3 Hz, 2H), 4.64 -- 4.59 (m, 0.5H), 4.02 – 3.78 (m, 2.5H), 3.40 (q, *J* = 11.7 Hz, 2H), 2.95 (t, *J* = 7.9 Hz, 2H), 2.87 – 2.76 (m, 1H), 2.54 (t, *J* = 11.6 Hz, 1H), 2.02 – 1.66 (m, 7H), 1.42 (m, 4H), 0.97 (tt, *J* = 32.7, 7.2 Hz, 6H), 0.67 (t, *J* = 7.3 Hz, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 169.7, 169.2, 151.2, 148.9, 136.1, 135.9, 131.0, 128.6, 128.5, 128.4, 127.6, 127.6, 127.4, 127.3, 120.9, 120.5, 56.3, 52.5, 49.5, 45.9, 45.6, 45.0, 42.5, 33.4, 31.5, 30.9, 29.9, 25.1, 25.0, 21.8, 21.7, 20.7, 20.0, 13.9, 13.6, 13.6, 13.5.

LC/MS (ESI) 432.45 *m/z* $[M+H]^{+}$

KLB_NB01_037



To a mixture of KLB_NB01_035 (0.137 g, 0.50 mmol, 1 Equiv.), EDCI (0.115 g, 0.60 mmol, 1.2 equiv.), HOBt (0.092 g, 0.60 mmol, 1.2 equiv.), and DIEA (0.131 mL, 0.75 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.087 g, 0.50 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water,

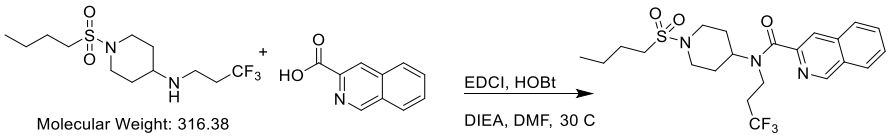
extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate.

Yellow oil (166.32 mg, 77%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.21 (s, 1H), 8.07 – 7.86 (m, 3H), 7.73 (dt, *J* = 35.0, 7.2 Hz, 3H), 4.58 (m, 0.5H), 4.04 – 3.75 (m, 2.5H), 3.39 (d, *J* = 6.6 Hz, 2H), 3.03 – 2.46 (m, 4H), 2.18 – 1.65 (m, 6H), 1.51 – 1.34 (m, 2H), 1.02 – 0.81 (m, 4H), 0.66 – 0.52 (m, 1H), 0.47 – 0.32 (m, 2H), -0.11 – -0.21 (m, 1H).

LC/MS (ESI) 430.68 *m/z* $[M+H]^+$

KLB_NB01_045



To a mixture of KLB_NB01_044 (0.158 g, 0.50 mmol, 1 Equiv.), EDCI (0.115 g, 0.60 mmol, 1.2 equiv.), HOBt (0.092 g, 0.60 mmol, 1.2 equiv.), and DIEA (0.131 mL, 0.75 mmol, 1.5 equiv.) in DMF (2.0 mL) was added isoquinoline carboxylic acid (0.087 g, 0.50 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with ethyl acetate: hexanes (1:1).

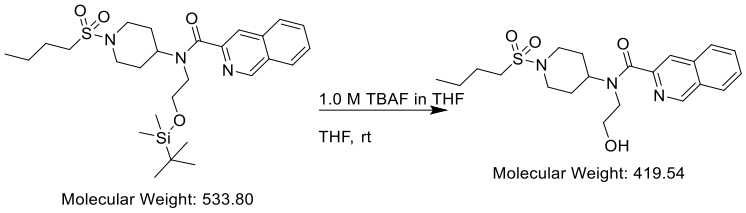
Yellow oil (125.91 mg, 53%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.20 (s, 1H), 8.14-8.10 (m, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.78 (t, *J* = 7.3 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 4.64-4.58(m,

0.4H), 4.15 – 3.83 (m, 2.6H), 3.72 – 3.62 (m, 2H), 3.00 – 2.81 (m, 3H), 2.73 – 2.55 (m, 3H), 2.07 – 1.87 (m, 4H), 1.87 – 1.70 (m, 2H), 1.53 – 1.34 (m, 2H), 1.03 – 0.88 (m, 3H).

LC/MS (ESI) *m/z* $[M+H]^+$ (NOTE: Didn't show up on mass spectra. Didn't ionize.)

KLB_NB01_063



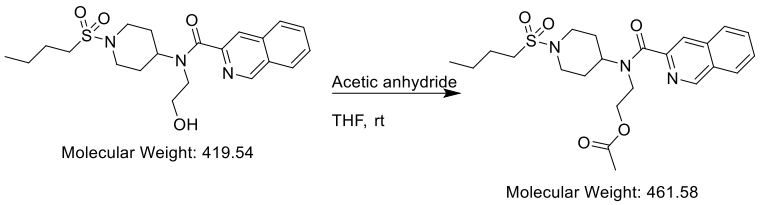
To a mixture of KLB_NB01_062_2 (0.200 g, 0.38 mmol, 1 Equiv.) in THF (2.00 mL) was added 1.0 M tetrabutylammonium fluoride solution (0.46 mL, 0.46 mmol, 1 equiv.) at 0 C and stirred at room temperature for 24 hrs. The mixture was diluted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. Column chromatography was performed using ethyl acetate.

White oily solid (87.52 mg, 55%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 (s, 1H), 8.24-8.15 (m, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.80 (t, *J* = 7.5 Hz, 1H), 7.73 (t, *J* = 8.1 Hz, 1H), 6.58 (s, 1H), 4.49 – 4.33 (m, 1H), 4.07 – 3.77 (m, 4H), 3.65 (d, *J* = 54.1 Hz, 2H), 3.05 – 2.78 (m, 3H), 2.25 – 1.99 (m, 3H), 1.99 – 1.67 (m, 3H), 1.47 (dt, *J* = 17.8, 8.3 Hz, 2H), 0.95 (dt, *J* = 15.5, 7.0 Hz, 3H).

LC/MS (ESI) *m/z* $[M+H]^+$ 420.17

KLB_NB01_064



Molecular Weight: 419.54

Molecular Weight: 461.58

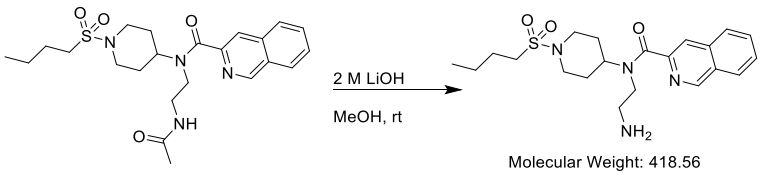
To a mixture of KLB_NB01_063 (0.042 g, 0.10 mmol, 1 Equiv.) in THF (0.500 mL) was added acetic anhydride (0.010 mL, 0.010 mmol, 1 equiv.) and DMAP (5 mg) and was stirred at room temperature for 24 hrs. The reaction mixture was washed with 1M HCl and concentrated.

White, oily solid (40.36 mg, 58%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.20 (s, 1H), 8.09 – 8.01 (m, 2H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.77 (t, *J* = 7.3 Hz, 1H), 7.71 (t, *J* = 7.3 Hz, 1H), 4.38 (t, *J* = 5.4 Hz, 1H), 4.21 – 3.67 (m, 6H), 3.02 – 2.79 (m, 3H), 2.62 – 2.52 (m, 1H), 2.13 – 1.72 (m, 9H), 1.52 – 1.37 (m, 2H), 0.93 (dt, *J* = 14.1, 6.6 Hz, 3H).

LC/MS (ESI) *m/z* $[M+H]^+$ 462.05

KLB_NB01_061



Molecular Weight: 460.59

Molecular Weight: 418.56

To a mixture of KLB_NB01_059_2 (0.080 g, 0.17 mmol, 1.0 eq.) in methanol (4 mL) was added 2.0 M LiOH (0.210 mL). The reaction mixture was stirred at 60 C overnight. The temperature was increased to 80 C. More 2.0 M LiOH (0.210 mL) was added to the reaction

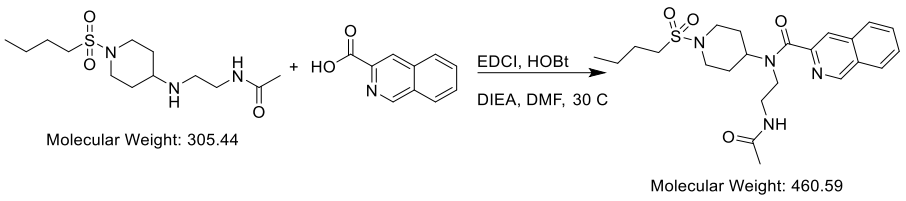
mixture. It stirred from Monday to Monday in total. Purification was performed using methanol: ethyl acetate (10-20%) as eluent.

Yellow oil (12.76 mg, 18%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H), 9.00 (s, 1H), 8.57 (s, 1H), 8.25 (d, J = 8.2 Hz, 1H), 8.20 (d, J = 7.7 Hz, 1H), 7.88 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 7.81 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 3.58 – 3.43 (m, 4H), 3.03 – 2.93 (m, 2H), 2.86 (td, J = 12.3, 2.6 Hz, 4H), 1.95 – 1.85 (m, 2H), 1.67 – 1.55 (m, 2H), 1.38 (dq, J = 14.6, 7.4 Hz, 4H), 0.88 (t, J = 7.3 Hz, 3H).

LC/MS (ESI) *m/z* $[M+H]^+$ 419.28

KLB_NB01_059



To a mixture of KLB_NB01_057_2 (0.687 g, 2.25 mmol, 1 Equiv.), EDCI (0.518 g, 2.70 mmol, 1.2 equiv.), HOBt (0.413 g, 2.70 mmol, 1.2 equiv.), and DIEA (0.590 mL, 3.38 mmol, 1.5 equiv.) in DMF (10.0 mL) was added isoquinoline carboxylic acid (0.390 g, 2.25 mmol, 1 equiv.) and stirred at 30 °C for 24 hrs. The mixture was diluted with water, extracted with ethyl acetate, washed with water and brine, dried over MgSO4, and concentrated. MPLC was performed with methanol: dichloromethane (2-5 %) twice. The impure compound was dissolved in ethyl acetate and washed with saturated sodium

bicarbonate solution, 1 M citric acid solution, and brine. MPLC was performed again with methanol: ethyl acetate (5%).

Yellow oil (102.9 mg), slightly less pure (79.3 mg) Yield: 18%

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.21 (s, 1H), 8.40 (s, 0.5H), 8.18 – 8.02 (m, 2H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.76 – 7.70 (m, 1H), 6.76 (s, 0.5H), 4.25-4.20 (m, 0.5H), 4.01 – 3.78 (m, 2.5H), 3.70 – 3.45 (m, 4H), 3.01 – 2.80 (m, 3H), 2.56 (t, *J* = 11.7 Hz, 1H), 2.30 – 2.15 (m, 1H), 2.06 – 1.70 (m, 8H), 1.52 – 1.35 (m, 2H), 1.01 – 0.87 (m, 3H).

LC/MS (ESI) *m/z* $[M+H]^+$ 461.46