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The Consequences of Chirality in Crowded Arenes––Macromolecular Helicity, Hierarchical Ordering, and Directed Assembly

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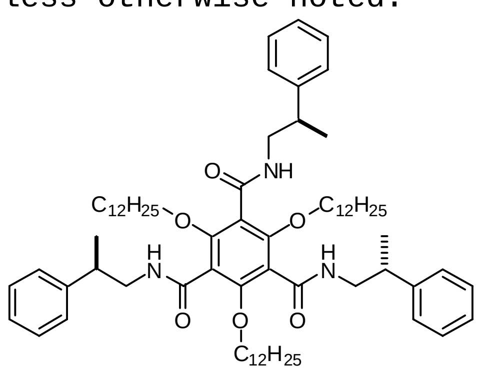
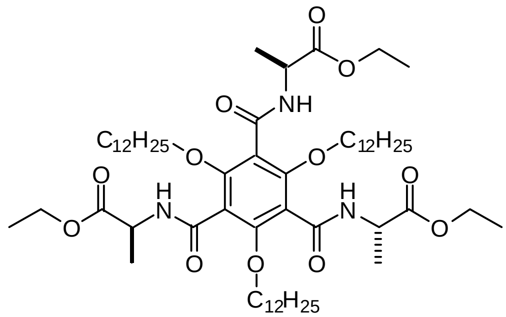
Synthesis.

General. ^{1}H NMR (400 MHz or 300MHz) and ^{13}C NMR (100 MHz or 75MHz) were recorded on a Bruker DRX 300 or DRX 400 spectrometer. Infrared spectra were recorded on a BioRad FTS 7000 FT-IR spectrometer, using a Specac Benchmark Series 11160 ATR with a thermostatically controlled zinc selenide crystal heating stage for elevated temperature spectra. All reagents were purchased from Aldrich, Acros, Bachem, or Fluka and used as received. Flash chromatography was performed using 230-400 mesh silica gel.

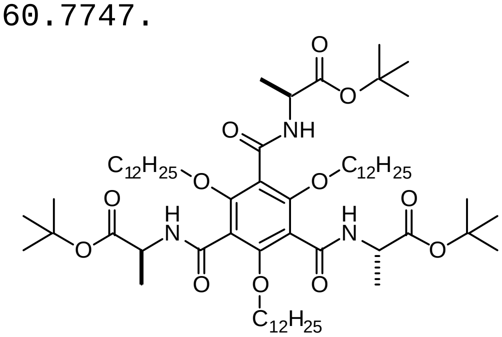
General procedure for the synthesis. To a 10 mL flask charged with a magnetic stir bar was added sequentially 2,4,6-tridodecyloxy-1,3,5-benzenetricarbonyl trichloride (0.110 g, 0.1344 mmol), CH_2Cl_2 (1.5 mL), Et_3N [62 μL, 0.4 mmol (twice the equivalents if the amine hydrochloride was used)], and the amine or amine hydrochloride (0.4 mmol). After stirring for 18 h, the mixture was diluted with CH_2Cl_2 (10 mL) and H_2O (10 mL). The phases were seperated and the aqueous one extracted three times with CH_2Cl_2 (10 mL each). The organic phases were combined, dried over sodium sulfate, and concentrated under reduced pressure. All samples were purified with flash chromatography or recrystallization unless otherwise noted.



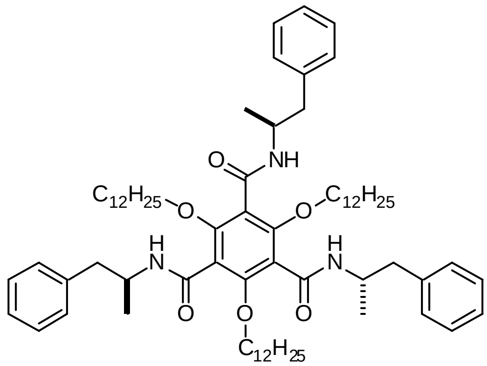
(3a). (103 mg, 0.0925 mmol, 69%). $[\alpha]^{23}_{D}$=-37.8° (c=0.12, $CHCl_3$), from (S)-(-)-β-Methylphenethylamine; $[\alpha]^{23}_{D}$=+37.9° (c=1.0, $CHCl_3$), from (R)-(+)-β-Methylphenethylamine;. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.22 (m, 5H), 5.88 (bt, 1H), 3.84 (t, *J* = 6.5 Hz, 2H), 3.72 (p, *J* = 6.75 Hz, 1H), 3.48 (m, 1H), 3.01 (h, *J* = 7.1 Hz, 1H), 1.58 (m, 3H), 1.27 (m, 20H), 0.90 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 155.9, 144.3, 130.1, 128.3, 126.4, 122.4, 76.7, 47.1, 41.2, 39.1, 32.2, 30.6, 30.0, 29.9, 28.6, 26.3, 23.1, 19.5, 19.2, 15.3, 13.8. IR (thin film) 3295, 3086, 3060, 3029, 2952, 2920, 2851, 1638, 1581, 1537, 1467, 1454, 1429, 1378, 1289, 1130, 1105, 1048, 1016, 959 cm^{-1}; HRMS (FAB $M+H^{+}$) calcd for $C_{72}H_{112}N_3O_6$ 1114.8551, found 1114.8530.



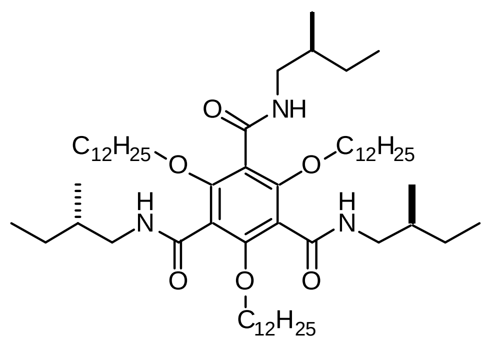
(3b). (95 mg, 0.0897 mmol, 58%). $[\alpha]^{23}_{D}$=-5.9° (c=0.90, $CHCl_3$), from (L)-Alanine Ethyl Ester. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (d, *J* = 7.0 Hz, 1H), 4.73 (p, *J* = 7.1Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.00 (m, 2H), 1.65 (p, *J* = 7.2 Hz, 2H), 1.52 (d, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.26 (m, 18H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 164.1, 156.7, 122.0, 77.1, 62.0, 49.1, 32.3, 30.5, 30.1, 30.0, 29.9, 29.8, 26.1, 23.1, 18.9, 14.6. IR (thin film, 160°C) 3289, 2922, 2850, 1750, 1739, 1639, 1572, 1522, 1461, 1450, 1428, 1372, 1328, 1267, 1194, 1139, 1094, 1022, 967 cm^{-1}; HRMS (FAB $M+H^{+}$) calcd for $C_{60}H_{106}N_3O_{12}$ 1060.7777, found 1060.7747.



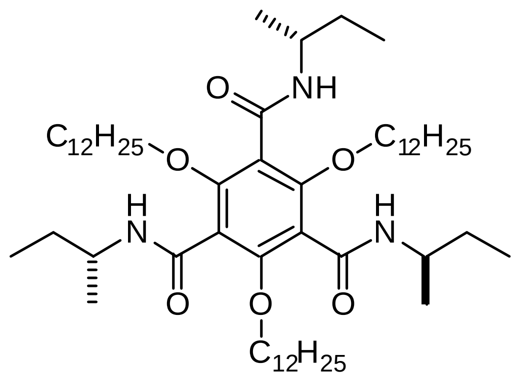
(3d). (96 mg, 0.0839 mmol, 71%). $[\alpha]^{23}_{D}$=-7.8° (c=0.90, $CHCl_3$), from (L)-Alanine *tert*-Butyl Ester. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.52 (d, *J* = 7.0 Hz, 1H), 4.60 (p, *J* = 7.1Hz, 1H), 3.98 (t, *J* = 6.7 Hz, 2H), 1.61 (p, *J* = 7.0 Hz, 2H), 1.48 (s, 12H), 1.25 (m, 18H), 0.88 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 164.1, 156.5, 122.1, 82.4, 50.3, 48.7, 32.3, 30.4, 30.0, 29.8, 29.1, 28.6, 28.3, 27.5, 26.0, 23.1, 19.8, 18.1, 15.3, 13.8. IR (thin film, 100°C) 3411, 3300, 2983, 2961, 2922, 2856, 1739, 1644, 1578, 1511, 1450, 1367, 1339, 1256, 1217, 1144, 1100, 972 cm^{-1}; HRMS (FAB $M+H^{+}$) calcd for $C_{66}H_{118}N_3O_{12}$ 1144.8716, found 1144.8658.



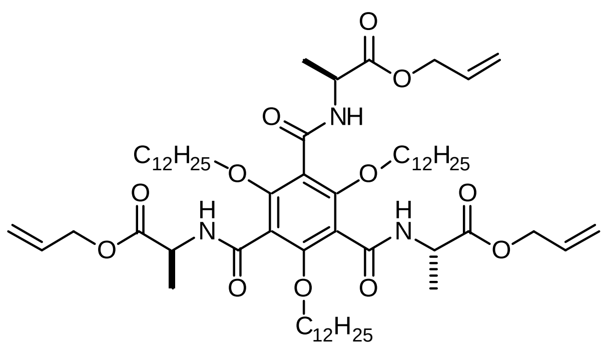
(3e). (115 mg, 0.1033 mmol, 74%). $[\alpha]^{23}_{D}$=-4.9° (c=0.65, $CHCl_3$), from (S)-(-)-α-Methylphenethylamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.23 (m, 5H), 5.86 (br d, *J* = 7.7 Hz, 1H), 4.42 (h, *J* = 6.4 Hz, 1H), 3.90 (t, *J* = 6.5 Hz, 2H), 3.05 (dd, *J* = 5.2, 13.3 Hz, 1H), 2.70 (dd, *J* = 8.0, 13.3 Hz, 1H), 1.61 (p, *J* = 6.9 Hz, 3H), 1.23 (m, 20H), 0.90 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 156.0, 138.3, 129.8, 128.9, 127.0, 122.5, 76.7, 47.5, 43.0, 32.3, 30.6, 30.1, 30.0, 29.8, 26.2, 23.1, 20.0, 14.6. IR (thin film) 3295, 3085, 3060, 3029, 2952, 2921, 2851, 1632, 1581, 1530, 1467, 1454, 1435, 1378, 1340, 1302, 1270, 1130, 1098, 1079, 1048, 1029, 978 cm^{-1}; HRMS (FAB $M+H^+$) calcd for $C_{72}H_{112}N_3O_6$ 1114.8551, found 1114.8568.



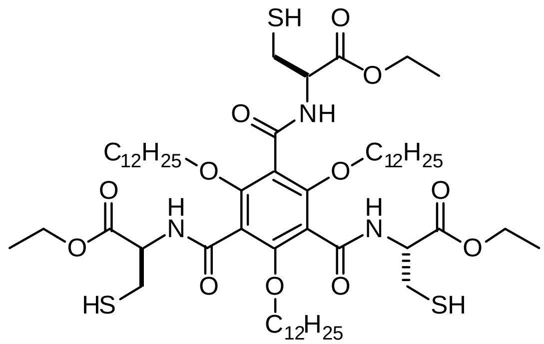
(3f). (114 mg, 0.1174 mmol, 78%). $[\alpha]^{23}_{D}$=+3.4° (c=0.12, $CHCl_3$), from (S)-(-)-2-Methylbutylamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (br s, 1H), 3.98 (t, *J* = 6.3 Hz, 2H), 3.37 (m, 1H), 3.23 (m, 1H), 1.65 (m, 2H), 1.49 (m, 1H), 1.27 (m, 20H), 0.96 (t, *J* = 6.1 Hz, 6H), 0.90 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 156.0, 122.9, 76.9, 46.2, 35.2, 32.4, 30.6, 30.1, 30.1, 29.9, 29.8, 27.4, 26.2, 23.1, 17.7, 14.6, 11.7. IR (thin film) 3295, 3073, 2959, 2921, 2851, 1638, 1575, 1537, 1460, 1429, 1378, 1289, 1238, 1111, 1054, 978 cm^{-1}; HRMS (FAB $M+H^+$) calcd for $C_{60}H_{112}N_3O_6$ 970.8551, found 970.8538.



(3g). (137 mg, 0.1470 mmol, 65%). $[\alpha]^{23}_{D}$=-25.7° (c=0.13, $CHCl_3$), from (R)-(-)-*sec*-Butylamine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (d, *J* = 7.9 Hz, 1H), 4.07 (h, *J* = 7.0 Hz, 1H), 3.99 (t, *J* = 6.8 Hz, 2H), 1.67 (p, *J* = 7.2 Hz, 2H), 1.57 (m, 1H), 1.26 (m, 20H), 1.22 (d, *J* = 6.6 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 155.8, 123.0, 76.8, 47.8, 32.4, 30.6, 30.1, 30.1, 30.0, 29.9, 29.8, 29.8, 26.1, 23.1, 20.4, 14.6, 10.9. IR (thin film) 3283, 2952, 2921, 2851, 1632, 1581, 1530, 1460, 1448, 1378, 1340, 1289, 1251, 1156, 1098, 1029, 997, 952 cm^{-1}; HRMS (FAB M+H$^+$) calcd for $C_{57}H_{106}N_3O_6$ 928.8082, found 928.8097.



(3h). (102 mg, 0.0933 mmol, 64%). $[\alpha]^{23}_{D}$=-8.0° (c=0.93, $CHCl_3$), from (L)-Alanine Allyl Ester. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (d, *J* = 6.7 Hz, 1H), 5.92 (m, 1H), 5.35 (d, *J* = 17.2 Hz, 1H), 5.27 (d, *J* = 10.4 Hz, 1H), 4.76 (t, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 4.8 Hz, 2H), 3.98 (d, *J* = 4.8 Hz, 2H), 1.63 (m, 2H), 1.53 (d, *J* = 7.0 Hz, 3H), 1.25 (m, 18H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 164.1, 156.7, 131.9, 121.9, 119.3, 77.1, 66.4, 49.0, 32.3, 30.4, 30.1, 29.9, 29.8, 26.1, 23.1, 18.9, 14.6. IR (thin film, 100°C) 3270, 2956, 2920, 2854, 1738, 1637, 1576, 1530, 1454, 1378, 1328, 1282, 1216, 1196, 1130, 1099, 988, 922 cm^{-1}; HRMS (FAB M+H$^+$) calcd for $C_{63}H_{105}N_3O_{12}$ 1096.7777, found 1096.7765.



Procedure for the synthesis of (3c). To a 10 mL flask with a magnetic stirbar was added sequentially 2,4,6-tridodecyloxy-1,3,5-benzenetricarbonyl trichloride (0.111 g, 0.1356 mmol), CH_2Cl_2 (4 mL), pyridine (73 µL, 0.8951 mmol), and cysteine hydrochloride ethyl ester (83.1 mg, 0.4476 mmol). After stirring for 18 h, the mixture was diluted with NH_4Cl (sat. aqueous, 10 mL). The phases were seperated and the aqueous one extracted twice with CH_2Cl_2 (10 mL each). The organic phases were combined, dried over magnesium sulfate, concentrated under reduced pressure. Silica gel chromatography (1% MeOH/CH_2Cl_2) resulted in a white waxy solid (72.8 mg, 0.06294 mmol, 47%). $[\alpha]^{23}_{D}$=+10.1° (c=0.24, $CHCl_3$), from (L)-Cysteine Ethyl Ester. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (d, J = 6.7 Hz, 1H), 5.01 (m, 1H), 4.30 (m, 2H), 4.03 (t, J = 6.7 Hz, 2H), 3.22 (m, 1H), 3.07 (m, 1H), 1.66 (m, 2H), 1.54 (t, J = 8.5 Hz, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.26 (s, 18H), 0.90 (t, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 164.4, 156.7, 121.9, 77.4, 62.6, 54.7, 32.4, 30.5, 30.1, 30.1, 29.9, 29.8, 27.1, 26.1, 23.1, 14.7, 14.6. IR (thin film, 100°C) 3294, 2956, 2922, 2850, 1744, 1656, 1644, 1572, 1511, 1500, 1461, 1428, 1367, 1333, 1311, 1261, 1200, 1094, 1028 cm^{-1}; HRMS (FAB M+H$^+$) calcd for $C_{60}H_{106}N_3O_{12}S_3$ 1156.6939, found 1156.6947.

Differential scanning calorimetry:

	heating cycle			cooling cycle		
3a	162 (4.8)	191 (3.8)	233 (38.5)	226 (-31.4)	183 (-3.5)	84 (-4.2)
3b	113 (5.9)	141 (3.1)	172 (17.6)	163 (-17.9)	138 (-2.7)	106 (-6.1)
3c			164 (27.2)	151 (-23.8)		
3d			103 (8.8)	82 (-7.5)		
3e			249 (50.4)	243 (-46.9)		
3f	65 (4.8)	90 (2.6)	254 (30.1)	243 (-22.0)		63 (-4.1)
3g	54 (2.2)	98 (2.6)	248 (18.6)	240 (-15.4)		48 (-2.9)
3h	82 (12.9)	113 (10.5)	174 (27.2)	167 (-26.1)	100 (-9.7)	56 (-12.0)

Table 1. Differential Scanning Calorimetry for **3a-h,** temperature in degrees Celsius (ΔH in kJ/mole).