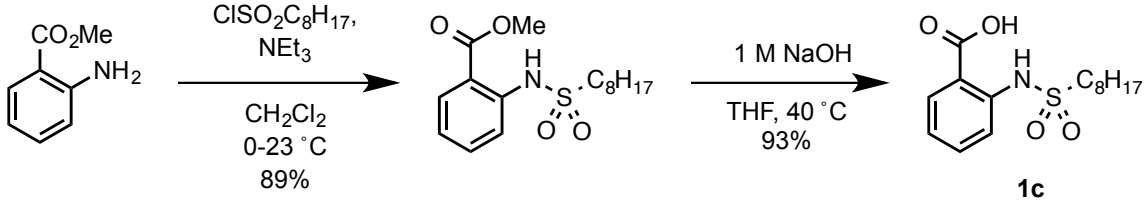
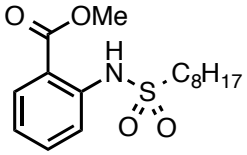
Chemistry

All reagents and solvents were obtained from commercial sources, and used as supplied unless otherwise indicated. Reactions requiring anhydrous conditions were conducted under an inert atmosphere of argon using anhydrous solvents. CH_2Cl_2, toluene and MeOH were distilled over CaH_2. Et_2O and THF were distilled over Na and benzophenone. All reactions were monitored by analytical thin-layer chromatography (TLC) using indicated solvent systems on Analtech Uniplate Silica Gel TLC plates (250 microns). TLC plates were visualized using UV light (254 nm) and/or by staining in potassium permanganate, cerium ammonium molybdate, or phosphomolybdic acid followed by heating. All NMR spectra were recorded on either Bruker Advance 400 MHz or 300 MHz spectrometers as indicated. Chemical shifts (δ H) are quoted in ppm (parts per million) and referenced to residual solvent signals: 1H δ = 7.26 ($CDCl_3$), 2.50 (DMSO- d_6), 3.31 (CD_3OD), 13C δ = 77.0 ($CDCl_3$), 39.43 (DMSO-d_6), 49.05 (CD_3OD). Coupling constants (*J*) are given in Hz. Elemental analysis was performed by Atlantic Microlabs, Inc.

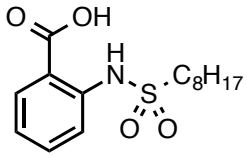
Preparation of 2-(octanesulfonamido)benzoic acid (1c)



1c

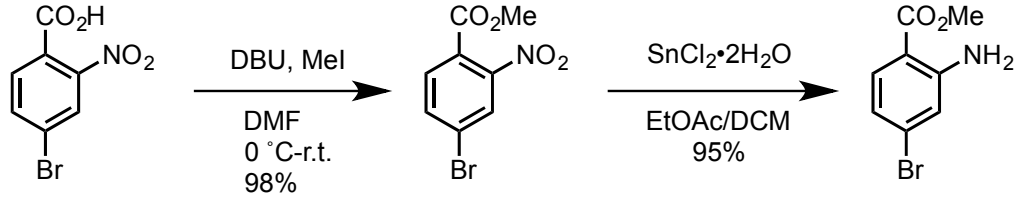


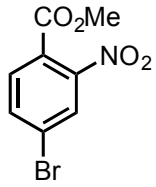
Methyl 2-(octanesulfonamido)benzoate. To a stirring solution of methyl anthranilate (2.5 mL, 19.3 mmol) in CH_2Cl_2 at 0 ˚C was added octanesulfonyl chloride (4.5 mL, 23.2 mmol) dropwise followed by freshly distilled triethylamine (8.1 mL, 57.9 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 16 h, then quenched with saturated NH_4Cl and extracted with CH_2Cl_2 (×3). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to provide 6.0 g of a crude off-white solid. Recrystallization from warm EtOAc/hexanes afforded the desired sulfonamide as white crystals (5.6 g, 17.1 mmol, 89%). ^{1}H-NMR (400 MHz; $CDCl_3$): δ 8.07 (ddd, *J* = 8.0, 1.7, 0.4 Hz, 1H), 7.76 (ddd, *J* = 8.4, 1.2, 0.5 Hz, 1H), 7.64 (ddd, *J* = 8.4, 7.3, 1.7 Hz, 1H), 7.19 (ddd, *J* = 8.0, 7.3, 1.2 Hz, 1H), 3.95 (s, 3H), 3.29-3.25 (m, 2H), 1.79-1.71 (m, 2H), 1.39 (s, 2H), 1.23 (s, 8H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz; DMSO-d_6): δ 167.8, 139.8, 134.7, 131.0, 123.0, 118.5, 116.1, 52.6, 51.2, 31.0, 28.7, 28.6, 28.0, 22.8, 21.9, 13.9.



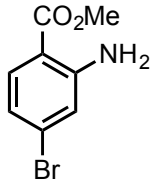
2-(Octanesulfonamido)benzoic acid (1c). To a stirring solution of methyl 2-(octanesulfonamido)benzoate (5.6 g, 17.1 mmol) in THF (86 mL) at room temperature was added 1 M NaOH (171 mL, 171 mmol). The reaction mixture was stirred at 40 ˚C for 18 h, then the reaction was quenched with 1 M HCl and extracted with EtOAc (×3). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to afford 5.3 g of a crude off-white solid. Recrystallization from warm EtOAc/hexanes afforded the desired carboxylic acid as white crystals (5.0 g, 16.0 mmol, 93%). ^{1}H-NMR (400 MHz; aceton-d_6): δ 10.67 (s, 1H), 8.14 (ddd, *J* = 8.0, 1.7, 0.4 Hz, 1H), 7.76 (ddd, *J* = 8.4, 1.2, 0.4 Hz, 1H), 7.65 (ddd, *J* = 8.4, 7.3, 1.7 Hz, 1H), 7.21-7.18 (m, 1H), 3.28-3.24 (m, 2H), 1.75 (m, 2H), 1.39 (m, 2H), 1.29-1.23 (m, 7H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (101 MHz, DMSO-d_6): δ 170.19, 141.04, 134.73, 131.85, 122.52, 117.42, 115.79, 51.26, 31.32, 28.55, 28.52, 27.42, 23.16, 22.23, 13.94; HRMS (FAB) calcd for $C_{15}H_{24}NO_4S$ [M+H]+, 314.14260; found, 314.14278.

Preparation of methyl 2-amino-4-bromobenzoate (2)[1]





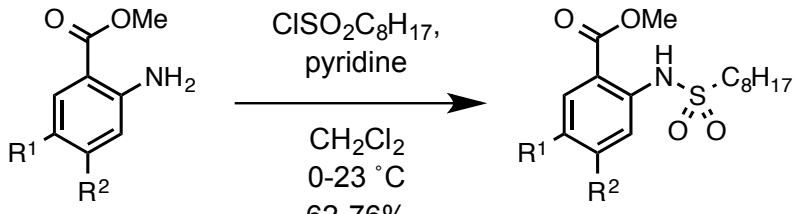
Methyl 4-bromo-2-nitrobenzoate. To a stirring solution of 4-bromo-2-nitrobenzoic acid (5.0 g, 21.7 mmol) in DMF (33 mL) at 0 ˚C was added DBU (3.91 mL, 26.1 mmol) followed by iodomethane (2.04 mL, 32.8 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 12 h, then quenched with $NaHCO_3$, and extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification by flash chromatography (10% EtOAc in hexanes) afforded methyl 4-bromo-2-nitrobenzoate (98%). Spectral data match literature values.[1]



Methyl 2-amino-4-bromobenzoate 2. To a stirring solution of methyl 4-bromo-2-nitrobenzoate (4.75 g, 18.3 mmol) in 3:1 EtOAc/DCM (45 mL) at room temperature was added $SnCl_2$•$2H_2O$ (20.6 g, 91.3 mmol). The reaction mixture was stirred at room temperature for 16 h, then quenched with $NaHCO_3$. The gelatinous mixture was filtered

over Celite, and the filtrate was extracted with DCM (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification by flash chromatography (10% EtOAc in hexanes) afforded aniline **2** (95%). Spectral data match literature values.[1]

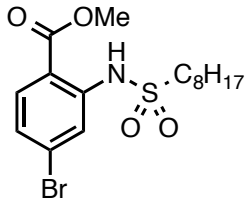
Preparation of Sulfonamides 4 and 5.



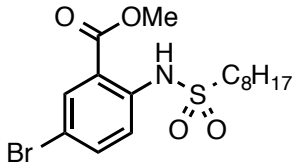
2 R^1=H, R^2=Br
3 R^1=Br, R^2=H

4 R^1=H, R^2=Br
5 R^1=Br, R^2=H

General Procedure. To a stirring solution of the starting aniline (6.6 mmol) in DCM (24 mL) at 0 ˚C was added pyridine (4 mL). Octanesulfonyl chloride (1.2 equiv) was then added slowly via syringe. The solution was stirred and allowed to warm to room temperature. Reaction progress was monitored by TLC (20 % EtOAc in hexanes). Upon completion, the reaction was poured into saturated $NaHCO_3$ solution (50 mL), extracted with DCM (3 × 30 mL), and washed with 1 M HCl (50 mL). The combined organic layers were concentrated *in vacuo* and purified by flash chromatography (10% EtOAc in hexanes).

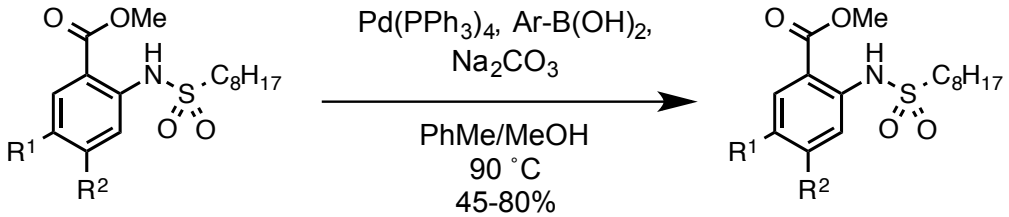


Methyl 4-bromo-2-(octanesulfonamido)benzoate (4). (62% from aniline **2**). ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 7.94 (d, J = 2.0 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.23 (dd, J = 2.0, 8.4 Hz, 1H), 3.93 (s, 3H), 3.15 (t, J = 8.0 Hz, 2H), 1.79 (m, 2H), 1.37 (m, 2H), 1.23 (m, 8H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 167.8, 142.0, 132.5, 129.7, 125.7, 120.4, 113.5, 52.6, 52.4, 31.5, 28.8, 28.7, 27.9, 23.2, 22.5, 13.9.



Methyl-5-bromo-2-(octanesulfonamido)benzoate (5). (76% yield from aniline **3** (>99%, TCI America)). ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.17 (d, J = 2.4 Hz, 1H), 7.66 (m, 2H), 3.95 (s, 3H), 3.11(t, J = 8.0 Hz, 2H), 1.78(m, 2H), 1.26(m, J = 10H),0.89 (t, J = 6.8Hz, 3H); ^{13}C CNMR ($CDCl_3$) δ 167.2, 140.1, 137.5, 134.0, 119.5, 116.5, 115.0, 52.8, 52.3, 31.6, 28.8, 28.8, 28.0, 23.3, 22.5, 14.0.

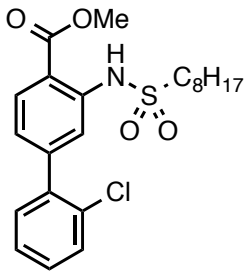
Preparation of Suzuki Coupling Products 6a-l and 7a-l.



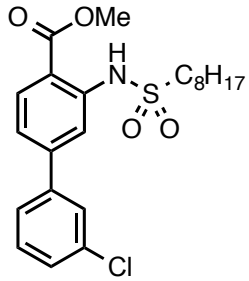
4 R^1=H, R^2=Br
5 R^1=Br, R^2=H

6a-l R^1=H, R^2=Ar
7a-l R^1=Ar, R^2=H

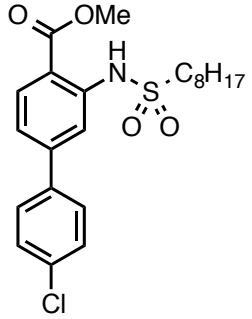
General Procedure. Aryl bromide **4** or **5** (0.247 mmol) was placed into a vial flushed with argon, and a solution of 10 mg $Pd(PPh_3)_4$ in 0.40 mL toluene was added, followed by 0.25 mL 2 M Na_2SO_3 solution. The solution was stirred at room temperature for 5 min, and then a solution of the boronic acid (0.318 mmol, 1.25 equiv.) in 0.40 mL MeOH was added. The vial was capped and heated to 90 °C for 24 h. The reaction was then cooled to room temperature and diluted with CH_2Cl_2, the organic phase was separated from the aqueous phase, and the organic phase was concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/hexanes) to yield the desired suzuki coupling product.



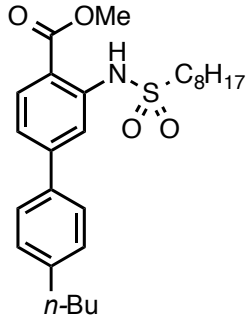
2-Chloro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6a). 76% yield; ^{1}H NMR ($CDCl_3$) δ 10.46 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.77 (s, 1H), 7.41 (m, 1H), 7.27 (m, 3H), 7.09 (d, *J* = 8.4 Hz, 1H), 3.85 (s, 3H), 3.14 (t, *J* = 8.0 Hz, 2H), 1.75 (m, 2H), 1.31 (m, 2H), 1.18 (m, 8H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1, 145.8, 140.7, 138.6, 132.0, 131.2, 130.9, 130.0, 129.4, 127.0, 123.4, 118.4, 113.8, 52.5, 52.0, 31.5, 28.7, 28.7, 27.9, 23.2, 22.4, 13.9.



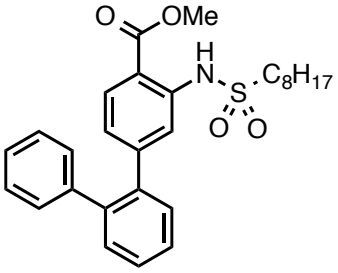
3-Chloro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6b). 74% yield; ^{1}H NMR ($CDCl_3$) δ 10.51 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 1.6 Hz, 1H), 7.59 (s, 1H), 7.51 (m, 1H), 7.39 (m, 2H), 7.29 (dd, *J* = 1.6, 8.4 Hz, 1H), 3.97 (s, 3H), 3.18 (t, *J* = 8.0 Hz, 2H), 1.82 (m, 2H), 1.37 (m, 2H), 1.25 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1, 145.9, 141.5, 140.9, 134.8, 132.0, 130.2, 128.6, 127.2, 125.4, 121.1, 116.1, 114.1, 52.5, 52.2, 31.5, 28.8, 28.7, 27.9, 23.3, 22.4, 13.9.



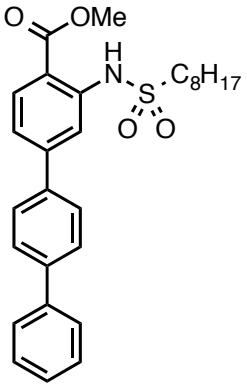
4-Chloro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6c). 74% yield; ^{1}H NMR ($CDCl_3$) δ 10.49 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.97 (s, 1H), 7.56 (d, *J* = 6.8 Hz, 2H), 7.43 (d, *J* = 6.8 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 1H), 3.96 (s, 3H), 3.16 (t, *J* = 8.0 Hz, 2H), 1.82 (m, 2H), 1.36 (m, 2H), 1.22 (m, 8H), 0.84 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1, 146.1, 141.5, 137.4, 134.9, 132.0, 129.1, 128.5, 120.9, 115.9, 113.9, 52.5, 52.2, 31.5, 28.8, 28.7, 27.9, 23.3, 22.4, 13.9.



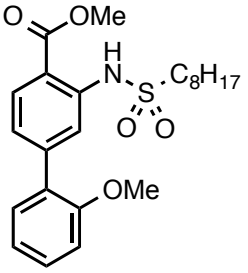
4-*n*-Butyl-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6d). 72% yield; ^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.65 (s, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 8.16 (d, *J* = 1.7 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.46 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 2H), 4.08 (s, 3H), 3.33-3.29 (m, 2H), 2.81 (t, *J* = 7.7 Hz, 2H), 2.00-1.90 (m, 2H), 1.80-1.76 (m, 2H), 1.59-1.45 (m, 4H), 1.45-1.30 (m, 8H), 1.10 (t, *J* = 7.3 Hz, 3H), 1.00 (t, *J* = 6.9 Hz, 3H).; ^{13}C-NMR (101 MHz, $CDCl_3$): δ 168.54, 147.68, 144.00, 141.67, 136.55, 132.07, 129.25, 127.31, 121.14, 115.94, 113.57, 52.63, 52.31, 35.51, 33.72, 31.83, 29.08, 29.00, 28.20, 23.55, 22.73, 22.53, 14.20, 14.12.



2-Phenyl-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6e). 67% yield; ^{1}H NMR ($CDCl_3$) δ 10.41 (s, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.45 (m, 5H), 7.25 (m, 5H), 7.03 (dd, *J* = 8.4, 1.6 Hz, 1H), 3.93 (s, 3H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.67 (m, 2H), 1.32 (m, 2H), 0.92 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 148.6, 141.0, 140.5, 140.3, 138.7, 131.2, 130.8, 130.2, 129.8, 128.3, 128.0, 127.5, 126.6, 123.6, 118.9, 112.7, 52.3, 51.2, 31.6, 28.9, 28.8, 27.8, 23.3, 22.5, 13.9.

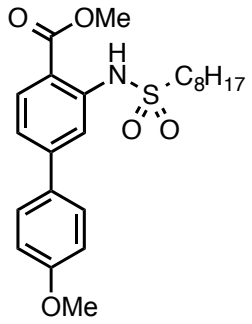


4-Phenyl-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6f). 71% yield; ^{1}H NMR (DMSO-d_6) δ 10.28 (s, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.90 (s, 1H), 7.81 (q, *J* = 8.4 Hz, 4H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 3.91 (s, 3H), 3.37 (t, *J* = 8.0 Hz, 2H), 1.64 (m, 2H), 1.32 (m, 2H), 1.20 (m, 8H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ 167.7, 145.5, 140.5, 140.4, 139.2, 137.2, 131.8, 128.9, 127.7, 127.5, 127.3, 126.6, 121.2, 116.0, 114.8, 52.7, 51.4, 31.0, 28.2, 28.2, 27.0, 22.9, 21.9, 13.8.

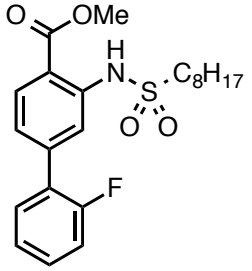


2-Methoxy-3-(octanesulfonamido)-biphenyI-4-carboxylic acid methyl ester (6g). 70% yield; ^{1}H NMR ($CDCl_3$) δ 10.48 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.98 (s, 1H), 7.37 (m, 2H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.05 (m, 2H), 3.95 (s, 3H), 3.84 (s, 3H), 3.20 (t, *J* = 8.0 Hz, 2H), 1.82 (m, 2H), 1.40 (m, 2H), 1.23 (m, 8H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C

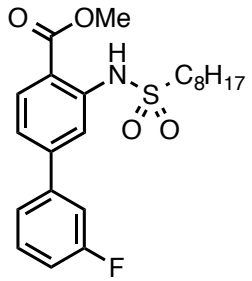
NMR ($CDCl_3$) δ 168.3, 156.3, 145.2, 140.6, 130.9, 130.5, 129.8, 128.6, 123.6, 120.9, 118.6, 113.1, 111.3, 55.5, 52.3, 51.8, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.



4-Methoxy-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6h). 71% yield; ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 1.6 Hz, 1H), 7.57 (dd, *J* = 6.8, 2.0 Hz, 2H), 7.28 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.97 (dd, *J* = 6.8, 2.0 Hz, 2H), 3.93 (s, 3H), 3.84 (s, 3H), 3.14 (t, *J* = 8.0 Hz, 2H), 1.80 (m, 2H), 1.23 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.3, 160.2, 147.0, 141.4, 131.8, 131.3, 128.4, 120.5, 115.4, 114.3, 113.0, 55.3, 52.4, 52.0, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.

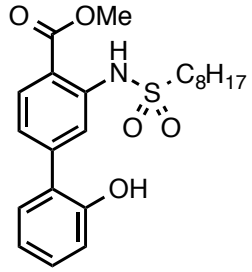


2-Fluoro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6i). 69% yield; ^{1}H NMR ($CDCl_3$) δ 10.51 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 1.6 Hz, 1H), 7.48 (dt, *J* = 7.6, 2.0 Hz, 1H), 7.40 (m, 1H), 7.28 (m, 1H), 7.19 (m, 1H), 3.97 (s, 3H), 3.21 (t, *J* = 8.0 Hz, 2H), 1.83 (m, 2H), 1.37 (m, 2H), 1.25 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1, 159.6 (d, *J* = 249 Hz), 142.3 (d, *J* = 1.4 Hz), 141.1, 131.4, 130.5 (d, *J* = 2.9 Hz), 130.2 (d, *J* = 8.4 Hz), 127.3, 124.6 (d, *J* = 3.7 Hz), 123.0 (d, *J* = 3.6 Hz), 117.9 (d, *J* = 3.5 Hz), 116.2 (d, *J* = 22.5 Hz), 113.8, 52.5, 52.1, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.

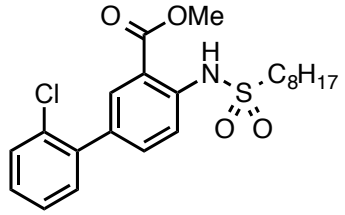


3-Fluoro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6j). 70% yield; ^{1}H NMR ($CDCl_3$) δ 10.49 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 1.6 Hz,

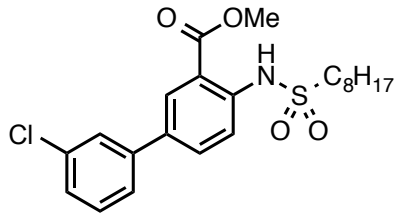
1H), 7.41 (m, 2H), 7.30 (m, 2H), 7.10 (m, 1H), 3.96 (s, 3H), 3.16 (t, J = 8.0 Hz, 2H), 1.81 (m, 2H), 1.36 (m, 2H), 1.21 (m, 8H), 0.86 (t, J = 6.8 Hz, 3H); ^{1}H NMR ($CDCl_3$) δ 168.1, 163.0 (d, J = 246 Hz), 146.0 (d, J = 2.2 Hz), 141.5, 141.3 (d, J = 7.3 Hz), 132.0, 130.5 (d, J = 8.0 Hz), 122.9 (d, J = 2.9 Hz), 121.0, 116.1, 115.4 (d, J = 21.1 Hz), 114.1, 114.1 (d, J = 22.4 Hz), 52.5, 52.2, 31.5, 28.8, 28.7, 27.9, 23.3, 22.4, 13.9.



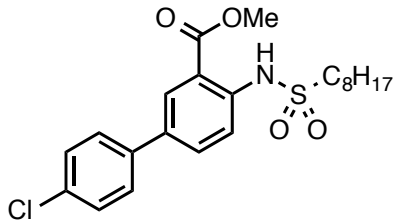
2-Hydroxy-3-(octanesulfonamido)-biphenyl-4-carboxylic acid methyl ester (6k). 45% yield; ^{1}H NMR ($CDCl_3$) δ 10.50 (s, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 1.6 Hz, 1H), 7.29 (m, 3H), 6.99 (m, 2H), 5.90 (br s, 1H), 3.96 (s, 3H), 3.20 (t, J = 8.0 Hz, 2H), 1.80 (m, 2H), 1.33 (m, 10H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 152.7, 144.6, 141.1, 131.7, 130.2, 129.9, 126.4, 123.1, 121.0, 118.2, 116.4, 113.5, 52.5, 52.2, 31.6, 28.8, 28.7, 27.9, 23.3, 22.5, 13.9.



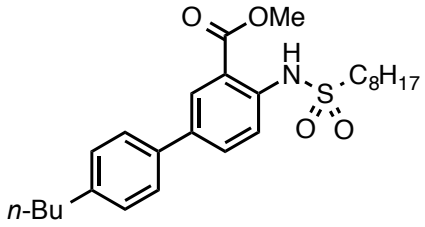
2-Chloro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7a). 74% yield; ^{1}H NMR ($CDCl_3$) δ 10.51 (s, 1H), 8.15 (d, J = 2.0 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.64 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (m, 1H), 7.33 (m, 3H), 3.94 (s, 3H), 3.20 (t, J = 8.0 Hz, 2H), 1.85 (m, 2H), 1.26 (m, 10H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 140.4, 138.4, 135.8, 133.5, 132.3, 132.3, 131.0, 130.0, 128.9, 127.0, 117.2, 114.6, 52.5, 52.3, 31.5, 28.8, 28.7, 27.9, 23.3, 22.4, 13.9.



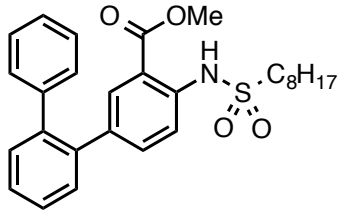
3-Chloro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7b). 78% yield; ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.23 (d, J = 2.4 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.71 (dd, J = 2.4, 8.8 Hz, 1H), 7.53 (m, 1H), 7.43 (m, 1H), 7.35 (m, 2H), 3.98 (s, 3H), 3.17 (t, J = 8.0 Hz, 2H), 1.82 (m, 2H), 1.37 (m, 2H), 1.24 (m, 8H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.0, 140.8, 140.5, 134.7, 133.8, 133.0, 130.1, 129.7, 127.5, 126.6, 124.7, 118.1, 115.2, 52.5, 52.2, 31.5, 28.7, 28.7, 27.9, 23.2, 22.4, 13.8.



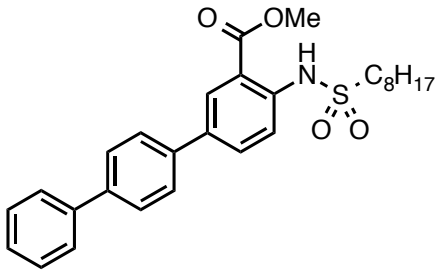
4-Chloro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7c). 80% yield; ^{1}H NMR ($CDCl_3$) δ 10.43 (s, 1H), 8.24 (d, *J* = 2.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.72 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 2H), 3.97 (s, 3H), 3.17 (t, *J* = 8.0 Hz, 2H), 1.82 (m, 2H), 1.36 (m, 2H), 1.23 (m, 8H), 0.85 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1, 140.3, 137.5, 134.2, 133.7, 133.0, 129.6, 129.0, 127.8, 118.3, 115.4, 52.6, 52.2, 31.5, 28.8, 28.7, 27.9, 23.3, 22.5, 13.9.



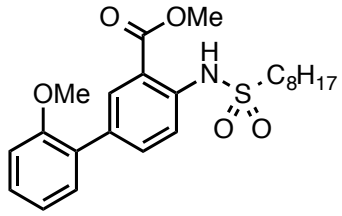
4'-Butyl-4-(octanesulfonamido)-[1,1'-biphenyl]-3-carboxylic acid methyl ester (7d). 74% yield; 74% yield; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J* = 6.8), 0.96 (t, 3H, *J* = 7.2), 1.24 (m, 8H), 1.39 (m, 4H), 1.65 (m, 2H), 1.83 (m, 2H), 2.66 (t, 2H, *J* = 8.0), 3.18 (t, 2H, *J* = 8.0), 3.97 (s, 3H), 7.27 (d, 2H, *J* = 8.4), 7.49 (d, 2H, *J* = 8.0), 7.75 (d, 1H, *J* = 8.4), 7.83 (d, 1H, *J* = 8.8), 8.28 (s, 1H), 10.42 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 22.4, 22.6, 23.4, 28.1, 28.9, 29.0, 31.7, 33.3, 33.6, 35.3, 52.2, 52.6, 115.5, 118.4, 126.6, 129.1, 129.6, 133.2, 135.7, 136.5, 139.9, 142.6, 168.4.



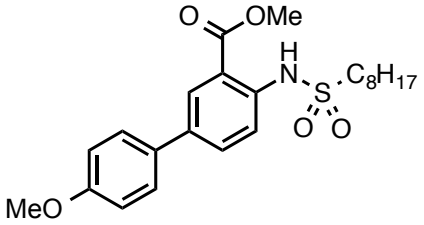
2-Phenyl-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7e). 65% yield; ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 7.93 (d, *J* = 2.0 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.43 (m, 4H), 7.22 (m, 4H), 7.13 (m, 2H), 3.87 (s, 3H), 3.11 (t, *J* = 8.0 Hz, 2H), 1.77 (m, 2H), 1.36 (m, 2H), 1.25 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 140.9, 140.6, 139.4, 138.4, 136.2, 135.8, 132.5, 130.6, 130.0, 129.8, 128.0, 127.9, 127.6, 126.7, 117.1, 114.6, 52.3, 52.0, 31.6, 28.8, 28.8, 28.0, 23.2, 22.5, 14.0.



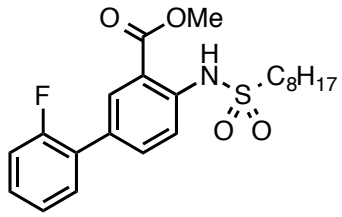
4-Phenyl-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7f). 72% yield; ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.34 (d, *J* = 2.4 Hz, 1H), 7.85 (m, 2H), 7.67 (m, 6H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.40 (m, 1H), 3.99 (s, 3H), 3.19 (t, *J* = 8.0 Hz, 2H), 1.84 (m, 2H), 1.39 (m, 2H), 1.24 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.3, 140.5, 140.3, 140.1, 138.0, 135.0, 133.1, 129.6, 128.8, 127.6, 127.5, 127.0, 126.9, 118.3, 115.4, 52.6, 52.2, 31.6, 28.9, 28.8, 28.0, 23.3, 22.5, 14.0.



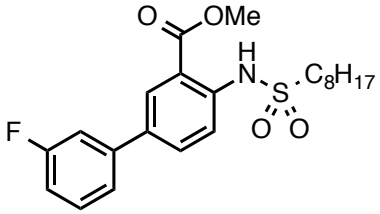
2-Methoxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl eser (7g). 67% yield; ^{1}H NMR ($CDCl_3$) δ 10.46 (s, 1H), 8.22 (d, *J* = 2.8 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.74 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.32 (m, 2H), 7.03 (m, 2H), 3.94 (s, 3H), 3.83 (s, 3H), 3.19 (t, *J* = 8.0 Hz, 2H), 1.84 (m, 2H), 1.36 (m, 2H), 1.26 (m, 8H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.4, 156.2, 139.6, 135.9, 132.9, 132.1, 130.3, 129.0, 128.4, 120.8, 117.2, 114.7, 111.1, 55.4, 52.4, 52.1, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.



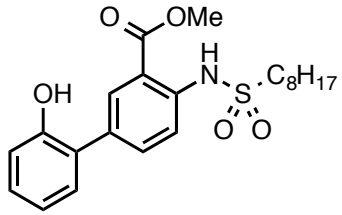
4-Methoxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7h). 71% yield; ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.22 (d, *J* = 2.4 Hz, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.71 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.96 (s, 3H), 3.85 (s, 3H), 3.16 (t, *J* = 8.0 Hz, 2H), 1.81 (m, 2H), 1.37 (m, 2H), 1.23 (m, 8H), 0.85 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.3, 159.3, 139.5, 135.3, 132.8, 131.6, 129.2, 127.7, 118.4, 115.4, 114.3, 55.3, 52.5, 52.1, 31.6, 28.8, 28.8, 28.0, 23.3, 22.5, 13.9.



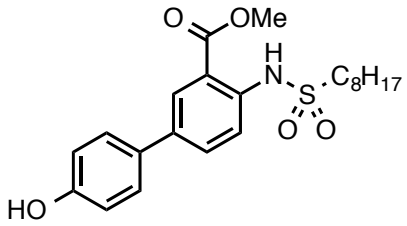
2-Fluoro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7i). 73% yield; ^{1}H NMR ($CDCl_3$) δ 10.48 (s, 1H), 8.24 (s, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.72 (td, *J* = 8.8, 2.0 Hz, 1H), 7.41 (dt, *J* = 7.6, 2.0 Hz, 1H), 7.32 (m, 1H), 7.22 (m, 1H), 7.15 (m, 1H), 3.94 (s, 3H), 3.18 (t, *J* = 8.0 Hz, 2H), 1.82 (m, 2H), 1.38 (m, 2H), 1.24 (m, 8H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1, 159.5 (d, *J* = 248 Hz), 140.3, 135.1 (d, *J* = 3.3 Hz), 131.7 (d, *J* = 3.0 Hz), 130.2 (d, *J* = 3.0 Hz), 130.0, 129.3 (d, *J* = 8.1 Hz), 127.0 (d, *J* = 13.0 Hz), 124.5 (d, *J* = 3.7 Hz), 117.7, 116.1 (d, *J* = 22.6 Hz), 115.0, 52.5, 52.2, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.



3-Fluoro-4-(octanesulfonamido)-biphenyI-3-carboxylic acid methyl ester (7j). 77% yield; ^{1}H NMR ($CDCl_3$) δ 10.46 (s, 1H), 8.27 (d, *J* = 2.4 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.74 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.41 (dd, *J* = 8.0, 6.0 Hz, 1H), 7.35 (d, 7.6 Hz, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.06 (m, 1H), 3.99 (s, 3H), 3.19 (t, *J* = 8.0 Hz, 2H), 1.83 (m, 2H), 1.39 (m, 2H), 1.24 (m, 8H), 0.86 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1, 163.1 (d, *J* = 246 Hz), 141.2 (d, *J* = 7.3 Hz), 140.5, 134.0, 133.0, 130.4 (d, *J* = 8.2 Hz), 129.7, 122.2 (d, *J* = 2.8 Hz), 118.2, 115.3, 114.3 (d, *J* = 21.0 Hz), 113.4 (d, *J* = 22.3 Hz), 52.6, 52.2, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.

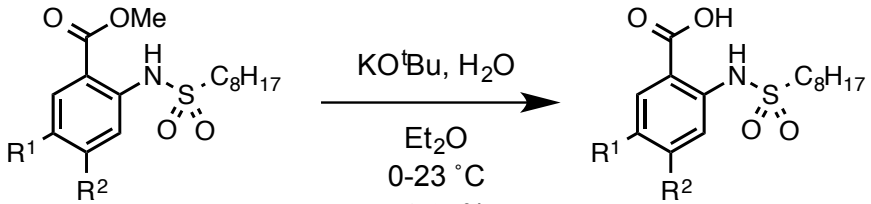


2-Hydroxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7k). 48% yield; ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 8.22 (d, *J* = 2.0 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.71 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.26 (m, 2H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 5.31 (s, 1H), 3.94 (s, 3H), 3.19 (t, *J* = 8.0 Hz, 2H), 1.82 (m, 2H), 1.27 (m, 2H), 1.25 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 152.4, 140.2, 135.6, 132.0, 131.8, 130.3, 129.3, 126.4, 121.1, 118.0, 116.1, 115.2, 52.6, 52.4, 31.6, 28.9, 28.8, 28.0, 23.3, 22.5, 14.0.



4-Hydroxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid methyl ester (7l). 51% yield; ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.21 (d, *J* = 2.4 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.70 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 3.96 (s, 3H), 3.16 (t, *J* = 8.0 Hz, 2H), 1.81 (m, 2H), 1.36 (m, 2H), 1.21 (m, 8H), 0.84 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.3, 155.7, 139.4, 135.4, 132.8, 131.6, 129.2, 127.9, 118.4, 115.8, 115.5, 52.6, 52.2, 31.6, 28.8, 28.8, 28.0, 23.3, 22.5, 13.9.

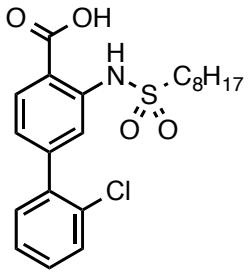
Preparation of Carboxylic Acids 12a-l and 13a-l.



6a-l R^1=H, R^2=Ar
7a-l R^1=Ar, R^2=H

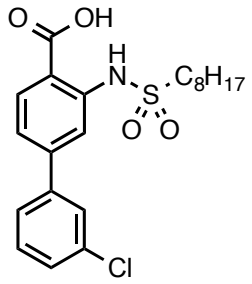
12a-l R^1=H, R^2=Ar
13a-l R^1=Ar, R^2=H

General Procedure. To a stirring suspension of potassium *tert*-butoxide (5.88 mmol) in Et_2O (15 mL) cooled to 0 °C, was added water (1.4 mmol) via syringe. The slurry was stirred for 5 min, and **6a-l** or **7a-l** (0.67 mmol) was added. The mixture was stirred at room temperature until starting material disappeared by TLC analysis (20% EtOAc in hexanes). Ice water was added until 2 clear layers formed. The aqueous layer was separated and acidified with 1 M HCl. The product was then extracted with EtOAc (3 × 20 mL), evaporated *in vacuo,* and recrystallized (EtOAc/hexanes) or purified by column chromatography (3:17:80 AcOH:EtOAc:hexanes).

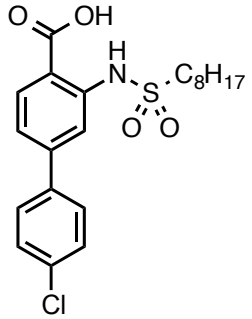


2-Chloro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12a). 89% yield; mp = 200-201 °C; ^{1}H NMR (DMSO-d_6) δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.48 (s, 1H), 7.42 (m, 3H), 6.96 (d, *J* = 8.0 Hz, 1H), 3.08 (t, *J* = 7.6 Hz, 2H), 1.62 (m, 2H), 1.20 (m, 10H), 0.80 (t, *J* = 7.2 Hz, 3H); ^{1}H NMR (MeOD) δ 171.1, 146.8, 142.0,

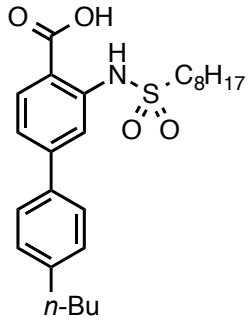
140.0, 133.0, 133.0, 132.1, 131.1, 130.7, 128.4, 124.7, 119.6, 115.9, 52.3, 32.7, 29.8, 29.8, 28.7, 24.3, 23.5, 14.4. Anal. ($C_{21}H_{26}ClNO_4S$) C, H, N.



3-Chloro-3-(octyIsulfonamido)-biphenyI-4-carboxylic acid (12b). 90% yield; mp = 120-121 °C; ^{1}H NMR (MeOD) δ 8.21 (d, *J* = 8.4 Hz, 1H), 7.98 (s, 1H), 7.68 (s, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.46 (m, 3H), 3.25 (t, *J* = 7.6 Hz, 2H), 1.78 (m, 2H), 1.38 (m, 2H), 1.23 (m, 8H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.2, 146.7, 142.9, 142.6, 135.9, 133.8, 131.6, 129.6, 128.0, 126.6, 122.3, 117.1, 116.7, 52.5, 32.8, 29.9, 29.8, 28.8, 24.4, 23.6, 14.4. Anal. ($C_{21}H_{26}ClNO_4S$) C, H, N.

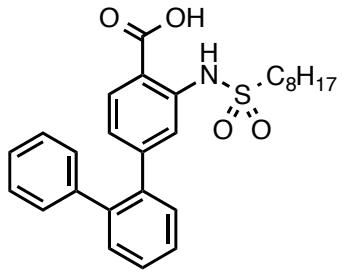


4-Chloro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12c). 86% yield; mp = 162-163 °C; ^{1}H NMR (MeOD) δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 1.6 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 2H), 7.48 (d, *J* = 6.8 Hz, 2H), 7.35 (dd, *J* = 2.0, 8.0 Hz, 1H), 3.14 (t, *J* = 8.0 Hz, 2H), 1.76 (m, 2H), 1.35 (m, 2H), 1.22 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (MeOD) δ 165.9, 147.0, 142.9, 139.3, 135.9, 133.8, 130.2, 129.7, 122.3, 117.0, 115.2, 52.5, 32.8, 29.9, 29.8, 28.8, 24.5, 23.6, 14.3. Anal. ($C_{21}H_{26}ClNO_4S$) C, H, N.

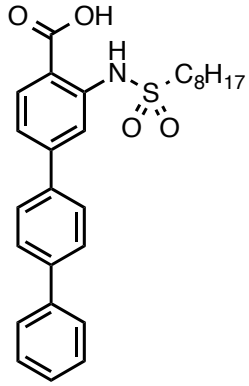


4'-Butyl-4-(octanesulfonamido)-[1,1'-biphenyl]-3-carboxylic acid (12d). 85% yield; mp = 134-135 ˚C; ^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.23 (s, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 1.6 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.39 (dd, *J* = 8.4, 1.6 Hz, 1H),

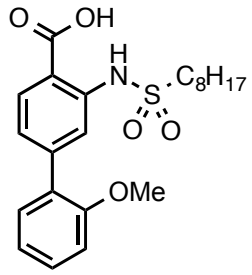
7.30 (d, J = 8.1 Hz, 2H), 3.22 (t, J = 7.9 Hz, 2H), 2.68 (t, J = 7.7 Hz, 2H), 1.87-1.83 (m, 2H), 1.68-1.61 (m, 2H), 1.42-1.35 (m, 4H), 1.23 (s, 9H), 0.96 (t, J = 7.3 Hz, 3H), 0.84 (t, J = 6.8 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 172.82, 148.92, 144.30, 142.16, 136.30, 133.16, 129.27, 127.33, 121.37, 115.83, 112.26, 52.45, 35.47, 33.65, 31.76, 29.03, 28.96, 28.16, 23.50, 22.66, 22.47, 14.14, 14.05; Anal. ($C_{25}H_{35}NO_4S$) C, H, N.



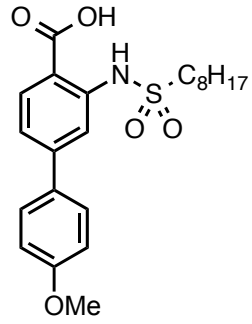
2-Phenyl-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12e). 84% yield; mp = 110-111 °C: ^{1}H NMR (MeOD) δ 8.06 (d, J = 8.4 Hz, 1H), 7.45 (m, 5H), 7.23 (m, 5H), 7.12 (dd, J = 8.0, 1.2 Hz, 1H), 2.61 (t, J = 8.0 Hz, 2H), 1.56 (m, 2H), 1.26 (m, 10H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 149.8, 142.6, 141.8, 141.8, 140.4, 133.1, 131.8, 131.2, 130.9, 129.5, 129.3, 128.7, 127.9, 124.9, 120.1, 114.9, 51.5, 32.8, 30.0, 29.9, 28.7, 24.5, 23.6, 14.4. Anal. ($C_{27}H_{31}NO_4S$) C, H, N.



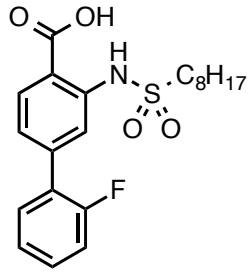
4-Phenyl-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12f). 83% yield; mp = 220-221 °C; ^{1}H NMR (DMSO-d_6) δ 8.08 (d, J = 8.4 Hz, 1H), 7.81 (m, 7H), 7.49 (m, 3H), 7.39 (t, J = 7.2 Hz, 1H), 3.31 (t, J = 8.0 Hz, 2H), 1.64 (m, 2H), 1.31 (m, 2H), 1.18 (m, 8H), 0.79 (t, J = 6.8 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ 169.8, 145.0, 141.5, 140.3, 139.3, 137.6, 132.3, 128.9, 127.7, 127.4, 127.3, 126.6, 120.5, 115.3, 114.9, 51.0, 31.0, 28.2, 28.1, 27.0, 23.0, 21.9, 13.8. HRMS (FAB) calcd for $C_{27}H_{31}NO_4S$ [M]+, 465.19738; found, 465.19692.



2-Methoxy-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12g). 89% yield; mp = 100-101 °C; ^{1}H NMR (MeOD) δ 8.12 (d, *J* = 8.4 Hz, 1H), 7.93 (s, 1H), 7.40 (m, 2H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.11 (m, 2H), 3.85 (s, 3H), 3.25 (t, *J* = 7.8 Hz, 2H), 1.71 (m, 2H), 1.22 (m, 10H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (MeOD) δ 173.9, 157.9, 146.4, 132.7, 131.4, 131.0, 130.0, 124.8, 122.0, 119.9, 119.2, 112.8, 112.3, 56.1, 51.8, 32.8, 29.8, 29.8, 28.8, 24.4, 23.5, 14.3. Anal. ($C_{22}H_{28}NNaO_5S$) C, H, N.

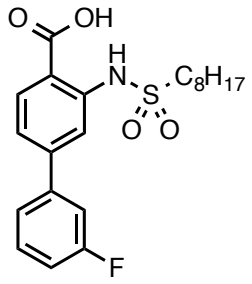


4-Methoxy-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12h). 94% yield; mp = 144 °C; ^{1}H NMR (MeOD) δ 8.12 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 1.6 Hz, 1H), 7.60 (d, *J* = 6.8 Hz, 2H), 7.37 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.02 (dd, *J* = 2.0, 6.8 Hz, 2H), 3.84 (s, 3H), 3.20 (t, *J* = 7.6 Hz, 2H), 1.73 (m, 2H), 1.34 (m, 2H), 1.20 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (MeOD) δ 171.4, 161.8, 148.2, 142.9, 133.6, 132.7, 129.3, 121.8, 116.3, 115.5, 115.2, 55.8, 52.3, 32.8, 29.9, 29.8, 28.8, 24.4, 23.6, 14.4. Anal. ($C_{22}H_{29}NO_5S$) C, H, N.

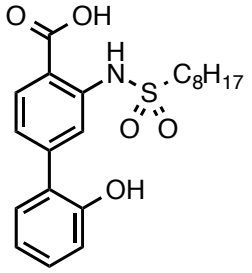


2-Fluoro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12i). 91% yield; mp = 117-118 °C; ^{1}H NMR (MeOD) δ 8.16 (dd, *J* = 2.8, 8.4 Hz, 1H), 7.92 (d, *J* = 1.6 Hz, 1H), 7.53 (m, 1H), 7.42 (m, 1H), 7.31 (m, 2H), 7.24 (m, 1H), 3.21 (t, *J* = 7.6 Hz, 2H), 1.73 (m, 2H), 1.33 (m, 2H), 1.24 (m, 8H), 0.85 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.2, 161.0 (d, *J* = 250 Hz), 143.3, 142.5, 133.3, 131.6 (d, *J* = 2.7 Hz), 131.5, 128.6 (d, *J* = 13.0 Hz). 125.9 (d, *J* = 2.6 Hz), 124.2 (d, *J* = 2.9 Hz), 119.1 (d, *J* = 3.5 Hz), 117.2 (d, *J* =

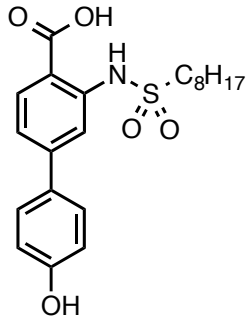
22.4 Hz), 116.1, 52.3, 32.7, 29.8, 29.8, 28.8, 24.4, 23.5, 14.3. Anal. ($C_{21}H_{26}FNO_4S$) C, H, N.



3-Fluoro-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12j). 86% yield; mp = 128-129 °C; ^{1}H NMR (MeOD) δ 8.19 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 1.6 Hz, 1H), 7.50 (m, 2H), 7.43 (m, 2H), 7.16 (m, 1H), 3.22 (t, *J* = 7.6 Hz, 2H), 1.76 (m, 2H), 1.39 (m, 2H), 1.23 (m, 8H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.7, 164.5 (d, *J* = 243.8 Hz), 146.3 (d, *J* = 2.0 Hz), 143.1, 142.7, 133.7, 131.8 (d, *J* = 8.6 Hz), 124.0 (d, *J* = 2.7 Hz), 122.2, 118.2, 117.1, 116.1 (d, *J* = 21.3 Hz), 114.8 (d, *J* = 22.5 Hz), 52.4, 32.7, 29.9, 29.8, 28.8, 24.4, 23.5, 14.3. Anal. (($C_{21}H_{26}FNO_4S$)·0.5(AcOH)) C, H, N.

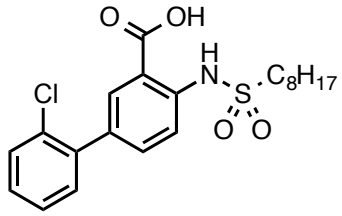


2-Hydroxy-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12k). 74% yield; mp = 45 °C; ^{1}H NMR (MeOD) δ 8.12 (d, *J* = 8.4 Hz, 1H), 8.00 (s, 1H), 7.34 (m, 2H), 7.21 (m, 1H), 6.92 (m, 2H), 3.26 (d, *J* = 8.0 Hz, 2H), 1.73 (m, 2H), 1.35 (m, 2H), 1.18 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (MeOD) δ 175.2, 155.7, 146.5, 141.8, 132.7, 131.3, 130.6, 128.0, 124.5, 121.0, 119.5, 117.1, 116.4, 51.7, 32.7, 29.8, 29.8, 28.8, 24.3, 23.5, 14.3. Anal. (($C_{21}H_{27}NO_5S$)·(H_2O)) C, H, N.

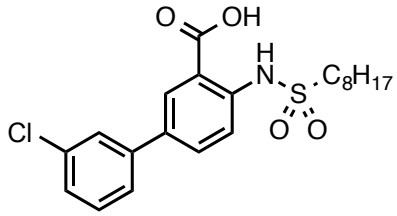


4-Hydroxy-3-(octanesulfonamido)-biphenyl-4-carboxylic acid (12l). Ester **6h** (0.3 mmol) was dissolved in 13 mL CH_2Cl_2, the solution was cooled to -78 °C, and 1M BBr_3 solution in CH_2Cl_2 (4 equiv) was added slowly. The solution was stirred and warmed to

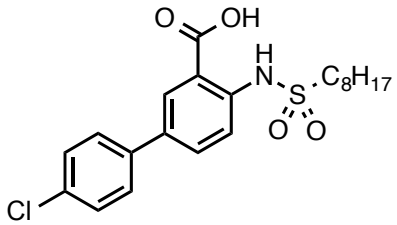
room temperature, and when complete by TLC (30% EtOAc in hexanes), the solution was acidified with 1M HCl and extracted with EtOAc (3 × 20 mL). The product was then evaporated *in vacuo*, and recrystallized (EtOAc/hexanes) or purified by column chromatography (3:17:80 AcOH:EtOAc:hexanes). 69% yield; mp = 61-62 °C; ^{1}H NMR (MeOD) δ 8.11 (d, *J* = 8.0 Hz, 1H), 7.92 (s, 1H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.37 (m, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.19 (t, *J* = 7.6 Hz, 2H), 1.72 (m, 2H), 1.34 (m, 2H), 1.19 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (MeOD) δ 171.5, 159.5, 148.4, 142.8, 133.6, 131.6, 129.3, 121.6, 116.9, 116.2, 110.7, 52.2, 32.8, 29.9, 29.8, 28.8, 24.4, 23.5, 14.3. Anal. (($C_{21}H_{27}NO_5S$)·0.3(AcOH)) C, H, N.



2-Chloro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13a). 85% yield; mp = 74-75 °C; ^{1}H NMR (MeOD) δ 8.17 (d, *J* = 2.4 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.60 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.37 (m, 3H), 3.21 (t, *J* = 8.0 Hz, 2H), 1.76 (m, 2H), 1.20 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 172.1, 141.6, 140.3, 135.6, 135.0, 133.9, 133.4, 132.3, 131.0, 130.0, 128.3, 118.4, 115.4, 52.2, 32.8, 29.9, 29.9, 28.9, 24.4, 23.6, 14.3. Anal. (($C_{21}H_{26}ClNO_4S$)·0.3(AcOH)) C, H, N.

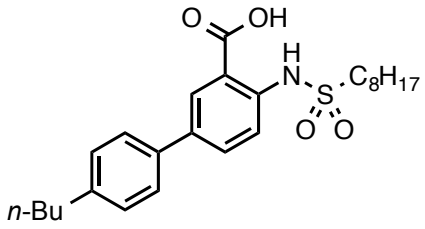


3-Chloro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13b). 89% yield; mp = 133-134 °C; ^{1}H NMR (MeOD) δ 8.29 (s, 1H), 7.81 (m, 2H), 7.57 (m, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 3.22 (t, *J* = 8.0 Hz, 2H), 1.72 (m, 2H), 1.23 (m, 10H), 0.83 (t, 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.1, 142.4, 142.1, 135.9, 135.2, 134.0, 131.5, 131.2, 128.5, 127.5, 126.0, 119.4, 117.4, 52.4, 32.8, 29.9, 29.9, 28.8, 24.4, 23.6, 14.3. Anal. ($C_{21}H_{26}ClNO_4S$) C, H, N.

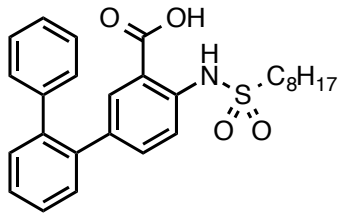


4-Chloro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13c). 91% yield; mp = 143-144 °C; ^{1}H NMR (MeOD) δ 8.31 (d, *J* = 2.0 Hz, 1H), 7.81 (m, 2H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 3.22 (t, *J* = 7.6 Hz, 2H), 1.73 (m, 2H), 1.35 (m, 2H),

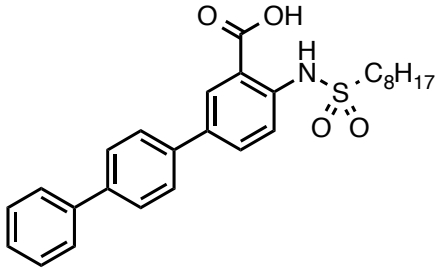
1.22 (m, 8H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.1, 141.8, 139.1, 135.5, 134.7, 133.8, 131.0, 130.1, 129.1, 119.5, 117.5, 52.4, 32.8, 29.9, 29.9, 28.8, 24.5, 23.6, 14.4. Anal. ($C_{21}H_{26}ClNO_4S$) C, H, N.



4'-Butyl-4-(octanesulfonamido)-biphenyl]-3-carboxylic acid (13d). 93% yield; mp = 103-104 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3H, J = 6.8), 0.97 (t, 3H, J = 7.2), 1.25 (m, 8H), 1.41 (m, 4H), 1.66 (m, 2H), 1.87 (m, 2H), 2.68 (t, 2H, J = 7.8), 3.24 (t, 2H, J = 7.5), 7.30 (d, 2H, J = 7.5), 7.52 (d, 2H, J = 7.8), 7.86 (m, 2H), 8.41 (s, 1H), 10.22 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.0, 14.0, 22.4, 22.6, 23.4, 28.1, 28.9, 28.9, 31.7, 33.6, 35.3, 52.4, 114.5, 118.3, 126.5, 129.1, 130.6, 134.2, 135.9, 136.1, 140.3, 142.8, 172.4; Anal. ($C_{25}H_{35}NO_4S$) C, H, N.

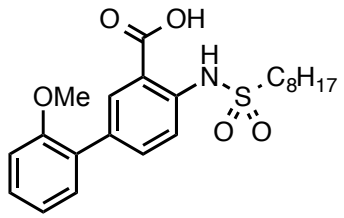


2-Phenyl-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13e). 88% yield; mp = 114-115 °C; ^{1}H NMR (MeOD) δ 7.89 (d, J = 2.0 Hz, 1H), 7.51 (d, J = 8.8 Hz, 1H), 7.38 (m, 4H), 7.19 (m, 4H), 7.09 (m, 2H), 3.10 (t, J = 8.0 Hz, 2H), 1.65 (m, 2H), 1.21 (m, 10H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 142.5, 141.9, 140.8, 139.9, 137.5, 137.0, 134.3, 131.2, 130.9, 129.0, 129.0, 128.8, 127.7, 118.4, 116.9, 52.2, 32.8, 29.9, 29.9, 28.9, 24.4, 23.6, 14.4; Anal. ($C_{27}H_{31}NO_4S$) C, H, N.

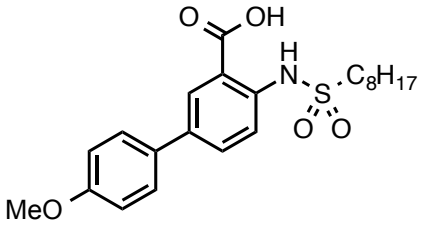


4-Phenyl-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13f). 92% yield; mp = 175-176 °C; ^{1}H NMR (DMSO-d_6) δ 10.79 (br s, 1H), 8.31 (d, J = 2.4 Hz, 1H), 8.01 (dd, J = 2.4, 8.8 Hz, 1H), 7.75 (m, 7H), 7.48 (t, J = 8.0 Hz, 2H), 7.37 (m, 1H), 3.33 (t, J = 7.6 Hz, 2H), 1.65 (m, 2H), 1.33 (m, 2H), 1.20 (m, 8H), 0.81 (t, J = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ 169.8, 139.9, 139.4, 139.2, 137.3, 133.7, 132.6, 129.1, 128.9, 127.5, 127.3,

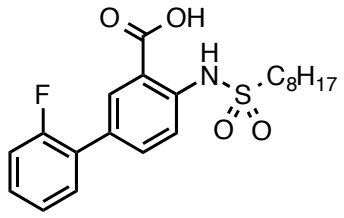
126.8, 126.5, 118.2, 116.4, 51.0, 31.0, 28.2, 28.2, 27.0, 22.9, 21.9, 13.8; HRMS (FAB) calcd for $C_{27}H_{31}NO_4S$ [M]+, 465.19738; found, 465.19766.



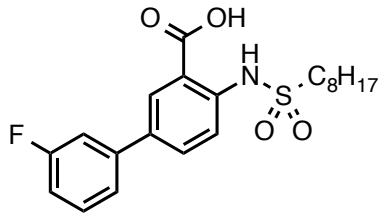
2-Methoxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13g). 91% yield; mp = 104-105 °C; ^{1}H NMR (MeOD) δ 8.24 (s, 1H), 7.71 (m, 2H), 7.28 (m, 2H), 6.98 (m, 2H), 3.77 (s, 3H), 3.17 (t, *J* = 8.0 Hz, 2H), 1.70 (m, 2H), 1.19 (m, 10H), 0.83 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.5, 157.7, 140.9, 136.6, 134.5, 133.8, 131.2, 130.1, 129.8, 122.0, 118.3, 116.9, 112.5, 55.9, 52.2, 32.7, 29.9, 29.8, 28.8, 24.4, 23.5, 14.4. Anal. ($C_{22}H_{29}NO_5S$) C, H, N.



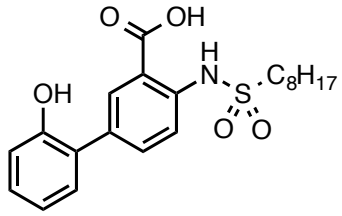
4-Methoxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13h). 91% yield; mp = 114-115 °C; ^{1}H NMR (MeOD) δ 8.26 (s, 1H), 7.71 (m, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.15 (t, *J* = 8.0 Hz, 2H), 1.70 (m, 2H), 1.20 (m, 10H), 0.81 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.5, 160.8, 140.8, 136.5, 133.2, 132.7, 130.5, 128.5, 119.4, 117.9, 115.3, 55.7, 52.2, 32.7, 29.9, 29.8, 28.8, 24.4, 23.5, 14.4. Anal. ($C_{22}H_{29}NO_5S$) C, H, N.



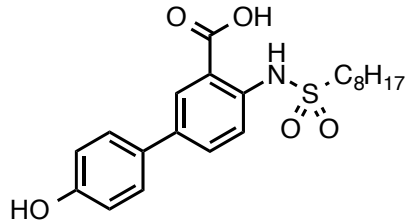
2-Fluoro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13i). 90% yield; mp = 91-92 °C; ^{1}H NMR (MeOD) δ 8.27 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.32 (m, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.15 (m, 1H), 3.19 (t, *J* = 7.6 Hz, 2H), 1.73 (m, 2H), 1.32 (m, 2H), 1.17 (m, 8H), 0.81 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 160.9 (d, *J* = 245 Hz), 141.7, 135.7 (d, *J* = 3.4 Hz), 133.3 (d, *J* = 3.3 Hz), 131.3 (d, *J* = 3.0 Hz), 130.5 (d, *J* = 8.4 Hz), 128.4, 128.2, 125.7 (d, *J* = 3.6 Hz), 118.7, 117.5, 117.0 (d, *J* = 22.8 Hz), 52.4, 32.7, 29.8, 29.8, 28.8, 24.4, 23.5, 14.3. Anal. ($C_{21}H_{26}FNO_4S$) C, H, N.



3-Fluoro-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13j). 82% yield; mp = 102-103 °C; ^{1}H NMR (MeOD) δ 8.31 (s, 1H), 7.79 (s, 2H), 7.41 (m, 2H), 7.30 (d, *J* = 10.4 Hz, 1H), 7.05 (m, 1H), 3.20 (t, *J* = 7.6 Hz, 2H), 1.73 (m, 2H), 1.33 (m, 2H), 1.21 (m, 8H), 0.82 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 164.6 (d, *J* = 243 Hz), 142.9 (d, *J* = 7.4 Hz), 141.9, 135.2, 133.6, 131.7 (d, *J* = 8.4 Hz), 131.2, 123.3 (d, *J* = 2.9 Hz), 119.3, 118.1, 115.1 (d, *J* = 21.1 Hz), 114.2 (d, *J* = 22.3 Hz), 52.4, 32.8, 29.9, 29.9, 28.8, 24.4, 23.5, 14.3. Anal. ($C_{21}H_{26}FNO_4S$) C, H, N.

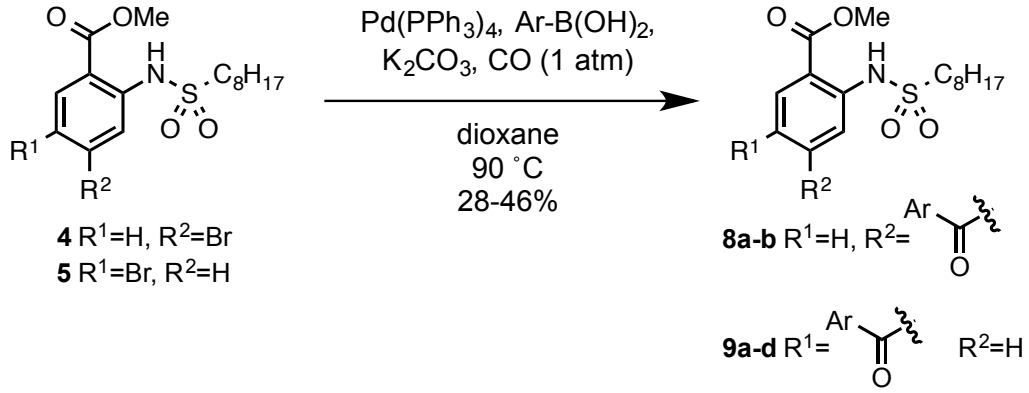


2-Hydroxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13k). 71% yield; mp = 59 °C; ^{1}H NMR (MeOD) δ 8.33 (s, 1H), 7.75 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.28 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.15 (dt, *J* = 7.6, 1.6 Hz, 1H), 6.90 (m, 2H), 3.17 (t, *J* = 8.0 Hz, 2H), 1.75 (m, 2H), 1.23 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 173.0, 155.4, 140.3, 135.1, 134.8, 133.6, 131.2, 129.6, 128.4, 120.9, 120.8, 118.4, 116.9, 51.9, 32.7, 29.9, 29.9, 28.9, 24.4, 23.5, 14.3. Anal. (($C_{21}H_{27}NO_5S$)·0.3(AcOH)) C, H, N.

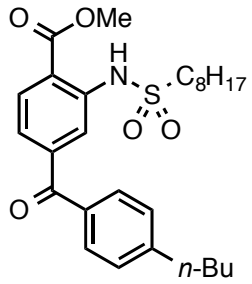


4-Hydroxy-4-(octanesulfonamido)-biphenyl-3-carboxylic acid (13l). 71% yield; mp = 142 °C; ^{1}H NMR (MeOD) δ 8.26 (s, 1H), 7.73 (m, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 3.17 (t, *J* = 8.0 Hz, 2H), 1.69 (m, 2H), 1.34 (m, 2H), 1.24 (m, 8H), 0.82 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 175.2, 158.3, 140.5, 137.0, 133.2, 131.7, 130.3, 128.6, 119.4, 117.7, 116.7, 52.1, 32.7, 29.8, 29.8, 28.7, 24.3, 23.5, 14.3. Anal. ($C_{21}H_{27}NO_5S$) C, H, N.

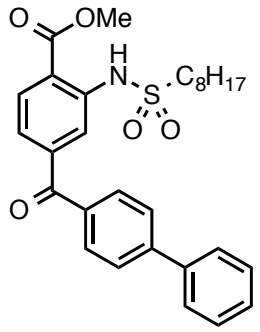
Preparation of Suzuki Coupling products 8a-b and 9a-d



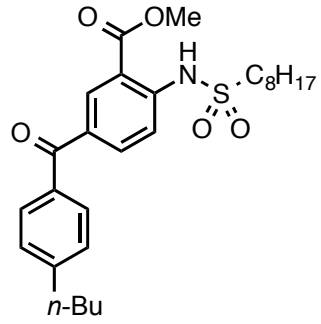
General Procedure. To an round bottom flask flushed with carbon monoxide was added 1.23 mmol of aryl bromide **4** or **5**, dioxane (9 mL), $Pd(PPh_3)_4$ (10 mol%), K_2CO_3 (3.0 eq), and boronic acid (1.1 eq). The catalyst was loaded by bubbling CO through the solution, and the reaction mixture was heated to 90 ˚C and stirred under 1 atm of carbon monoxide. Reaction progress was monitored by TLC (10% EtOAc in hexanes) until disappearance of starting material was observed (approx. 24 h). Upon completion, the reaction was quenched with 1 M HCl solution, and the crude product was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. Purification by flash chromatography (10% EtOAc in hexanes) afforded carbonyl insertion Suzuki products **8a-b** or **9a-d** as well as directly-coupled Suzuki side products without carbonyl insertion.



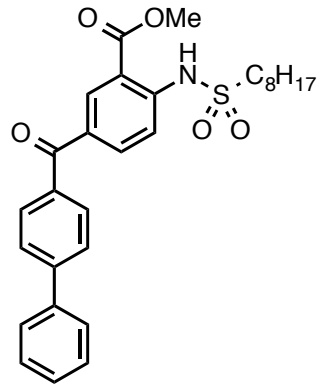
Methyl 4-(4-*n*-butylbenzoyl)-2-(octanesulfonamido)benzoate (8a). 25% yield (48% directly-coupled product); ^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.46 (s, 1H), 8.15 (d, J = 8.2 Hz, 1H), 8.03 (d, J = 1.5 Hz, 1H), 7.75 (d, J = 8.3 Hz, 2H), 7.43 (dd, J = 8.2, 1.5 Hz, 1H), 7.30 (d, J = 8.3 Hz, 2H), 3.98 (s, 3H), 3.17-3.14 (m, 2H), 2.69 (t, J = 7.8 Hz, 2H), 1.84-1.77 (m, 2H), 1.65-1.50 (m, 2H), 1.40-1.35 (m, 4H), 1.28-1.22 (m, 8H), 0.94 (t, J = 7.3 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 194.89, 167.90, 149.35, 143.67, 140.99, 133.75, 131.59, 130.47, 128.65, 122.94, 121.12, 118.61, 52.91, 52.83, 35.81, 33.22, 31.68, 28.96, 28.89, 28.06, 23.42, 22.59, 22.39, 14.07, 13.93.



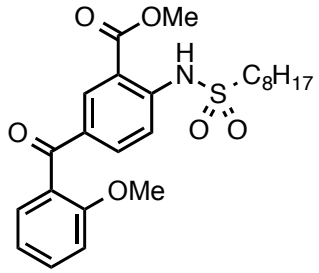
Methyl 4-([1,1'-biphenyl]-4-carbonyl)-2-(octanesulfonamido)benzoate (8b). 35% yield (44% directly-coupled product); ^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.48 (s, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 8.09 (d, *J* = 1.5 Hz, 1H), 7.93-7.90 (m, 2H), 7.73-7.71 (m, 2H), 7.66-7.64 (m, 2H), 7.55-7.40 (m, 4H), 3.99 (s, 3H), 3.20-3.16 (m, 2H), 1.86-1.78 (m, 2H), 1.39-1.35 (m, 2H), 1.28-1.22 (m, 8H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 194.94, 168.01, 146.31, 143.48, 141.19, 139.81, 134.94, 131.04, 129.14, 127.47, 127.36, 123.13, 118.85, 117.52, 53.08, 53.06, 31.81, 29.10, 29.02, 28.22, 23.57, 22.72, 14.20.



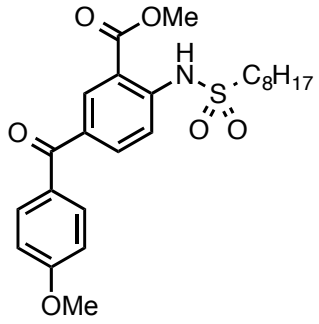
Methyl 5-(4-*n*-butylbenzoyl)-2-(octanesulfonamido)benzoate (9a). 40% yield (37% directly-coupled product); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3H, *J* = 6.3), 0.94 (t, 3H, *J* = 7.2), 1.23 (m, 8H), 1.37 (m, 4H), 1.65 (m, 2H), 1.84 (m, 2H), 2.70 (t, 2H, *J* = 7.5), 3.21 (t, 2H, *J* = 7.8), 3.94 (s, 3H), 7.30 (d, 2H, *J* = 8.1), 7.70 (d, 2H, *J* = 7.8), 7.83 (d, 1H, *J* = 8.7), 7.97 (d, 1H, *J* = 8.7), 8.55 (s, 1H), 10.76 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.9, 14.0, 22.4, 22.6, 23.4, 28.0, 28.9, 28.9, 31.7, 33.3, 35.7, 52.8, 52.8, 114.3, 116.6, 128.6, 130.1, 131.7, 133.8, 134.5, 136.3, 144.3, 148.6, 168.0, 194.1.



Methyl 5-([1,1'-biphenyl]-4-carbonyl)-2-(octanesulfonamido)benzoate (9b). 32% yield (42% directly-coupled product); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J* = 6.8), 1.15-1.30 (m, 8H), 1.35-1.45 (m, 2H), 1.80-1.90 (m, 2H), 3.24 (t, 2H, *J* = 8.0), 3.95 (s, 3H), 7.38-7.55 (m, 3H), 7.66 (d, 2H, *J* = 8.0), 7.73 (d, 2H, *J* = 8.0), 7.84-7.89 (m, 3H), 8.03 (d, 1H, *J* = 8.8), 8.59 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.0, 22.5, 23.3, 28.0, 28.8, 28.9, 31.6, 52.8, 52.8, 114.2, 116.7, 127.1, 127.2, 128.3, 129.0, 130.5, 131.4, 133.9, 135.6, 136.3, 139.7, 144.5, 145.5, 167.9, 194.1.

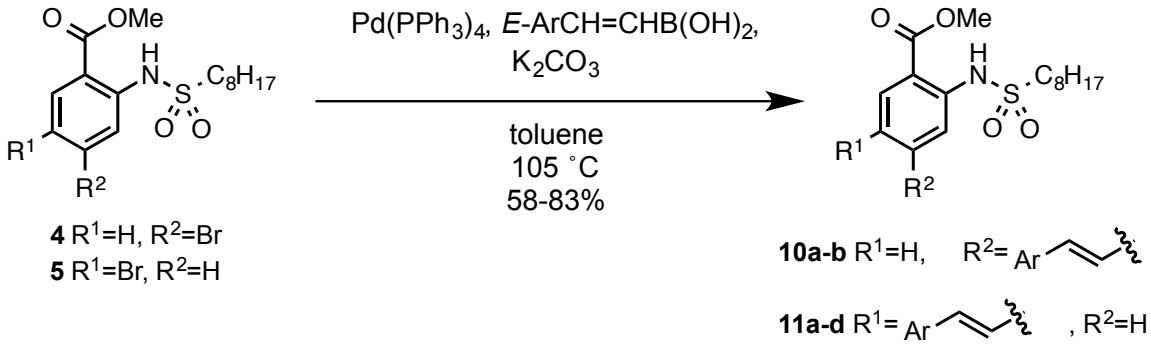


Methyl 5-(2-methoxybenzoyl)-2-(octanesulfonamido)benzoate (9c). 28% yield (57% directly-coupled product); ^{1}H-NMR (400 MHz, $CDCl_3$) ppm 0.82 (t, 3H, *J* = 6.8), 1.20 (m, 8H), 1.34 (m, 2H), 1.79 (m, 2H), 3.18 (t, 2H, *J* = 8.0), 3.69 (s, 3H), 3.89 (s, 3H), 6.98 (t, 1H, *J* = 8.0), 7.04 (d, 1H, *J* = 7.6), 7.33 (d, 1H, *J* = 7.6), 7.47 (t, 1H, *J* = 7.6), 7.74 (d, 1H, *J* = 7.2), 7.89 (dd, 1H, J_1 = 8.8, J_2 = 2.0), 8.53 (d, 1H, *J* = 2.0), 10.77 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) ppm 14.0, 22.5, 23.4, 28.0, 28.8, 28.9, 31.6, 52.7, 52.8, 55.6, 111.6, 114.2, 116.4, 120.8, 128.0, 129.7, 129.7, 132.4, 133.5, 136.3, 144.7, 157.2, 168.1, 194.1.

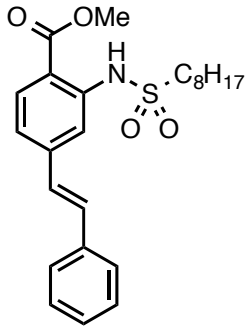


Methyl 5-(4-methoxybenzoyl)-2-(octanesulfonamido)benzoate (9d). 46% yield (28% directly-coupled product); ^{1}H-NMR (400 MHz, $CDCl_3$) ppm 0.84 (t, 3H, *J* = 6.8), 1.10-1.30 (m, 8H), 1.35-1.40 (m, 2H), 1.70-1.85 (m, 2H), 3.20 (t, 2H, *J* = 8.0), 3.88 (s, 3H), 3.93 (s, 3H), 6.97 (d, 2H, *J* = 8.8), 7.77 (d, 2H, *J* = 8.8), 7.81 (d, 1H, *J* = 8.4), 7.93 (d, 1H, *J* = 8.4), 8.48 (s, 1H), 10.72 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) ppm 13.9, 22.5, 23.3, 27.9, 28.7, 28.8, 31.5, 52.6, 52.7, 55.5, 113.7, 114.1, 116.6, 129.5, 131.9, 132.2, 133.5, 136.0, 144.0, 163.3, 167.9, 193.1

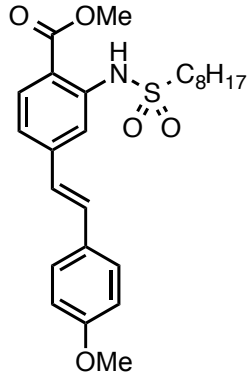
Preparation of Compounds 10a-b and 11a-b



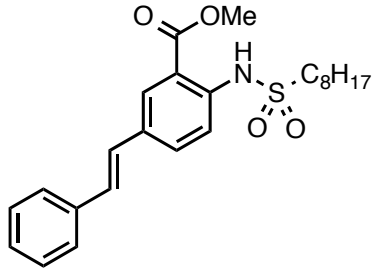
General Procedure. To a vial flushed with argon was placed 0.247 mmol of aryl bromide **4** or **5**, followed by 10 mol% $Pd(PPh_3)_4$, 0.40 mL of toluene, and 0.25 mL of a 2 M Na_2CO_3 solution. The solution was stirred at room temperature for 5 min, and then a solution of the boronic acid (40 mg, 1.25 equiv) in 0.40 mL MeOH was added. The vial was capped and heated to 90 °C for 24 h. The reaction was then cooled to room temperature and diluted $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/hexanes) to yield the desired Suzuki coupling product.



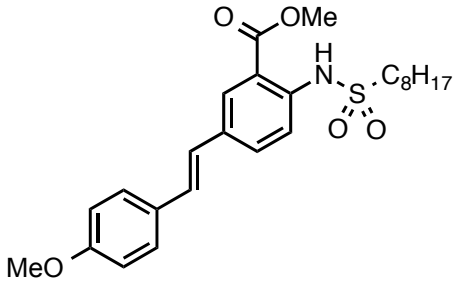
(*E*)-Methyl 2-(octanesulfonamido)-4-styrylbenzoate (10a). 64% yield; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 6.8), 1.31 (m, 10H), 1.82 (m, 2H), 3.19 (t, 2H, *J* = 8.0), 3.94 (s, 3H), 7.05-7.43 (m, 6H), 7.55 (d, 2H, *J* = 8.0), 7.88 (s, 1H), 8.02 (d, 1H, *J* = 8.0), 10.52 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9, 22.4, 23.2, 27.9, 28.7, 28.8, 31.5, 51.9, 52.3, 113.5, 115.5, 120.0, 126.8, 126.9, 128.4, 128.7, 131.6, 132.5, 136.2, 141.3, 143.7, 168.1.



(*E*)-Methyl 4-(4-methoxystyryl)-2-(octanesulfonamido)benzoate (10b). 58% yield; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J* = 7.2), 1.33 (m, 10H), 1.80 (m, 2H), 3.15 (t, 2H, *J* = 8.1), 3.82 (s, 3H), 3.91 (s, 3H), 6.88 (m, 3H), 7.20 (m, 2H), 7.46 (d, 2H, *J* = 8.7), 7.82 (s, 1H), 7.97 (d, 1H, *J* = 8.4), 10.48 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 23.2, 27.9, 28.7, 28.8, 31.4, 51.8, 52.2, 55.1, 113.1, 114.1, 115.2, 119.8, 124.7, 128.2, 128.9, 131.6, 132.1, 141.4, 144.2, 159.9, 168.1.



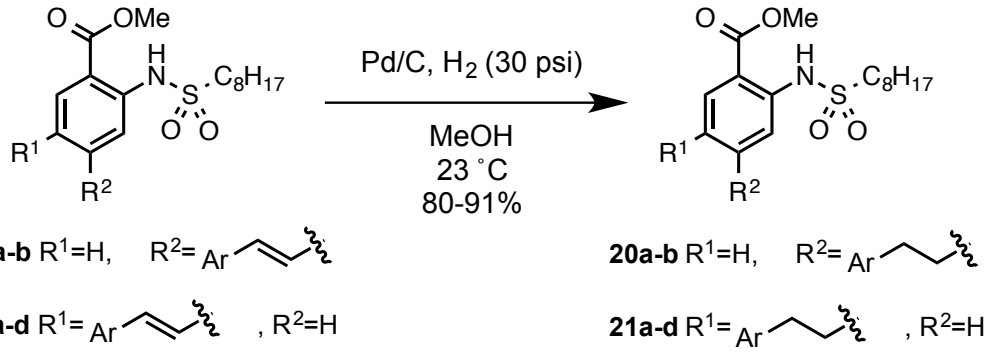
(*E*)-Methyl 2-(octanesulfonamido)-5-styrylbenzoate (11a). 83% yield; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J* = 7.2), 1.23 (m, 10H), 1.81 (m, 2H), 3.16 (t, 2H, *J* = 8.1), 3.97 (s, 3H), 7.04 (d, 2H, *J* = 2.1), 7.28 (m, 1H), 7.37 (t, 2H, *J* = 7.5), 7.51 (d, 2H, *J* = 7.2), 7.66 (dd, 1H, *J* = 2.1, 8.7), 7.76 (d, 1H, *J* = 8.7), 8.15 (d, 1H, *J* = 2.1), 10.43; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.9, 22.4, 23.1, 27.8, 28.6, 28.7, 31.4, 52.0, 52.4, 115.1, 117.9, 126.3, 126.3, 127.7, 128.5, 128.8, 129.3, 131.8, 132.1, 136.6, 139.8, 168.0.



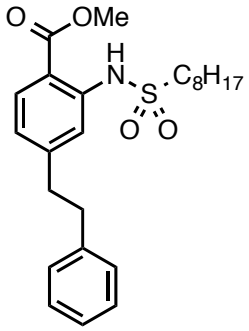
(*E*)-Methyl 5-(4-methoxystyryl)-2-(octanesulfonamido)benzoate (11b). 73% yield; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.85 (t, 2H, *J* = 7.2), 1.26(m, 10H), 1.77 (m, 2H), 3.14 (t, 2H, *J* = 7.8), 3.77 (s, 3H), 3.94 (s, 3H), 6.82-7.01 (m, 4H), 7.42 (d, 2H, *J* = 8.7), 7.61 (d, 1H, *J* = 8.7), 7.73 (d, 1H, *J* = 8.7), 8.09 (s, 1H), 10.40 (s, 1H); ^{13}C-NMR (100 MHz,

$CDCl_3$) δ 13.8, 22.3, 23.1, 27.8, 28.6, 28.7, 31.4, 51.9, 52.4, 55, 113.9, 115.0, 117.9, 124.1, 127.5, 128.3, 128.9, 129.3, 131.8, 132.2, 139.4, 159.3, 168.3.

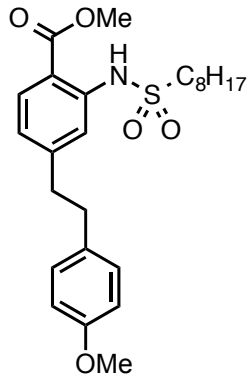
Preparation of Compounds 20a-b and 21a-b.



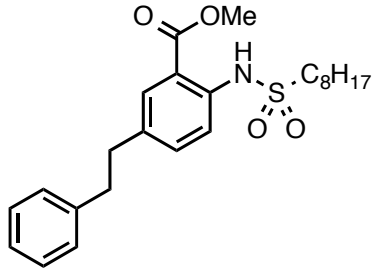
General Procedure. The alkene (0.5 mmol) was dissolved in anhydrous MeOH (5 mL), 10% Pd/C catalyst (30 mg) was added, and the solution was hydrogenated at 30 psi for 5h. When complete, the catalyst was removed by filtration and the reduced product was purified by column chromatography (10% EtOAc in hexanes).



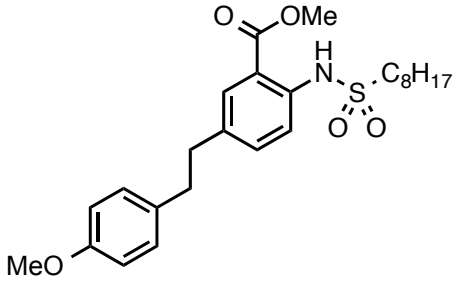
Methyl 2-(octanesulfonamido)-4-phenethylbenzoate (20a). 89% yield; ^{1}H NMR ($CDCl_3$) δ 10.43 (s, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 7.54 (s, 1H), 7.31-7.15 (m, 5H), 6.92 (d, *J* = 8.1 Hz, 1H), 3.93 (s, 3H), 2.99 (m, 6H), 1.77 (m, 2H), 1.30 (m, 10H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 149.5, 141.0, 140.6, 131.3, 128.3, 128.2, 126.0, 122.8, 117.5, 112.7, 52.2, 51.7, 37.7, 36.8, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.



Methyl 4-(4-methoxyphenethyl)-2-(octanesulfonamido)benzoate (20b). 87% yield; ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.53 (s, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 2H), 3.91 (s, 3H), 3.77 (s, 3H), 3.01 (t, *J* = 8.1 Hz, 2H), 2.92 (m, 4H), 1.75 (m, 2H), 1.26 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 157.7, 149.5, 140.9, 132.5, 131.3, 129.2, 122.9, 117.5, 113.6, 112.6, 55.0, 52.2, 51.5, 37.9, 35.9, 31.5, 28.7, 28.6, 27.8, 23.1, 22.4, 13.8.



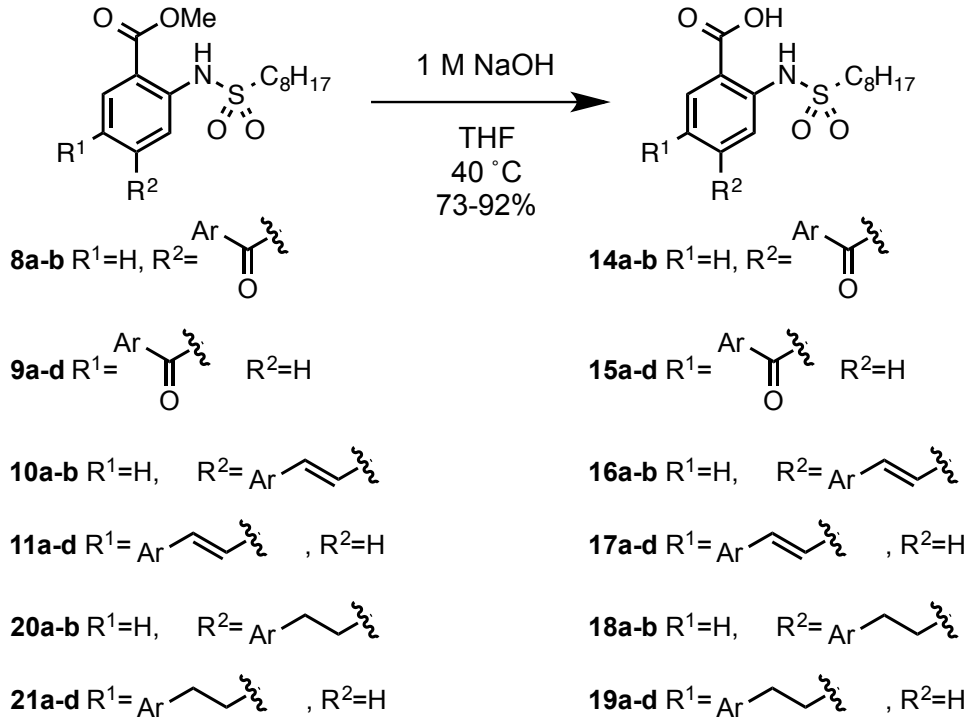
Methyl 2-(octanesulfonamido)-5-phenethylbenzoate (21a). 91% yield; ^{1}H NMR ($CDCl_3$) δ 10.32 (s, 1H), 7.88 (d, *J* = 2.1 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.31 (m, 3H), 7.20 (m, 3H), 3.95 (s, 3H), 3.14 (t, *J* = 7.8 Hz, 2H), 2.93 (s, 4H), 1.80 (m, 2H), 1.32 (m, 10H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.2, 140.8, 138.8, 136.0, 134.9, 130.9, 128.2, 128.2, 125.9, 117.9, 115.0, 52.3, 51.8, 37.4, 36.7, 31.5, 28.7, 28.6, 27.8, 23.1, 22.4, 13.9.



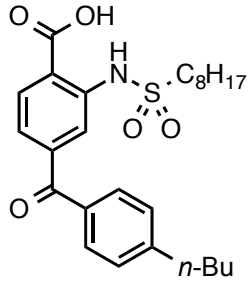
Methyl 5-(4-methoxyphenethyl)-2-(octanesulfonamido)benzoate (21b). 80% yield; ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 7.84 (d, *J* = 1.8 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.30 (dd, *J* = 2.1, 8.7 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 3.93 (s, 3H), 3.79 (s, 3H), 3.11 (t, *J* = 8.0 Hz, 2H), 2.85 (s, 4H), 1.77 (m, 2H), 1.30 (m, 10H), 0.85 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 168.3, 157.8, 138.9, 136.1, 135.0, 133.0, 131.0,

129.2, 117.9, 115.0, 113.7, 55.1, 52.4, 51.8, 37.0, 36.6, 31.5, 28.8, 28.7, 27.9, 23.2, 22.4, 13.9.

Preparation of Benzoic Acids 14a-b, 15a-d, 16a-b, 17a-b, 18a-b, and 19a-b

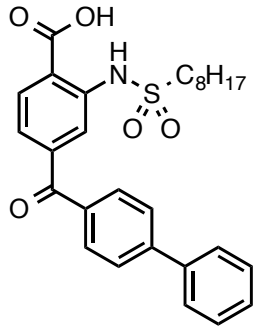


General Procedure. To the starting ester (0.5 mmol) dissolved in THF (3 mL) at room temperature was added 1 M NaOH (3 mL). The reaction mixture was heated to 40 ˚C until the starting material had disappeared by TLC (20% EtOAC in hexanes). When complete, the solution was acidified with 1 M HCl and extracted with 3 × 10 mL EtOAc. The combined organic extracts were dried over Na_2SO_4, concentrated *in vacuo*, and the resulting product was purified by recrystallization (EtOAc/hexanes) or column chromatography (3:7:90 AcOH:EtOAc:hexanes).

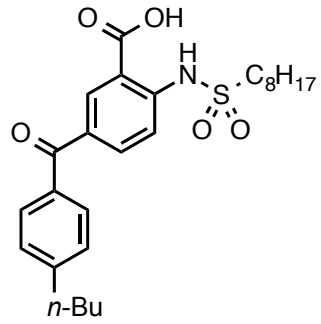


4-(4-*n*-Butylbenzoyl)-2-(octanesulfonamido)benzoic acid (14a). 85% yield; mp = 149-150 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.27 (s, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 8.04 (d, *J* = 1.5 Hz, 1H), 7.76-7.74 (m, 2H), 7.45 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 2H), 3.21-3.17 (m, 2H), 2.69 (t, *J* = 7.7 Hz, 2H), 1.85-1.77 (m, 2H), 1.67-1.60 (m, 2H),

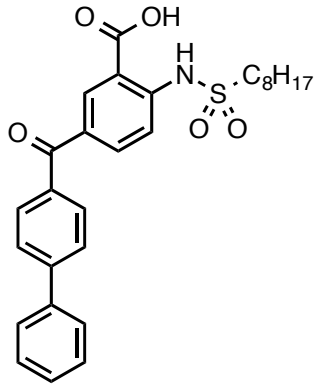
1.40-1.35 (m, 4H), 1.32-1.20 (m, 8H), 0.94 (t, J =7.3 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 195.11, 178.03, 172.12, 149.64, 144.50, 141.52, 133.71, 132.72, 130.63, 128.79, 123.15, 118.54, 116.61, 52.99, 35.91, 33.30, 31.78, 29.05, 28.99, 28.18, 23.50, 22.68, 22.48, 14.16, 14.02; Anal. ($C_{26}H_{35}NO_5S$) C, H, N.



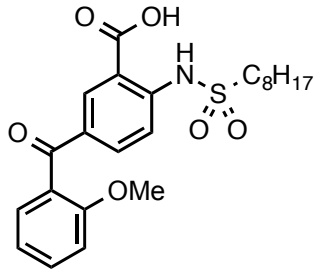
4-([1,1'-Biphenyl]-4-carbonyl)-2-(octanesulfonamido)benzoic acid (14b). 87% yield; mp = 188-189 ˚C; ^{1}H-NMR (400 MHz; $CDCl_3$): δ 8.27 (d, J = 8.2 Hz, 1H), 8.10 (d, J = 1.4 Hz, 1H), 7.92 (d, J = 8.3 Hz, 2H), 7.73 (d, J = 8.3 Hz, 2H), 7.67-7.64 (m, 2H), 7.51-7.42 (m, 4H), 3.21 (t, J = 7.9 Hz, 2H), 1.87-1.79 (m, 2H), 1.40-1.35 (m, 2H), 1.27-1.22 (m, 8H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ 194.73, 146.30, 144.17, 141.53, 139.64, 134.68, 132.69, 130.92, 129.01, 128.44, 127.34, 127.25, 123.08, 118.48, 52.98, 31.65, 28.95, 28.86, 28.08, 23.42, 22.57, 14.05; Anal. ($C_{28}H_{31}NO_5S$) C, H, N.



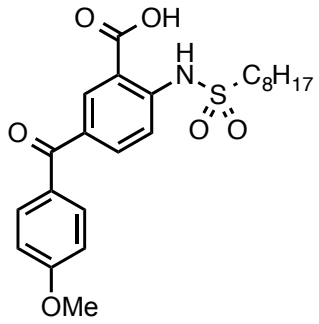
5-(4-*n*-Butylbenzoyl)-2-(octanesulfonamido)benzoic acid (15a). 90% yield; mp = 149-150 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.84 (t, 3H, J = 6.8), 0.95 (t, 3H, J = 7.2), 1.24 (m, 8H), 1.40 (m, 4H), 1.65 (m, 2H), 1.85 (m, 2H), 2.71 (t, 2H, J = 7.6), 3.25 (t, 2H, J = 8.0), 7.32 (d, 2H, J = 8.0), 7.72 (d, 2H, J = 8.0), 7.85 (d, 1H, J = 7.2), 8.05 (d, 1H, J = 7.2), 8.64 (s, 1H), 10.61 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9, 14.0, 22.4, 22.6, 23.4, 28.1, 28.9, 28.9, 31.6, 33.2, 35.8, 53.0, 113.3, 116.8, 128.7, 130.2, 131.7, 134.3, 135.0, 137.2, 144.9, 148.9, 171.1, 194.5; Anal. ($C_{26}H_{35}NO_5S$) C, H, N.



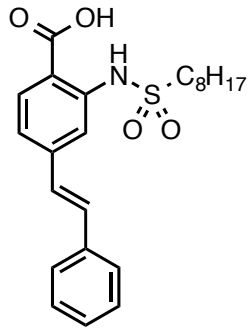
5-([1,1'-Biphenyl]-4-carbonyl)-2-(octanesulfonamido)benzoate (15b). 91% yield; mp = 210-211 °C; ^{1}H-NMR (400 MHz, DMSO) δ 0.87 (t, 3H, *J* = 6.8), 1.15-1.30 (m, 8H), 1.35-1.45 (m, 2H), 1.80-1.90 (m, 2H), 3.24 (t, 2H, *J* = 8.0), 3.95 (s, 3H), 7.40-7.55 (m, 3H), 7.70-7.90 (m, 7H), 8.06 (d, 1H, *J* = 8.8), 8.41 (s, 1H); ^{13}C-NMR (100 MHz, DMSO) δ 13.9, 22.0, 22.9, 27.1, 28.2, 28.3, 29.9, 31.1, 51.5, 115.1, 116.9, 126.8, 127.0, 128.4, 129.1, 130.3, 130.5, 133.6, 135.6, 135.8, 138.8, 144.2, 144.4; Anal. ($C_{28}H_{31}NO_5S$) C, H, N.



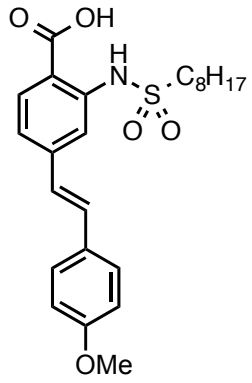
5-(2-methoxybenzoyl)-2-(octanesulfonamido)benzoic acid (15c). 81% yield; mp = 125-126 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) ppm 0.83 (t, 3H, *J* = 6.8), 1.22 (m, 8H), 1.40 (m, 2H), 1.78 (m, 2H), 3.37 (t, 2H, *J* = 8.0), 3.74 (s, 3H), 7.11 (t, 1H, *J* = 7.2), 7.18 (d, 1H, *J* = 7.6), 7.37 (dd, 1H, J_1 = 7.6, J_2 = 2.0), 7.55 (t, 1H, *J* = 7.6), 7.82 (d, 1H, *J* = 7.2), 7.99 (dd, 1H, J_1 = 8.8, J_2 = 2.0), 8.51 (d, 1H, *J* = 2.0), 11.00 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) ppm 13.4, 22.3, 23.3, 27.6, 28.7, 28.8, 31.5, 51.9, 55.1, 111.8, 114.1, 116.6, 120.8, 128.5, 129.2, 131.6, 132.2, 133.7, 135.6, 145.3, 157.2, 169.2, 193.3; Anal. ($C_{23}H_{29}NO_6S$) C, H, N.



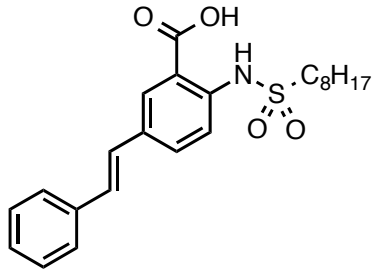
5-(4-Methoxybenzoyl)-2-(octanesulfonamido)benzoic acid (15d). 83% yield; mp = 132-133 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) ppm 0.84 (t, 3H, *J* = 6.8), 1.10-1.30 (m, 8H), 1.35-1.40 (m, 2H), 1.75-1.90 (m, 2H), 3.23 (t, 2H, *J* = 8.0), 3.90 (s, 3H), 6.98 (d, 2H, *J* = 8.0), 7.79 (d, 2H, *J* = 8.4), 7.83 (d, 1H, *J* = 8.8), 8.00 (d, 1H, *J* = 8.8), 8.58 (s, 1H), 10.63 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) ppm 14.0, 22.5, 23.3, 28.0, 28.8, 28.9, 31.6, 52.9, 55.5, 113.5, 113.8, 116.7, 129.4, 131.9, 132.4, 134.7, 136.8, 144.6, 163.6, 171.3, 193.5; Anal. ($C_{23}H_{28}NNaO_6S\bullet{}^{1}/_{4}(H_2O)$) C, H, N.



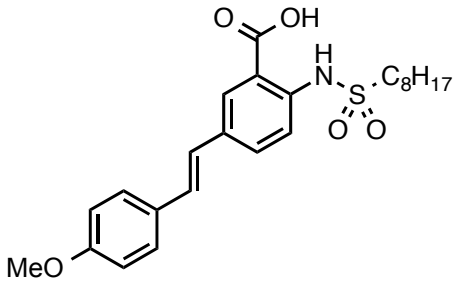
(*E*)-2-(octanesulfonamido)-4-styrylbenzoic acid (16a). 80% yield; mp = 91-92 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H, *J* = 7.2), 1.20-1.30 (m, 8H), 1.35-1.48 (m, 2H), 1.80-1.90 (m, 2H), 3.24 (t, 2H, *J* = 8.0), 7.10-7.44 (m, 7H), 7.57 (d, 2H, *J* = 11.2), 7.89 (s, 1H), 8.13 (d, 1H, *J* = 8.4), 10.28 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.0, 22.5, 23.3, 28.0, 28.8, 28.9, 31.6, 52.2, 112.5, 115.6, 120.3, 126.8, 127.0, 128.7, 128.8, 132.9, 133.3, 136.2, 142.0, 145.0, 172.5***;*** Anal. ($C_{23}H_{29}NO_4S$) C, H, N.



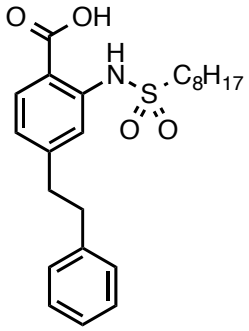
(*E*)-4-(4-methoxystyryl)-2-(octanesulfonamido)benzoic acid (16b). 91% yield; mp = 98-98 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.84 (t, 3H, *J* = 7.2), 1.10-1.30 (m, 8H), 1.30-1.40 (m, 2H), 1.75-1.85 (m, 2H), 3.20 (t, 2H, *J* = 8.0), 3.85 (s, 3H), 6.90-7.00 (m, 3H), 7.20-7.30 (m, 3H), 7.49 (d, 2H, *J* = 8.8), 7.84 (s, 1H), 8.08 (d, 1H, *J* = 8.4), 10.25; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.0, 22.5, 23.4, 28.0, 28.8, 28.9, 31.6, 52.1, 55.4, 112.0, 114.3, 115.2, 120.1, 124.7, 128.5, 129.0, 132.8, 132.9, 142.1, 145.4, 160.2, 172.2; Anal. ($C_{24}H_{30}NNaO_5S\bullet 1(H_2O)$) C, H, N.



(*E*)-2-(Octanesulfonamido)-5-styrylbenzoic acid (17a). 92% yield; mp = 94-95 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H, *J* = 7.2), 1.15-1.30 (m, 8H), 1.30-1.45 (m, 2H), 1.80-1.90 (m, 2H), 3.20 (t, 2H, *J* = 8.0), 7.00-7.10 (m, 2H), 7.20-7.40 (m, 3H), 7.52 (d, 2H, *J* = 8.4), 7.70-7.80 (m, 2H), 8.25 (s, 1H), 10.25 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.0, 22.5, 23.3, 28.0, 28.8, 28.9, 31.6, 52.3, 114.6, 118.1, 126.3, 126.5, 128.0, 128.7, 129.3, 130.4, 132.3, 133.2, 136.7, 140.4, 169.1; Anal. ($C_{23}H_{29}NO_4S\bullet{}^1/_4(H_2O)$) C, H, N.

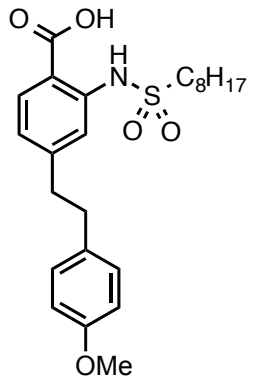


(*E*)-5-(4-methoxystyryl)-2-(octanesulfonamido)benzoic acid (17b). 90% yield; mp = 98-99 °C; ^{1}H-NMR (400 MHz, MeOD) δ 0.84 (t, 3H, *J* = 7.2), 1.15-1.25 (m, 8H), 1.30-1.40 (m, 2H), 1.65-1.75 (m, 2H), 3.17 (t, 2H, *J* = 8.0), 3.79 (s, 3H), 6.89 (d, 2H, *J* = 8.8), 6.95-7.10 (m, 2H), 7.46 (d, 2H, *J* = 8.8), 7.65-7.75 (m, 2H), 8.19 (s, 1H); ^{13}C-NMR (100 MHz, MeOD) δ 14.4, 23.6, 24.5, 28.8, 28.9, 29.9, 32.9, 52.3, 55.7, 115.2, 119.4, 121.1, 125.5, 128.9, 130.0, 130.8, 131.2, 132.8, 134.3, 141.0, 161.0, 172.3; Anal. ($C_{24}H_{31}NO_5S$) C, H, N.

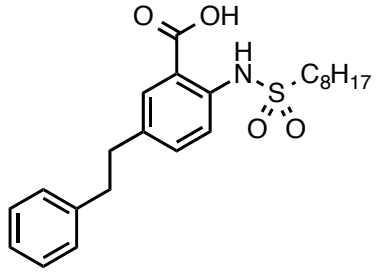


2-(Octanesulfonamido)-4-phenethylbenzoic acid (18a). 85% yield; mp = 94-95 °C; ^{1}H NMR (MeOD) δ 7.97 (d, *J* = 8.1 Hz, 1H), 7.46 (s, 1H), 7.22 (m, 2H), 7.13 (m, 3H), 6.97 (d, *J* = 8.1 Hz, 1H), 2.94 (m, 6H), 1.64 (m, 2H), 1.23 (m, 10H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 150.7, 142.3, 142.0, 133.1, 129.4, 129.3, 127.0, 124.3, 118.7,

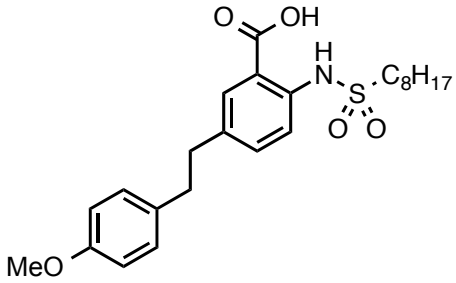
114.6, 51.9, 38.6, 37.8, 32.7, 29.9, 29.9, 28.7, 24.4, 23.6, 14.4. Anal ($C_{23}H_{31}NO_4S$) C, H, N.



4-(4-Methoxyphenethyl)-2-(octanesulfonamido)benzoic acid (18b). 87% yield; mp = 106-107 °C; ^{1}H NMR (MeOD) δ 7.95 (d, *J* = 8.1 Hz, 1H), 7.42 (s, 1H), 7.00 (d, *J* = 8.1 Hz, 2H), 6.93 (d, *J* = 8.1 Hz, 1H), 6.75 (d, *J* = 8.1 Hz, 2H), 3.70 (s, 3H), 2.89 (m, 6H), 1.61 (m, 2H), 1.17 (m, 10H), 0.85 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 159.3, 150.8, 142.3, 133.9, 133.0, 130.4, 124.2, 118.7, 114.7, 114.5, 55.5, 51.8, 38.8, 36.9, 32.7, 29.9, 29.8, 28.7, 24.3, 23.5, 14.4. Anal. ($C_{24}H_{33}NO_5S$) C, H, N.



2-(Octanesulfonamido)-5-phenethylbenzoic acid (19a). 89% yield; mp = 92-93 °C; ^{1}H NMR (MeOD) δ 7.89 (d, *J* = 2.1 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.34 (dd, *J* = 2.1, 8.7 Hz, 1H), 7.23 (m, 2H), 7.13 (m, 3H), 3.11 (t, *J* = 8.0 Hz, 2H), 2.88 (s, 4H), 1.68 (m, 2H), 1.23 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 142.3, 140.3, 137.6, 135.9, 132.8, 129.4, 129.2, 126.9, 119.0, 116.9, 52.0, 38.6, 37.9, 32.7, 29.8, 29.8, 28.8, 24.3, 23.5, 14.4. Anal. ($C_{23}H_{31}NO_4S$) C, H, N.



5-(4-Methoxyphenethyl)-2-(octanesulfonamido)benzoic acid (19b). 89% yield; mp = 102-103 °C; ^{1}H NMR (MeOD) δ 7.87 (d, *J* = 2.1 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 7.33 (dd, *J* = 2.4, 8.4 Hz, 1H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 3.73 (s, 3H),

3.12 (t, J = 8.0 Hz, 2H), 2.84 (s, 4H), 1.68 (m, 2H), 1.28 (m, 10H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (MeOD) δ 171.3, 159.3, 140.2, 137.8, 135.9, 134.3, 132.8, 130.4, 119.8, 117.0, 114.6, 55.5, 52.0, 38.1, 37.7, 32.7, 29.8, 29.8, 28.7, 24.3, 23.5, 14.3. Anal. ($C_{24}H_{33}NO_5S$) C, H, N.

Protein-Ligand Docking

The squash glycerol-3-phosphate acyltransferase coordinates used were from the PDB entry 1IUQ.[2] The resolution of the structure is 1.55 Å. Both *in silico* viewing and manipulation were carried out using Accelrys Discovery Studio, version 2.1. Glycerol, sulfate, and water molecules were removed prior to ligand docking experiments. The A chain was then designated as the receptor and typed with the CHARMm forcefield. A model of compound **1** was then created as the input ligand and docked into the active site of the receptor using the CDOCKER protocol. The docked ligand in Figure 2A in the main text was one of the resulting poses. Figure 2B was created by manually docking compound **14b** into the binding site obtained for compound **1** in Figure 2A.

Biological Testing

Mitochondrial Preparation. The mtGPAT assay has been reported previously.[3] The mitochondrial preparation was performed with the Mitochondria Isolation Kit (Sigma-Aldrich, Catalog # MITOISO1) according to the manufacturer's instructions. Specifically, the liver from a freshly-sacrificed BALB/c mouse was homogenized in 12 mL extraction buffer (isotonic solution, 10 mM HEPES, pH 7.5, containing 200 mM mannitol, 70 mM sucrose, 1 mM EGTA, 24 mg albumin), transferred to a 2 mL microcentrifuge tubes, and centrifuged at 1000 × g. The pellet was discarded and the supernatant was centrifuged at 3500 × g. The pellet was resuspended in extraction buffer, and the previous two centrifugation steps were repeated. After the final 3500 × g spin, the pellet was resuspended in storage buffer (10 mM HEPES, pH 7.4, containing 250 mM sucrose, 1mM ATP, 0.08 mM ADP, 5 mM sodium succinate, 2 mM K_2HPO_4, and 1 mM DTT) and used as the mitochondrial preparation in the GPAT Assay

GPAT Assay. The mitochondrial preparation (3 µL) including mtGPAT was added to 200 µL of an incubation mixture containing 75 mM Tris/HCl, pH 7.4; 4 mM $MgCl_2$; 2 mg/mL bovine serum albumin; 7.6 mCi/mmol ^{14}C-labeled glycerol-3-phosphate, 50 µM palmitoyl-CoA, and 1 µL of varying inhibitor concentrations (0, 0.625, 2.5, 10, 40 µg/mL in DMSO) to initiate the reaction. After 10 min, the reaction was terminated by adding 3 mL $CHCl_3$:MeOH (1:2) and 600 µL of 1% perchloric acid. After an additional 5 min, 1 mL $CHCl_3$ and 1 mL 1% perchloric acid were added, and the upper aqueous layer was removed. After washing three times with 2 mL of 1% perchloric acid, the organic layer was evaporated under nitrogen, and the amount of ^{14}C present was measured by scintillation counting to determine the extent of reaction inhibition. Data points were recorded in triplicate, and IC_{50} values were calculated based on the amount of test

inhibitor required to produce 50% of mtGPAT activity observed in the absence of inhibitor but in the presence of DMSO vehicle control.

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