Synthesis of axially chiral dendrimers containing *meta*-terphenyl peripheral groups and a chiral binol core

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Fréchet-type poly(arylether) dendritic bromides carrying *m*-terphenyl peripheral groups were synthesised up to second generation by convergent methodology. Simple *O*-alkylation of chiral (*S*)-BINOL with the dendritic bromides afforded the corresponding axially chiral dendrimers. The molar optical rotation values of the dendrimers become increasingly negative as the dendrimer generation increases.

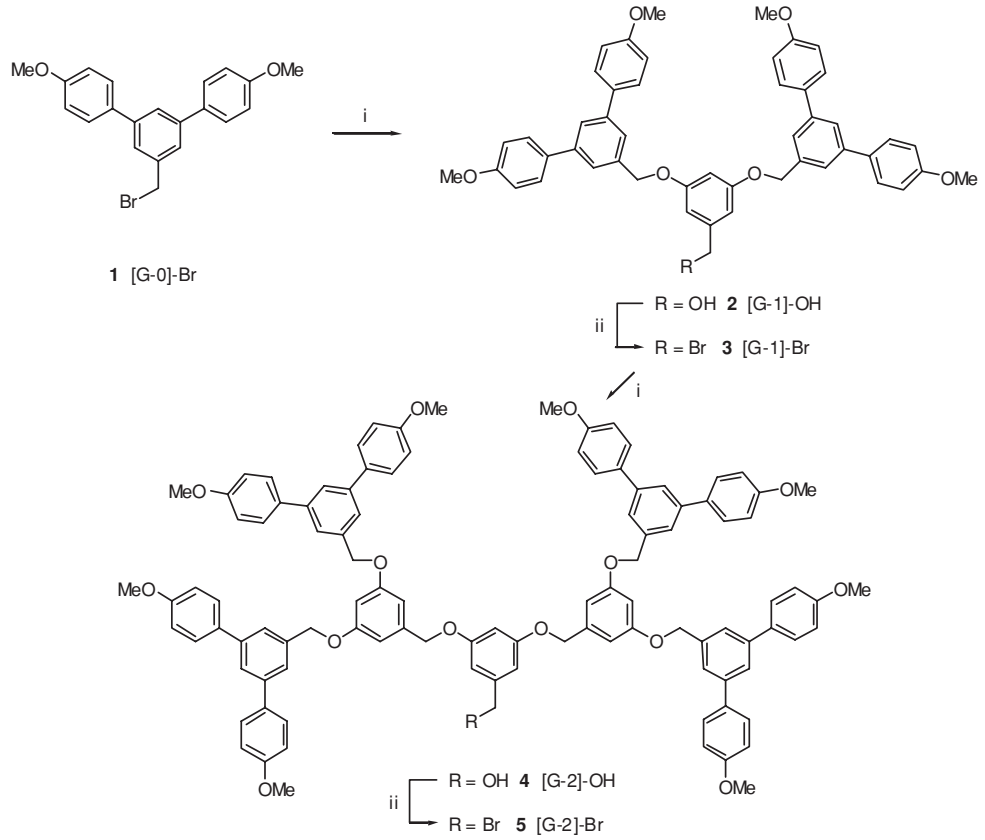
Keywords: chiral dendrimers, *m*-terphenyl, (*S*)-BINOL, optical rotation

The angular nature of *m*-terphenyls makes them ideal building blocks for the synthesis of various types of cyclophanes,[1-10] including chiral cyclophanes based on (*S*)-(−)-1,1′-bi-2-naphthol [(*S*)-BINOL].[9] In order to extend their utility to other supramolecular systems, we planned to introduce *m*-terphenyls as peripheral groups in Fréchet-type poly(arylether) dendrimers[11] having a (*S*)-BINOL core. The resulting axially chiral dendrimers[12-14] might find application as asymmetric catalysts, enantioselective fluorescent sensors and in chiral molecular recognition. Further, the *m*-terphenyl peripheral groups might provide conformational rigidity to the dendrimers in addition to electron rich-pockets for achiral molecular recognition at the dendrimer surface. We report here synthesis and optical rotation values of axially chiral Fréchet-type dendrimers containing *m*-terphenyl peripheral groups and a (*S*)-BINOL core.

Results and discussion

The synthetic strategy for the preparation of the *m*-terphenyl-capped dendrons utilised a convergent methodology.[11,15] Coupling of 2.1 equiv. of the *m*-terphenyl bromide[15] **1**, [G-0]-Br, with 1 equiv. of 3,5-dihydroxybenzyl alcohol in the presence of K_2CO_3 and 18-crown-6 in refluxing acetone gave the first generation dendritic alcohol **2**, [G-1]-OH, in 73% yield. The alcohol **2** was treated with PBr_3 in CH_2Cl_2 to afford the corresponding dendritic bromide **3**, [G-1]-Br in 68% yield. The second generation dendritic bromide **5**, [G-2]-Br, was built in a similar way by the repetition of the above two reactions namely, *O*-alkylation and bromination (Scheme 1).

Heating 2 equiv. of each of the dendritic bromides **1**, **3** and **5** under reflux with 1 equiv. of (*S*)-BINOL in the presence of K_2CO_3 and 18-crown-6 in acetone afforded the dendrimers **6**, **7** and **8** in 80, 65 and 62% yields respectively after column chromatography (Scheme 2).



Scheme 1 *Reagents and conditions:* (i) 3,5-dihydroxy benzyl alcohol, K_2CO_3, 18-crown-6, acetone, reflux, 48 h; afforded **2** (73%)and 4 (64%); (ii) PBr_3, CH_2Cl_2, 0 °C to rt, 2 h; afforded **3** (68%) and **5** (54%).

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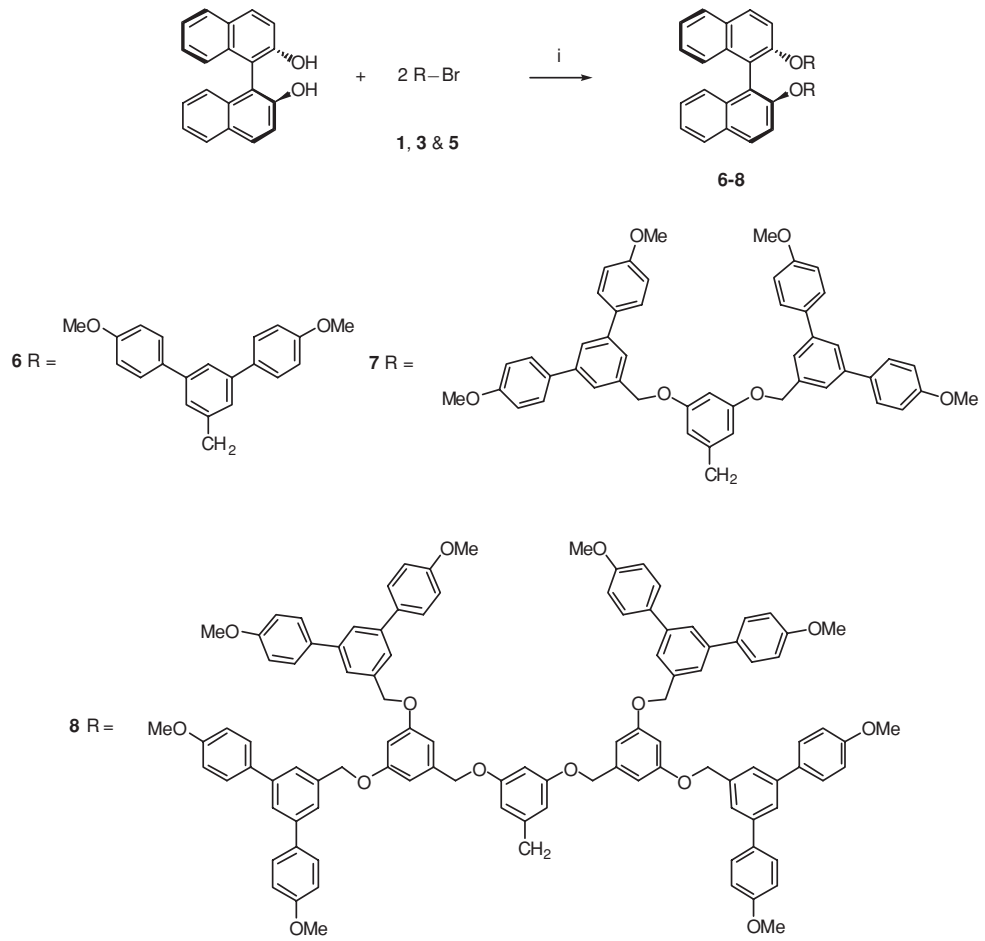

Scheme 2 *Reagents and conditions:* (i) K_2CO_3, 18-crown-6, acetone, reflux, 48 h; afforded **6** (80%), **7** (65%) and **8** (62%).

In the ^{1}H NMR spectra of the dendrimers, the intra-annular *m*-terphenyl protons (proton at 2'-position of the *m*-terphenyl unit) resonate in the region 7.31–7.65 ppm as singlets, the *m*-terphenyl protons *ortho* to methoxy groups resonate in the region 6.76–6.96 ppm as doublets and the aromatic and methylene protons of each layer of the monomer units resonate in separate regions. In case of dendrimer **7**, the methylene protons attached to BINOL unit appears as two doublets whereas they appear as singlets in case of dendrimers **6** and **8**. All the dendrimers show absorption maxima around 268 nm and emission maxima around 348 nm in $CHCl_3$.

The optical rotation values recorded for the dendrimers in $CHCl_3$ at 25 °C are shown in Table 1.

It is clear from Table 1 that the molar optical rotation value becomes increasingly negative as the dendrimer generation increases. This effect may be due to the increase in the torsional angle between the two naphthyl units caused by the steric repulsion between the dendritic wedges.[12]

Table 1 The optical rotation values for the dendrimers **6-8**

Dendrimer	$[\alpha]_D^{25}$	Molecular weight	Molar rotation
6	–24.2	891.08	–216
7	–18.7	1740.07	–325
8	–15.5	3438.06	–533

Experimental

General

Melting points were determined by using a Toshniwal melting point apparatus by open capillary tube method and were uncorrected. The optical rotations were recorded on Autopol-II automatic spectrometer with cell length of 10 cm using D-line of sodium at 25 °C. UV-vis spectra were recorded on a Shimadzu 260 spectrophotometer and emission spectra on Perkin-Elmer LS-5B spectrophotometer. IR spectra were recorded on Shimadzu FTIR-8300 spectrophotometers. ^{1}H and ^{13}C NMR spectra were recorded on Jeol 500 MHz and Jeol 400 MHz spectrometers. The FAB-MS spectra were recorded on a Jeol SX 102/DA-6000 mass spectrometer using a *m*-nitro benzyl alcohol (NBA) matrix and MALDI-TOF MS spectra on Voyager-DE PRO mass spectrometer using a α-cyano-4-hydroxycinnamic acid (CHCA) matrix. Elemental analyses were performed on a Perkin-Elmer 240B elemental analyser.

General procedure for the synthesis of dendritic alcohols

A mixture of the corresponding dendritic bromide (2.1 equiv.), 3,5-dihydroxy benzyl alcohol (1.0 equiv.), dried K_2CO_3 (3.0 equiv.) and 18-crown-6 (0.1 equiv.) in dry acetone (30 ml) was vigorously stirred at reflux for 48 h under a nitrogen atmosphere. The reaction mixture was then allowed to cool to room temperature and filtered. The filtrate was evaporated under vacuum and the residue was extracted with $CHCl_3$ (50 ml). The organic layer was separated, washed with water (2 × 50 ml), brine (1 × 50 ml), dried (anhydrous Na_2SO_4) and evaporated to give the crude alcohol, which was purified by column chromatography (SiO_2).

Dendritic alcohol **2** *{[G-1]-OH}*: The dendritic alcohol **2** was obtained as a white solid from 3,5-dihydroxybenzyl alcohol (600 mg, 4.28 mmol) and **1** (3.45 g, 8.99 mmol) after eluting the column with $CHCl_3$. Yield 73%; m.p. 112 °C; IR (cm^{-1}) 3421 (O–H); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 12H), 4.61 (s, 2H), 5.08 (s, 4H), 6.62 (distorted t, 1H), 6.66 (distorted d, 2H), 6.96 (d, *J* = 8.8 Hz, 8H), 7.52–7.56 (m, 12H), 7.65 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 65.2, 70.2, 101.3, 105.7, 114.2, 124.3, 124.9, 128.2, 133.4, 137.7, 141.6, 143.5, 159.3, 160.2; FAB-MS: *m/z* 744 (M^+); Anal. Calcd for $C_{49}H_{44}O_7$: C, 79.01, H, 5.95; Found: C, 79.33, H, 5.79%.

Dendritic alcohol **4** *{[G-2]-OH}:* The dendritic alcohol **4** was obtained as a white solid from 3,5-dihydroxy benzyl alcohol (120 mg, 0.856 mmol) and **2** (1.45 g, 1.80 mmol) after eluting the

column with $CHCl_3$/EtOAc (9.5:0.5, v/v). Yield 64%; m.p. 110 °C; IR (cm^{-1}) 3420 (O–H); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82 (s, 24H), 4.57 (s, 2H), 4.96 (s, 4H), 5.10 (s, 8H), 6.54 (distorted t, 1H), 6.59 (distorted d, 2H), 6.65 (distorted t, 2H), 6.73 (distorted d, 4H), 6.96 (d, *J* = 8.8 Hz, 16H), 7.53–7.57 (m, 24H), 7.66 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 65.2, 69.1, 70.3, 101.3, 101.8, 105.9, 106.5, 114.2, 124.3, 125.0, 128.3, 133.5, 137.7, 139.4, 141.7, 159.3, 160.1, 160.2; FAB-MS: *m/z* 1592 (M^+); Anal. Calcd for $C_{105}H_{92}O_{15}$: C, 79.12, H, 5.82; Found: C, 78.98, H, 5.87%.

General procedure for the conversion of the dendritic alcohol into the corresponding bromide

To a stirred suspension of the corresponding dendritic alcohol (1.0 equiv.) in CH_2Cl_2 (10 ml) was added dropwise a solution of PBr_3 (3.0 equiv.) in CH_2Cl_2 (20 ml) at 0 °C. The reaction mixture was stirred at room temperature for 2 h and then quenched by the addition of ice water. The organic layer was separated, washed with water (2 × 25 ml), satd. $NaHCO_3$ solution (1 × 25 ml), dried (anhydrous Na_2SO_4) and evaporated to give the crude dibromide, which was purified by column chromatography (SiO_2) using hexane/CH_2Cl_2 (1:1-1:8 v/v) as the eluent.

Dendritic bromide **3** *{[G-1]-Br}*: The dendritic bromide **3** was obtained as a white foam-like solid by the bromination of **2** (2.0 g, 2.68 mmol) with PBr_3 (0.77 ml, 8.10 mmol). Yield 68%; m.p. 202 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (s, 12H), 4.44 (s, 2H), 5.12 (s, 4H), 6.65 (distorted t, 1H), 6.71 (distorted d, 2H), 6.99 (d, *J* = 8.6 Hz, 8H), 7.54–7.59 (m, 12H), 7.69 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.8, 55.5, 70.4, 102.4, 108.3, 114.4, 124.5, 125.2, 128.4, 133.5, 137.6, 140.0, 141.8, 159.4, 160.2; FAB-MS: *m/z* 807 (M^+); Anal. Calcd for $C_{49}H_{43}BrO_6$: C, 72.86, H, 5.37; Found: C, 72.66, H, 5.42%.

Dendritic bromide **5** *{[G-2]-Br}*: The dendritic bromide **5** was obtained as a white foam-like solid by the bromination of **4** (500 mg, 0.314 mmol) with PBr_3 (0.09 ml, 0.948 mmol). Yield 54%; m.p. 125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 24H), 4.27 (s, 2H), 4.88 (s, 4H), 5.03 (s, 8H), 6.46 (distorted t, 1H), 6.53 (distorted d, 2H), 6.59 (distorted t, 2H), 6.64 (distorted d, 4H), 6.88 (d, *J* = 8.8 Hz, 16H), 7.45–7.49 (m, 24H), 7.58 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.6, 55.3, 70.1, 70.3, 101.8, 102.2, 106.5, 108.3, 113.4, 114.2, 124.3, 125.0, 128.3, 133.5, 137.7, 139.2, 141.7, 159.3, 160.0, 160.2; FAB-MS: *m/z* 1655 (M^+); Anal. Calcd for $C_{105}H_{91}BrO_{14}$: C, 76.12, H, 5.54; Found: C, 76.38, H, 5.56%.

General procedure for the synthesis of axially chiral dendrimers

A mixture of the corresponding dendritic bromide (2.0 equiv.), (S)-BINOL (1.0 equiv.), 18-crown-6 (0.1 equiv.) and dried K_2CO_3 (5.0 equiv.) in dry acetone (25 ml) was heated under reflux with vigorous stirring for 48 h under nitrogen. The reaction mixture was then allowed to cool to room temperature and the salts were removed by filtration. The filtrate was evaporated under vacuum and the residue was subjected to column chromatography (SiO_2).

The dendrimer **6**: The dendrimer **6** was obtained as a white solid from the dendritic bromide **1** (402 mg, 1.05 mmol) and (S)-BINOL (150 mg, 0.524 mmol) after eluting the column with hexane/$CHCl_3$ (1:1, v/v). Yield 80 %; m.p. 110 °C; $[\alpha]_D^{25}$ –24.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (s, 12H), 4.81 (s, 4H), 6.76 (d, *J* = 8.8 Hz, 8H), 6.83 (distorted d, 4H), 7.08 (d, *J* = 8.8 Hz, 8H), 7.12–7.23 (s, 8H), 7.31 (s, 2H), 7.68 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 71.2, 114.3, 115.7, 120.7, 123.7, 123.9, 124.3, 125.7, 126.7, 128.2, 128.4, 129.7, 133.6, 134.4, 138.5, 141.2, 154.3, 159.4; FAB-MS: *m/z* 890 (M^+); Anal. Calcd for $C_{62}H_{50}O_6$: C, 83.57, H, 5.66; Found: C, 83.38, H, 5.57.

The dendrimer **7**: The dendrimer **7** was obtained as a white solid from the dendritic bromide **3** (282 mg, 0.349 mmol) and (S)-BINOL (50 mg, 0.175 mmol) after eluting the column with hexane/$CHCl_3$ (1:4, v/v). Yield 65 %; m.p. 103 °C; $[\alpha]_D^{25}$ –18.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 24H), 4.66 (s, 8H), 5.01, 5.05 (2 × d, *J* = 12.6 Hz, 4H), 6.28 (distorted d, 4H), 6.42 (distorted t, 2H), 6.96 (d, *J* = 8.6 Hz, 16H), 7.20-7.28 (m, 6H), 7.44-7.47 (m, 10H), 7.55 (d, *J* = 8.6 Hz, 16H), 7.65 (s, 4H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.86 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4, 70.0, 71.0, 101.5, 105.2, 114.3, 115.9, 120.8, 124.0, 124.3, 124.6, 125.0, 125.5, 126.6, 128.4, 129.5 (two peaks), 133.6, 134.3, 137.8, 140.1, 141.7, 154.1, 159.4, 159.9; MALDI-TOF-MS: *m/z* 1761 (M^+ + Na); Anal. Calcd for $C_{118}H_{98}O_{14}$: C, 81.45, H, 5.68; Found: C, 81.67, H, 5.70%.

The dendrimer **8**: The dendrimer **8** was obtained as a white solid from the dendritic bromide **5** (116 mg, 0.070 mmol) and (S)-BINOL (10 mg, 0.035 mmol) after eluting the column with $CHCl_3$. Yield 62 %; m.p. 128 °C; $[\alpha]_D^{25}$ –15.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 48H), 4.32 (s, 8H), 4.86 (s, 16H), 5.01 (s, 4H), 6.01 (s, 4H), 6.15 (s, 2H), 6.51 (s, 12H), 6.80 (d, *J* = 8.3 Hz, 32H), 7.08-7.20 (m, 6H), 7.38–7.45 (m, 50H), 7.51 (s, 8H), 7.61 (distorted d, 2H), 8.01 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 69.6, 70.1, 70.3, 101.8, 105.2, 106.6, 113.4, 114.2, 115.5, 120.6, 123.5, 124.2, 124.8, 125.0, 126.4, 128.2, 129.3, 129.7, 130.6, 133.4, 134.1, 137.8, 139.3, 139.8, 141.6, 159.3, 159.6, 160.1, 160.2; MALDI-TOF-MS: *m/z* 3457 (M^+ + Na); Anal. Calcd for $C_{230}H_{194}O_{30}$: C, 80.35, H, 5.69; Found: C, 80.63, H, 5.55%.

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