

The Introduction of Asymmetry into Alkyl-Decorated Fréchet-Type Dendrons

Edwin C. Constable,^{*,[a]} Stefan Graber,^[a] B. A. Hermann,^[b] Catherine E. Housecroft,^{*,[a]} Michael S. Malarek,^[a] and Lukas J. Scherer^[a]**Keywords:** Fréchet dendrons / Alkyl tails / Dendrimers / Asymmetry

A strategy for the introduction of asymmetry into Fréchet-type dendrons bearing *n*-alkyl chains is described. Starting from a methyl 3,5-dihydroxybenzoate core, 3,5-bis(octyloxyphenyl)methoxy and 3,5-bis(alkoxyphenyl)methoxy units are introduced in a stepwise manner. The method is illustrated by the syntheses of four representative compounds having

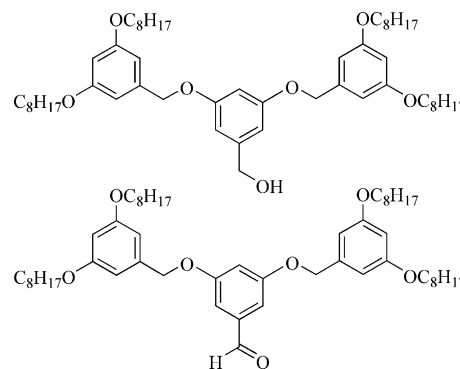
mixed *n*-octyl/*n*-butyl, *n*-octyl/*n*-hexyl, *n*-octyl/*n*-heptyl and *n*-octyl/*n*-dodecyl substituents. The new compounds have been characterized by spectroscopic and mass spectrometric techniques.

(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2008)

Introduction

Dendrimers and dendrons are becoming the scaffolds of choice for multifunctional species and are finding applications in all areas of chemistry and physics.^[1–5] One of the ubiquitous core structures was introduced by Fréchet^[6–8] in which the key building blocks are 3,5-bis(alkoxybenzyl) alcohols. Even though both convergent and divergent strategies are adopted, the critical growth steps involve reactions of the nucleophilic 3,5-bis(phenoxides) with electrophilic 3,5-bis(alkoxybenzyl) derivatives. Although prototype Fréchet dendrimers are decorated with benzyloxy substituents, replacement by aliphatic alkoxy substituents leads to novel hydrophobic species. Monolayers of Fréchet-type dendrons that are rich in aromatic units may be clearly imaged using scanning tunnelling microscopy (STM), and octyl-decorated dendrons constructed from the 3,5-dihydroxybenzyl alcohol core have been central to a series of STM studies reported to date.^[6–11] Of relevance to this paper are the highly resolved STM images^[12–14] of 3,5-bis[3,5-bis(octyloxyphenyl)methoxy]benzyl alcohol^[12,15] and the related aldehyde^[14] (Scheme 1). These long-chain octyl-decorated Fréchet-type dendrons prove to be a powerful assembly motif. Monolayers on highly oriented pyrolytic graphite (HOPG) initially form with a pattern based on trimeric units, with a pseudo unit cell of seven molecules (one of which remains highly mobile), and over time, the supramolecular ordering changes to a dimeric pattern. A combination of interdigitation of long alkyl chains, graphite–methylene interactions, and graphite–aromatic ring π -stacking interactions lead to the formation of particularly stable

monolayers. The dominant intermolecular interactions in the monolayer arise from the interdigitation of the alkyl chains. In efforts to control the topography of the monolayer, we considered the consequences of asymmetrical dendrons with different-length alkyl chains, which are expected to be non-commensurate and give novel structures. Fréchet-type dendrons with different substituents in the 3- and 5-positions are relatively rare, and in this paper, we report the synthesis of asymmetric first- and second-generation dendrons.



Scheme 1. Octyl-decorated second-generation Fréchet-type dendrons.^[12,15]

Results and Discussion

Our strategy for the synthesis of symmetrical octyl-decorated second-generation Fréchet-type dendrons (Scheme 1) has been the conversion of 1-(hydroxymethyl)-3,5-bis(octyloxy)benzene to the corresponding mesylate **1** followed by reaction with 3,5-dihydroxybenzyl alcohol. Oxidation of the resultant alcohol leads to the corresponding aldehyde. Following our STM investigations of these den-

[a] Department of Chemistry, University of Basel, Spitalstrasse 51, 4056 Basel, Switzerland
Fax: +41-61-267-1018
E-mail: edwin.constable@unibas.ch

[b] WMI/CeNS, LMU Munich, Walther-Meissner-Str. 8, 85748 Garching, Germany

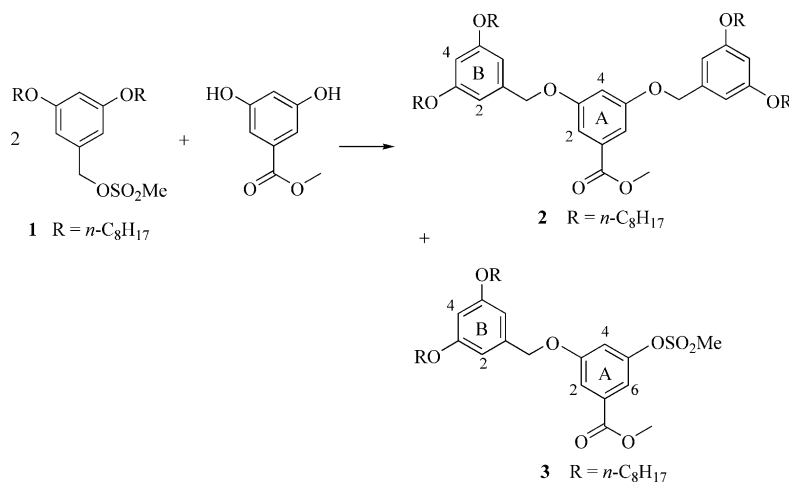
drons,^[12] we decided to prepare the corresponding methyl ester in order to study the effects of further altering the head group. While preparing a batch of **1**, serendipitous use of non-optimal quantities of hydrochloric acid (added to quench excess methanesulfonyl chloride) during the workup led to crude **1** being contaminated with methanesulfonyl chloride. Treatment of methyl 3,5-dihydroxybenzoate with 2 equiv. of the crude mesylate **1** in the presence of potassium carbonate and 18-crown-6^[16,17] yielded the symmetrical Fréchet-type dendron **2** as expected (Scheme 2). However, we observed that a second product, **3**, was also formed. This product was never observed when adequate HCl was added to completely remove excess methanesulfonyl chloride during the workup of compound **1**, and under such conditions, compound **2** may be obtained in up to 87% yield. Compounds **2** and **3** were separated by column chromatography, with **2** being isolated as a yellow oil and **3** as a white solid. The base peak ($m/z = 861$) in the EI mass spectrum of **2** corresponded to the parent ion with an isotope pattern that matched the one simulated. The ^1H and ^{13}C NMR spectra indicated a symmetrical product, and the resonances for the mesylate methyl group, present in **1** at $\delta(^1\text{H}) = 2.92$ ppm and $\delta(^{13}\text{C}) = 39$ ppm, were absent. The ^{13}C and ^1H NMR spectra were assigned by COSY, NOESY, HMQC and HMBC techniques. The ^1H and ^{13}C NMR spectroscopic signatures of **3** confirmed the retention of a mesylate substituent [signals for the Me group at $\delta(^1\text{H}) = 3.15$ ppm and $\delta(^{13}\text{C}) = 37.8$ ppm]. The asymmetry in the structure of **3** is immediately apparent from the ^{13}C NMR spectrum which shows signals for carbon atoms $\text{C}^{\text{A}}\text{-2}$, $\text{C}^{\text{A}}\text{-4}$ and $\text{C}^{\text{A}}\text{-6}$ at $\delta = 114.8$, 114.0 and 115.5 ppm, compared to resonances for $\text{C}^{\text{A}}\text{-2,6}$ and $\text{C}^{\text{A}}\text{-4}$ at $\delta = 108.6$ and 107.4 ppm in **2**. The MALDI-TOF mass spectrum of **3** exhibited a base peak at $m/z = 634$, assigned to $[\text{M} + \text{K}]^+$.

The formation of **3** in addition to **2** can readily be explained in terms of the presence of MeSO_3Cl which provides an electrophile that competes with **1** during the reaction with 3,5-dihydroxybenzoate. The isolation of compound **3** provided a starting point for the synthesis of asym-

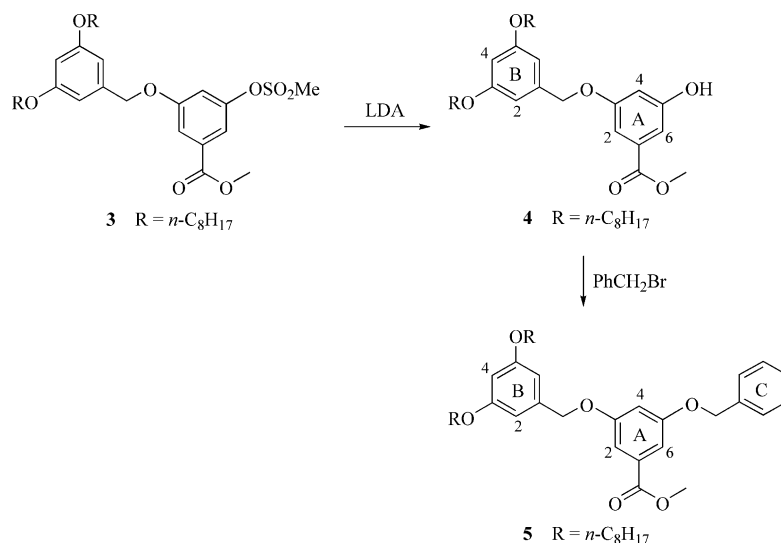
metrical alkyl-decorated Fréchet-type dendrons. Our strategy for the introduction of a second 3,5-bis(alkoxy)benzyloxy substituent was the reaction of the corresponding 3,5-bis(alkoxy)benzyl methanesulfonate with methyl 3-[3,5-bis(octyloxy)benzyloxy]-5-hydroxybenzoate (**4**). Treatment of **3** with LDA^[18] at 0 °C in THF followed by addition of aqueous HCl resulted in the formation of **4** in good yield (Scheme 3). The highest mass peak in the EI mass spectrum of **4** corresponded to the parent ion ($m/z = 514$), while the base peak ($m/z = 347$) confirmed fragmentation by loss of the $\text{CH}_2\text{C}_6\text{H}_3(\text{OC}_8\text{H}_{17})_2$ group. Complete NMR spectroscopic assignments were made using COSY, NOESY, HMQC and HMBC techniques. The ^{13}C NMR spectrum of **4** closely resembles that of **3**, except for the absence of the signal for the mesylate Me group and a significant shifting of the signal for $\text{C}^{\text{A}}\text{-5}$ from $\delta = 149.9$ to 156.8 ppm. The signals for $\text{C}^{\text{A}}\text{-2}$, $\text{C}^{\text{A}}\text{-4}$ and $\text{C}^{\text{A}}\text{-6}$ also shift (from $\delta = 114.8$, 114.0 and 115.5 ppm in **3** to $\delta = 108.5$, 107.5 and 109.6 ppm in **4**, respectively). Except for the loss of the resonance for H^{SMe} , the ^1H NMR spectrum of **4** is almost identical to that of **3**. The OH proton signal of **4** was not observed.

The reactivity of **4** was first tested by investigating its reaction with benzyl bromide in the presence of K_2CO_3 and 18-crown-6. Compound **5** (Scheme 3) was obtained in 85% yield. A parent ion peak at $m/z = 604$ was observed in the EI mass spectrum of **5**, along with intense fragmentation peaks assigned to $[\text{CH}_2\text{C}_6\text{H}_3(\text{OC}_8\text{H}_{17})_2]^+$ ($m/z = 347$) and $[\text{M} - \text{CH}_2\text{Ph}]^+$ ($m/z = 513$). The ^{13}C and ^1H NMR spectra were fully assigned by using COSY, NOESY, DEPT, HMQC and HMBC methods.

We next turned our attention to the synthesis of four 3,5-bis(alkoxy)benzyl methanesulfonates for introduction into the Fréchet-type dendrons. Scheme 4 summarizes the reaction strategy. Treatment of methyl 3,5-dihydroxybenzoate with 2 equiv. of RBr (R = *n*-butyl, *n*-hexyl, *n*-heptyl or *n*-dodecyl) in the presence of K_2CO_3 and 18-crown-6, resulted in the formation of compounds **6–9**. Crude compounds **6–8** were isolated as oils and were characterized by mass spectrometry and IR and NMR spectroscopy, with the latter



Scheme 2. Formation of a symmetrical octyl-decorated Fréchet dendron and the mesylate by-product used as a building block for the asymmetrical dendrons. Ring labels for NMR spectroscopic assignments.



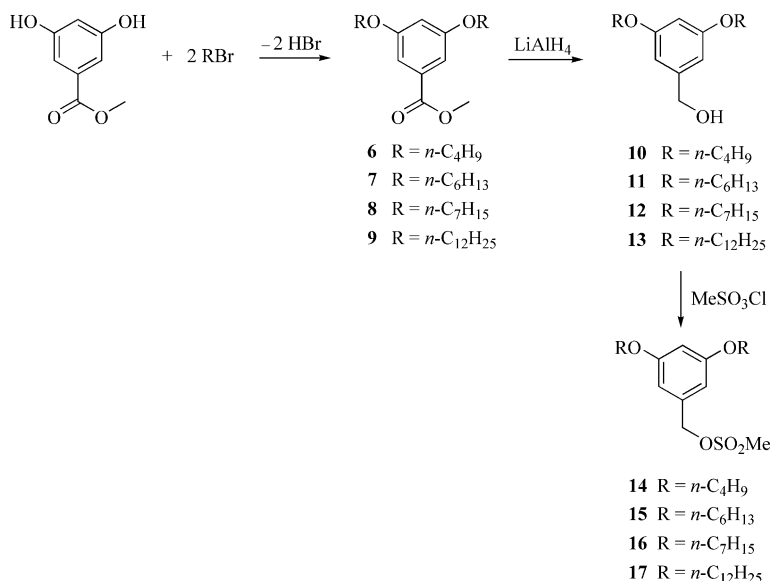
Scheme 3. Synthetic pathway to the asymmetrical dendron **5**. Ring labels for NMR spectroscopic assignments.

spectra being fully assigned (COSY, NOESY, HMQC and HMBC). These esters were used in the next steps of the syntheses without further purification. Compound **9** was isolated as an analytically pure, white, crystalline solid. A parent ion was observed at $m/z = 504$ in the MALDI-TOF mass spectrum of **9**, and the ^1H and ^{13}C NMR spectra were in accord with the expected symmetry of the structure.

Reduction of esters **6–9** with LiAlH_4 in diethyl ether produced the corresponding alcohols **10–13** in >90% yield. A parent ion was observed in the EI mass spectrum of each of compounds **10–12**, and in the MALDI-TOF mass spectrum of **13**. A comparison of the ^{13}C NMR spectra of **6–10** showed the expected loss of signals assigned to the ester group in **6** and the appearance of a signal in each spectrum arising from the methylene group of CH_2OH unit. Similar changes were observed on going from **7** to **11**, **8** to **12**, and **9** to **13**. The final step in the synthesis of the mesylates **14–**

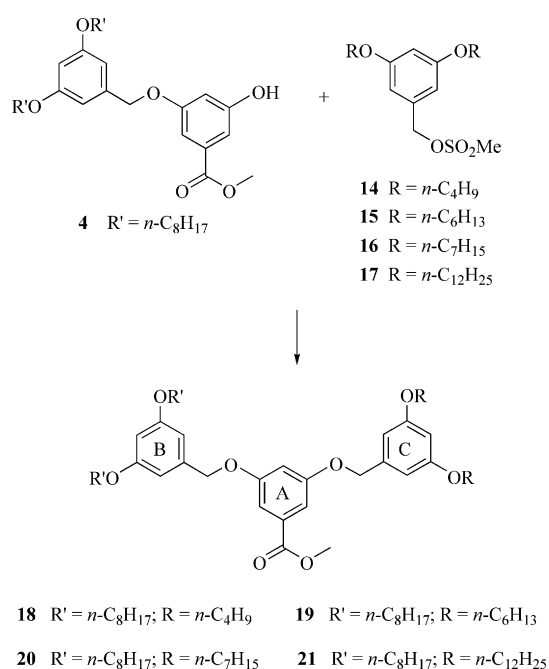
17 was the reaction of each alcohol with methanesulfonyl chloride. Because of the highly reactive nature of compounds **14–17**, each was prepared in situ, although it proved possible to isolate **17** as a yellow solid. NMR spectroscopy may be used to confirm the conversion of the CH_2OH group to the mesylate group, with characteristic signals appearing, for example, at $\delta = 2.9$ ppm and $\delta = 38.8$ ppm in the ^1H and ^{13}C NMR spectra, respectively, for the Me group in compound **17**, or monitoring the shift from $\delta = 4.6$ ppm for the CH_2OH group to $\delta = 5.0$ ppm for the $\text{CH}_2\text{OSO}_2\text{Me}$ group in the ^1H NMR spectrum on going from **13** to **17**.

Asymmetrical alkyl-decorated Fréchet dendrons were prepared by reactions of the octyl-decorated alcohol **4** with mesylates **14–17** in the presence of K_2CO_3 and 18-crown-6 (Scheme 5). Each of the *n*-octyl/*n*-butyl, *n*-octyl/*n*-hexyl, *n*-octyl/*n*-heptyl and *n*-octyl/*n*-decyl derivatives **18–21** were



Scheme 4. Reaction scheme for the formation of mesylate building blocks.

obtained in ca. 90% yield. The highest mass peak ($m/z = 788$) in the MALDI-TOF mass spectrum of compound **18** was assigned to $[M + K]^+$. For **19**, a parent ion ($m/z = 804$) was observed in the EI mass spectrum, with fragmentation by loss of the $\text{CH}_2\text{C}_6\text{H}_3(\text{OC}_8\text{H}_{17})_2$ ($m/z = 347$) and $\text{CH}_2\text{C}_6\text{H}_3(\text{OC}_6\text{H}_{13})_2$ ($m/z = 291$) groups. Similarly, the EI mass spectra of **20** and **21** exhibited parent ions ($m/z = 832$ and 973 , respectively) and fragmentation by loss of the $\text{CH}_2\text{C}_6\text{H}_3(\text{OR})_2$ groups. The asymmetry of the compounds is not apparent in either their ^{13}C or ^1H NMR spectra, because of coincidence of the signals for pairs of related carbon (or proton) atoms in rings B and C (Scheme 5). However, the relative integrals of the proton signals for the alkyl groups are consistent with the presence of two pairs of different alkyl chains. Attempts to grow X-ray quality crystals of compounds **18–21** were unsuccessful.



Scheme 5. Formation of asymmetrical alkyl-decorated Fréchet dendrons. Ring labels for NMR spectroscopic assignments.

Conclusions

We have detailed a strategy to introduce asymmetry into Fréchet-type dendrons bearing *n*-alkyl chains. Starting from a methyl 3,5-dihydroxybenzoate core, 3,5-bis(octyloxyphenyl)methoxy and 3,5-bis(alkoxyphenyl)methoxy units are introduced in a stepwise manner. The method has been illustrated by the syntheses and characterizations of four representative compounds having mixed *n*-octyl/*n*-butyl, *n*-octyl/*n*-hexyl, *n*-octyl/*n*-heptyl and *n*-octyl/*n*-dodecyl substituents. In a future paper, we shall report the results of STM studies of monolayers of esters **18–21** which self-organize on HOPG surfaces and compare the two-dimensional motifs with those formed by the symmetrical **2**.^[12]

Experimental Section

General: ^1H and ^{13}C NMR spectra were recorded with Bruker Avance DPX 400 or DRX 500 spectrometers; the numbering scheme adopted for the compounds is shown in the Schemes. Chemical shifts for ^1H and ^{13}C NMR spectra are referenced to residual solvent peaks with respect to TMS ($\delta = 0$ ppm); all spectra were recorded at ca. 298 K. MALDI-TOF and electron impact (EI) mass spectra were recorded with PerSeptive Biosystems Voyager and Finnigan MAT95Q mass spectrometers, respectively. Melting points were recorded with a Stuart Scientific SMP3 melting point apparatus. Methyl 3,5-dihydroxybenzoate was prepared according to a literature route.^[19]

Compound 1: Compound **1** was prepared according to a method based on that previously reported.^[12] A solution of 1-(hydroxymethyl)-3,5-bis(octyloxy)benzene (6.00 g, 16.4 mmol) in CH_2Cl_2 (50 mL) was cooled to -10°C , and NEt_3 (10 mL, 71 mmol) was added. Methanesulfonyl chloride (5.0 mL, 65 mmol) was added slowly over a period of 15 min. The reaction mixture was stirred at -10°C for 1 h, after which time it was poured into a mixture of concentrated HCl (5 mL, see text) and crushed ice, and extracted with CH_2Cl_2 . The organic layer was washed with a saturated solution of NaHCO_3 , dried with Na_2SO_4 , and the solvent removed to yield a brown oil. The crude product was used in the next step without purification.

Compounds 2 and 3: K_2CO_3 (3.73 g, 27.0 mmol), methyl 3,5-dihydroxybenzoate (1.14 g, 6.79 mmol) and 18-crown-6 (53 mg, 0.20 mmol) were added to a solution of crude **1** (5.98 g, 13.5 mmol, see text) in acetone (150 mL). The reaction mixture was heated under reflux for 48 h, and then H_2O (300 mL) was added. The organic layer was extracted three times with CH_2Cl_2 , and the combined organic layers were dried with MgSO_4 . The solvent was then removed. Column chromatography (SiO_2 ; ethyl acetate/hexane, 1:3) yielded **2** as a pale yellow oil ($R_f = 0.71$; 2.20 g, 2.56 mmol, 38%) and **3** as a white solid ($R_f = 0.29$; 1.8 g, 3.0 mmol, 45%). **2:** ^1H NMR (500 MHz, CDCl_3): $\delta = 0.89$ (t, $J = 7.0$ Hz, 12 H, Me), 1.23–1.38 [m, 32 H, $(\text{CH}_2)_4\text{Me}$], 1.44 (m, 8 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.77 (m, 8 H, OCH_2CH_2), 3.90 (s, 3 H, OMe), 3.94 (t, $J = 6.5$ Hz, 8 H, OCH_2CH_2), 4.98 [s, 4 H, $\text{CH}_2\text{O}(\text{ringA})$], 6.41 (t, $J = 2.2$ Hz, 2 H, 4- H^B), 6.55 (d, $J = 2.0$ Hz, 4 H, 2- H^B), 6.79 (t, $J = 2.2$ Hz, 1 H, 4- H^A), 7.28 (d, $J = 2.2$ Hz, 2 H, 2- H^A) ppm. ^{13}C NMR (125 MHz, CDCl_3): $\delta = 14.3$ (Me), 22.9 (CH_2), 26.3 (CH_2), 29.5 (2CH_2), 29.6 (CH_2), 32.0 (CH_2), 52.5 (OMe), 68.3 (OCH_2CH_2), 70.5 [$\text{CH}_2\text{O}(\text{ringA})$], 101.1 ($\text{C}^B\text{-4}$), 105.9 ($\text{C}^B\text{-2}$), 107.4 ($\text{C}^A\text{-4}$), 108.6 ($\text{C}^A\text{-2}$), 132.2 ($\text{C}^A\text{-1}$), 138.8 ($\text{C}^B\text{-1}$), 160.0 ($\text{C}^A\text{-3}$), 160.7 ($\text{C}^B\text{-3}$), 167.0 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu} = 2950$ (w), 2925 (s), 2870 (w), 2855 (m), 1725 (m), 1596 (s), 1455 (m), 1446 (w), 1378 (w), 1347 (w), 1324 (m), 1299 (m), 1233 (w), 1168 (s), 1054 (m), 1006 (w), 849 (w), 832 (w), 767 (w), 680 (w), 634 (w) cm^{-1} . EI-MS: $m/z = 861$ $[M]^+$. $\text{C}_{54}\text{H}_{84}\text{O}_8$ (861.2): calcd. C 75.31, H 9.83; found C 75.48, H 9.78. **3:** M.p. 60–61 $^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3): $\delta = 0.89$ (t, $J = 7.0$ Hz, 6 H, Me), 1.23–1.38 [m, 16 H, $(\text{CH}_2)_4\text{Me}$], 1.44 (m, 4 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.77 (m, 4 H, OCH_2CH_2), 3.15 (s, 3 H, SMe), 3.92 (s, 3 H, OMe), 3.94 (t, $J = 7.0$ Hz, 4 H, OCH_2CH_2), 5.03 [s, 2 H, $\text{CH}_2\text{O}(\text{ringA})$], 6.42 (t, $J = 2.0$ Hz, 1 H, 4- H^B), 6.54 (d, $J = 2.0$ Hz, 2 H, 2- H^B), 7.11 (t, $J = 2.0$ Hz, 1 H, 4- H^A), 7.53 (m, 1 H, 6- H^A), 7.63 (m, 1 H, 2- H^A) ppm. ^{13}C NMR (125 MHz, CDCl_3): $\delta = 14.3$ (Me), 22.8 (CH_2), 26.2 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 29.4 (CH_2), 29.5 (CH_2), 32.0 (CH_2), 37.8 (SMe), 52.7 (OMe), 68.3 (OCH_2CH_2), 70.8 [$\text{CH}_2\text{O}(\text{ringA})$], 101.2 ($\text{C}^B\text{-4}$), 105.9 ($\text{C}^B\text{-2}$), 114.0 ($\text{C}^A\text{-4}$), 114.8 ($\text{C}^A\text{-2}$), 115.5 ($\text{C}^A\text{-6}$), 132.9 ($\text{C}^A\text{-1}$), 137.9 ($\text{C}^B\text{-1}$), 149.9 ($\text{C}^A\text{-5}$), 159.9 ($\text{C}^A\text{-3}$), 160.8 ($\text{C}^B\text{-3}$), 165.7 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu} = 2922$ (m), 2867 (w), 2854 (m), 1738 (m), 1587 (m), 1472 (w), 1455 (m),

1435 (m), 1362 (s), 1345 (m), 1329 (m), 1319 (w), 1292 (s), 1266 (w), 1220 (m), 1171 (s), 1131 (s), 1096 (m), 1067 (w), 1043 (m), 1004 (m), 963 (s), 947 (w), 876 (s), 827 (m), 812 (s), 766 (m), 732 (m), 682 (m), 638 (m), 623 (m) cm^{-1} . MALDI-TOF MS: m/z = 634 $[\text{M} + \text{K}]^+$. $\text{C}_{32}\text{H}_{48}\text{O}_8\text{S}$ (592.8): calcd. C 64.84, H 8.16; found C 64.98, H 8.26.

Compound 4: Compound **3** (1.00 g, 1.69 mmol) was dissolved in THF (15 mL), and the solution was cooled to 0 °C. Freshly prepared LDA (5.1 mmol in 10 mL THF) was added by syringe, and the reaction mixture was stirred at 0 °C for 30 min, after which time HCl (4 mL, 5% aqueous) was added. The product was extracted with ethyl acetate and then the solvent removed. Column chromatography (SiO_2 ; ethyl acetate/hexane, 1:2) yielded **4** as a white solid (700 mg, 1.36 mmol, 80%). M.p. 49–52 °C. ^1H NMR (500 MHz, CDCl_3): δ = 0.88 (t, J = 7.0 Hz, 6 H, Me), 1.25–1.32 [m, 16 H, $(\text{CH}_2)_4\text{Me}$], 1.42 (m, 4 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.76 (m, 4 H, OCH_2CH_2), 3.90 (s, 3 H, OMe), 3.93 (t, J = 7.0 Hz, 4 H, OCH_2CH_2), 4.99 [s, 2 H, $\text{CH}_2\text{O}(\text{ringA})$], 6.41 (t, J = 2.3 Hz, 1 H, 4- H^{B}), 6.55 (d, J = 2.3 Hz, 2 H, 2- H^{B}), 6.66 (t, J = 2.0 Hz, 1 H, 4- H^{A}), 7.13 (m, 1 H, 6- H^{A}), 7.24 (m, 1 H, 2- H^{A}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.3 (Me), 22.9 (CH_2), 26.3 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 29.5 (2CH_2), 29.6 (CH_2), 32.0 (CH_2), 52.5 (OMe), 68.3 (OCH_2CH_2), 70.5 [$\text{CH}_2\text{O}(\text{ringA})$], 101.1 ($\text{C}^{\text{B-4}}$), 105.9 ($\text{C}^{\text{B-2}}$), 107.5 ($\text{C}^{\text{A-4}}$), 108.5 ($\text{C}^{\text{A-2}}$), 109.6 ($\text{C}^{\text{A-6}}$), 132.4 ($\text{C}^{\text{A-1}}$), 138.8 ($\text{C}^{\text{B-1}}$), 156.8 ($\text{C}^{\text{A-5}}$), 160.2 ($\text{C}^{\text{A-3}}$), 160.8 ($\text{C}^{\text{B-3}}$), 166.9 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu}$ = 3361 (br.), 2954 (w), 2942 (m), 2921 (m), 2849 (m), 1694 (m), 1607 (m), 1592 (s), 1470 (m), 1447 (m), 1392 (w), 1372 (w), 1334 (m), 1321 (m), 1256 (m), 1244 (m), 1156 (s), 1141 (s), 1117 (w), 1050 (s), 1026 (w), 1013 (w), 1009 (w), 999 (w), 990 (w), 957 (w), 861 (m), 852 (m), 823 (m), 766 (s), 728 (w), 712 (w), 675 (s), 640 (m) cm^{-1} . EI-MS: m/z = 514 $[\text{M}]^+$. $\text{C}_{31}\text{H}_{46}\text{O}_6$ (514.7): calcd. C 72.34, H 9.01; found C 71.86, H 9.22.

Compound 5: 18-Crown-6 (20.6 mg, 0.78 mmol), K_2CO_3 (161 mg, 1.17 mmol) and benzyl bromide (100 mg, 0.58 mmol) were added to a solution of **4** (200 mg, 0.39 mmol) in acetone (15 mL). The reaction mixture was heated at reflux for 48 h, after which time water was added. The organic layer was extracted with CH_2Cl_2 , dried with MgSO_4 , and the solvent was removed. Column chromatography (SiO_2 ; ethyl acetate/hexane, 1:3) yielded **5** as a white solid (200 mg, 0.33 mmol, 85%). M.p. 38 °C. ^1H NMR (500 MHz, CDCl_3): δ = 0.89 (t, J = 7.0 Hz, 6 H, Me), 1.25–1.36 [m, 16 H, $(\text{CH}_2)_4\text{Me}$], 1.44 (m, 4 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.77 (m, 4 H, OCH_2CH_2), 3.91 (s, 3 H, OMe), 3.94 (t, J = 6.5 Hz, 4 H, OCH_2CH_2), 4.99 [s, 2 H, $(\text{ringB})\text{CH}_2\text{O}$], 5.07 [s, 2 H, $(\text{ringC})\text{CH}_2\text{O}$], 6.41 (t, J = 2.0 Hz, 1 H, 4- H^{B}), 6.55 (d, J = 2.0 Hz, 2 H, 2- H^{B}), 6.80 (t, J = 2.0 Hz, 1 H, 4- H^{A}), 7.29 (m, 2 H, 2,6- H^{A}), 7.31–7.45 (m, 5 H, H^{C}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.3 (Me), 22.8 (CH_2), 26.2 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 29.4 (2CH_2), 29.5 (CH_2), 32.0 (CH_2), 52.4 (OMe), 68.2 (OCH_2CH_2), 70.4 [$(\text{ringB})\text{CH}_2\text{O} + (\text{ringC})\text{CH}_2\text{O}$], 101.0 ($\text{C}^{\text{B-4}}$), 105.8 ($\text{C}^{\text{B-2}}$), 107.4 ($\text{C}^{\text{A-4}}$), 108.5 ($\text{C}^{\text{A-2,6}}$), 108.6 ($\text{C}^{\text{A-2,6}}$), 127.7 ($\text{C}^{\text{C-2,3}}$), 128.3 ($\text{C}^{\text{C-4}}$), 128.8 ($\text{C}^{\text{C-2,3}}$), 132.2 ($\text{C}^{\text{A-1}}$), 136.6 ($\text{C}^{\text{C-1}}$), 138.7 ($\text{C}^{\text{B-1}}$), 159.9 ($\text{C}^{\text{A-3}}$), 160.7 ($\text{C}^{\text{B-3}}$), 166.9 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu}$ = 2950 (w), 2919 (m), 2855 (m), 1717 (m), 1597 (s), 1468 (m), 1455 (m), 1445 (m), 1431 (m), 1386 (m), 1378 (m), 1348 (s), 1299 (s), 1256 (m), 1231 (m), 1171 (s), 1154 (m), 1128 (w), 1056 (s), 1027 (s), 998 (w), 867 (w), 847 (m), 826 (m), 776 (w), 765 (m), 745 (w), 695 (m), 689 (w), 674 (w), 640 (w) cm^{-1} . EI-MS: m/z = 604 $[\text{M}]^+$. $\text{C}_{38}\text{H}_{52}\text{O}_6$ (604.8): calcd. C 75.46, H 8.67; found C 75.21, H 8.63.

Compound 6: 18-Crown-6 (350 mg, 1.3 mmol), K_2CO_3 (2.00 g, 14.5 mmol) and 1-bromobutane (2.0 mL, 19 mmol) were added to an acetone (50 mL) solution of methyl 3,5-dihydroxybenzoate

(1.0 g, 6.0 mmol). The reaction mixture was heated under reflux for 3 d, after which time all the solid material was removed by filtration. The filtrate was collected and the solvent removed. After the addition of water and CH_2Cl_2 , the organic layer was collected, dried with Na_2SO_4 , and the solvent was removed; **6** was isolated as a yellow oil and used in the next step without further purification. ^1H NMR (500 MHz, CDCl_3): δ = 0.96 (t, J = 7.5 Hz, 6 H, Me), 1.48 (m, 4 H, CH_2Me), 1.75 (m, 4 H, OCH_2CH_2), 3.89 (s, 3 H, OMe), 3.97 (t, J = 6.5 Hz, 4 H, OCH_2), 6.63 (t, J = 2.5 Hz, 1 H, 4- H^{Ar}), 7.15 (d, J = 2.5 Hz, 2 H, 2- H^{Ar}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.2 (Me), 19.6 (CH_2Me), 31.5 (OCH_2CH_2), 52.4 (OMe), 67.8 (OCH_2), 106.6 ($\text{C}^{\text{Ar-4}}$), 108.1 ($\text{C}^{\text{Ar-2}}$), 132.5 ($\text{C}^{\text{Ar-1}}$), 160.5 ($\text{C}^{\text{Ar-3}}$), 167.3 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu}$ = 2962 (m), 2878 (m), 2852 (m), 1705 (s), 1597 (s), 1450 (m), 1358 (m), 1327 (m), 1304 (m), 1234 (m), 1165 (s), 1049 (m), 1003 (w), 949 (w), 910 (w), 849 (w), 764 (m), 741 (w), 679 (w), 617 (w) cm^{-1} . EI-MS: m/z = 280 $[\text{M}]^+$.

Compound 7: 18-Crown-6 (350 mg, 1.3 mmol), K_2CO_3 (2.00 g, 14.5 mmol) and 1-bromohexane (2.3 mL, 16 mmol) were added to an acetone (50 mL) solution of methyl 3,5-dihydroxybenzoate (1.0 g, 6.0 mmol). The reaction procedure and workup were as for **6**. Compound **7** was isolated as a yellow oil and used in the next step without further purification. ^1H NMR (500 MHz, CDCl_3): δ = 0.90 (m, 6 H, Me), 1.30 (m, 8 H, $\text{CH}_2\text{CH}_2\text{Me}$), 1.44 (m, 4 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.76 (m, 4 H, OCH_2CH_2), 3.89 (s, 3 H, OMe), 3.96 (t, J = 6.5 Hz, 4 H, OCH_2), 6.62 (t, J = 2.5 Hz, 1 H, 4- H^{Ar}), 7.15 (d, J = 2.5 Hz, 2 H, 2- H^{Ar}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.2 (Me), 22.8 [$(\text{CH}_2)_2\text{Me}$], 25.9 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 29.3 (OCH_2CH_2), 31.7 [$(\text{CH}_2)_2\text{Me}$], 52.4 (OMe), 68.5 (OCH_2), 106.7 ($\text{C}^{\text{Ar-4}}$), 107.8 ($\text{C}^{\text{Ar-4}}$), 132.0 ($\text{C}^{\text{Ar-1}}$), 160.3 ($\text{C}^{\text{Ar-3}}$), 167.2 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu}$ = 2932 (m), 2862 (m), 1921 (w), 1852 (w), 1720 (s), 1597 (s), 1512 (m), 1443 (s), 1350 (m), 1327 (m), 1304 (m), 1234 (m), 1165 (s), 1080 (w), 1049 (m), 1026 (w), 980 (w), 918 (m), 848 (m), 771 (s), 752 (w), 687 (w), 656 (w), 625 (m) cm^{-1} . EI-MS: m/z = 336 $[\text{M}]^+$.

Compound 8: 18-Crown-6 (500 mg, 1.86 mmol), K_2CO_3 (3.0 g, 21.8 mmol) and 1-bromoheptane (3.6 mL, 23 mmol) were added to an acetone (80 mL) solution of methyl 3,5-dihydroxybenzoate (1.5 g, 9.0 mmol). The reaction procedure and workup were as for **6**, and **8** was isolated as a yellow oil and used in the next step of the synthesis without further purification. ^1H NMR (500 MHz, CDCl_3): δ = 0.89 (t, J = 7.0 Hz, 6 H, Me), 1.26–1.35 (m, 12 H, CH_2), 1.44 (m, 4 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.76 (m, 4 H, OCH_2CH_2), 3.89 (s, 3 H, OMe), 3.93 (t, J = 6.5 Hz, 4 H, OCH_2), 6.63 (t, J = 2.5 Hz, 1 H, 4- H^{Ar}), 7.15 (d, J = 2.5 Hz, 2 H, 2- H^{Ar}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.3 (Me), 22.8 (CH_2), 26.2 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 29.3 (CH_2), 29.4 (OCH_2CH_2), 32.0 (CH_2), 52.4 (OMe), 68.5 (OCH_2), 106.7 ($\text{C}^{\text{Ar-4}}$), 107.8 ($\text{C}^{\text{Ar-2}}$), 132.0 ($\text{C}^{\text{Ar-1}}$), 160.3 ($\text{C}^{\text{Ar-3}}$), 167.2 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu}$ = 2924 (s), 2854 (m), 1720 (s), 1597 (s), 1450 (m), 1381 (w), 1350 (w), 1327 (w), 1304 (w), 1234 (m), 1165 (s), 1057 (w), 849 (w), 771 (w), 679 (w), 633 (w) cm^{-1} . EI-MS: m/z = 364 $[\text{M}]^+$.

Compound 9: 18-Crown-6 (6.26 g, 23.7 mmol), K_2CO_3 (40.9 g, 296 mmol) and 1-bromododecane (70.9 mL, 296 mmol) were added to an acetone (190 mL) solution of methyl 3,5-dihydroxybenzoate (9.95 g, 59.2 mmol). The reaction mixture was heated at reflux for 39 h, after which it was cooled to room temperature. White needles of **9** formed and were removed by filtration and washed with Et_2O . Ethyl acetate (100 mL), Et_2O (200 mL) and water (300 mL) were added to the filtrate, and the organic layer was collected and dried with Na_2SO_4 . The solvent was then removed to yield **9** as a white solid. The combined products were recrystallized twice from acetone.

tone to give **9** as a white solid (26.6 g, 52.7 mmol, 89.0%). M.p. 61 °C. ¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.9 Hz, 6 H, Me), 1.19–1.38 (m, 32 H, CH₂), 1.39–1.49 (m, 4 H, CH₂), 1.77 (quint, *J* = 7.0 Hz, 4 H, OCH₂CH₂), 3.89 (s, 3 H, OMe), 3.96 (t, *J* = 6.6 Hz, 4 H, OCH₂), 6.63 (t, *J* = 2.3 Hz, 1 H, 4-H^{Ar}), 7.15 (d, *J* = 2.4 Hz, 2 H, 2-H^{Ar}) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.5 (Me), 23.1 (CH₂), 26.4 (CH₂), 29.6 (CH₂), 29.8 (2CH₂), 30.0 (3CH₂), 30.1 (CH₂), 32.3 (CH₂), 52.6 (OMe), 68.7 (OCH₂), 107.0 (C^{Ar}-4), 108.0 (C^{Ar}-2), 132.2 (C^{Ar}-1), 160.5 (C^{Ar}-3), 167.4 (C=O) ppm. IR (neat): ν̄ = 2919 (s), 2846 (m), 1720 (m), 1597 (m), 1466 (m), 1443 (m), 1389 (w), 1319 (s), 1234 (s), 1119 (w), 1049 (m), 995 (m), 856 (w), 764 (w), 717 (w) cm⁻¹. MALDI-MS: *m/z* = 504 [M]⁺. C₃₂H₅₆O₄ (504.8): calcd. C 76.14, H 11.18; found C 76.27, H 10.92.

Compound 10: LiAlH₄ (388 mg, 10.2 mmol) in Et₂O (40 mL) was cooled to 0 °C, and **6** (2.01 g, 7.17 mmol) was added slowly over a period of 1 h. The reaction mixture was heated at reflux for 3 h and then stirred at room temperature overnight. NaOH (6 mL, 1 M) was added until a white precipitate formed. The mixture was filtered through Celite and the solid washed thoroughly with Et₂O and water. The organic layer was washed with water, and the aqueous layers were combined and extracted with Et₂O. The organic layers were combined and dried with MgSO₄, and the solvent was then removed; **10** was isolated as a yellow oil (1.72 g, 6.81 mmol, 95%). ¹H NMR (500 MHz, CDCl₃): δ = 0.97 (t, *J* = 7.5 Hz, 6 H, Me), 1.48 (m, 4 H, CH₂Me), 1.75 (m, 4 H, OCH₂CH₂), 1.82 (br. s, 1 H, OH), 3.94 (t, *J* = 6.5 Hz, 4 H, OCH₂), 4.62 (s, 2 H, CH₂OH), 6.38 (t, *J* = 2.5 Hz, 1 H, 4-H^{Ar}), 6.50 (d, *J* = 2.5 Hz, 2 H, 2-H^{Ar}) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 14.1 (Me), 19.5 (CH₂Me), 31.5 (OCH₂CH₂), 65.7 (CH₂OH), 67.9 (OCH₂), 100.7 (C^{Ar}-4), 105.2 (C^{Ar}-2), 143.4 (C^{Ar}-1), 160.7 (C^{Ar}-3) ppm. IR (neat): ν̄ = 2955 (m), 2932 (m), 2870 (m), 1597 (s), 1458 (s), 1381 (m), 1342 (w), 1319 (w), 1296 (m), 1165 (s), 1041 (m), 833 (w), 671 (w), 640 (w), 594 (w) cm⁻¹. EI-MS: *m/z* = 252 [M]⁺. C₁₅H₂₄O₃ (252.3): calcd. C 71.39, H 9.59; found C 71.53, H 9.55.

Compound 11: LiAlH₄ (358 mg, 9.42 mmol) in Et₂O (40 mL) was cooled to 0 °C, and **7** (1.98 g, 5.88 mmol) was added slowly over a period of 1 h. The reaction mixture was heated under reflux for 3 h. and then stirred at room temperature overnight. NaOH (6 mL, 1 M) was added until a white precipitate formed. Purification was as for **10**. Compound **11** was isolated as a yellow oil (1.69 g, 5.47 mmol, 93%). ¹H NMR (500 MHz, CDCl₃): δ = 0.90 (t, *J* = 7.0 Hz, 6 H, Me), 1.33 [m, 8 H, (CH₂)₂Me], 1.45 (m, 4 H, OCH₂CH₂CH₂), 1.76 (m, 4 H, OCH₂CH₂), 3.93 (t, *J* = 6.5 Hz, 4 H, OCH₂), 4.61 (s, 2 H, CH₂OH), 6.38 (t, *J* = 2.0 Hz, 1 H, 4-H^{Ar}), 6.50 (d, *J* = 2.0 Hz, 2 H, 2-H^{Ar}) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 14.3 (Me), 22.8 [(CH₂)₂Me], 25.9 (OCH₂CH₂CH₂), 29.4 (OCH₂CH₂), 31.8 [(CH₂)₂Me], 65.7 (CH₂OH), 68.2 (OCH₂), 100.7 (C^{Ar}-4), 105.2 (C^{Ar}-2), 143.4 (C^{Ar}-1), 160.7 (C^{Ar}-3) ppm. IR (neat): ν̄ = 2924 (s), 2862 (m), 1597 (s), 1458 (s), 1381 (m), 1342 (w), 1319 (w), 1296 (m), 1165 (s), 1057 (m), 833 (w), 679 (w), 586 (m) cm⁻¹. EI-MS: *m/z* = 308 [M]⁺. C₁₉H₃₂O₃ (308.5): calcd. C 73.98, H 10.46; found C 73.82, H 10.35.

Compound 12: LiAlH₄ (250 mg, 6.58 mmol) in Et₂O (30 mL) was cooled to 0 °C, and **8** (1.49 g, 4.09 mmol) was added slowly over a period of 1 h. The reaction mixture was heated at reflux for 10 h, after which time NaOH (4 mL, 1 M) was added until a white precipitate formed. The solid was filtered through Celite and washed thoroughly with Et₂O and water. Purification was as for **10**. Compound **12** was isolated as a yellow oil (1.29 g, 3.85 mmol, 94%). ¹H NMR (500 MHz, CDCl₃): δ = 0.89 (t, *J* = 7.0 Hz, 6 H, Me), 1.25–1.38 [m, 12 H, (CH₂)₃Me], 1.44 (m, 4 H, OCH₂CH₂CH₂), 1.76 (m,

4 H, OCH₂CH₂), 3.93 (t, *J* = 6.5 Hz, 4 H, OCH₂), 4.62 (s, 2 H, CH₂OH), 6.37 (t, *J* = 2.0 Hz, 1 H, 4-H^{Ar}), 6.50 (d, *J* = 2.0 Hz, 2 H, 2-H^{Ar}) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 14.3 (Me), 22.8 [(CH₂)₃Me], 26.2 (OCH₂CH₂CH₂), 29.3 [(CH₂)₃Me], 29.5 (OCH₂CH₂), 32.0 [(CH₂)₃Me], 65.7 (CH₂OH), 68.2 (OCH₂), 100.7 (C^{Ar}-4), 105.2 (C^{Ar}-2), 143.4 (C^{Ar}-1), 160.7 (C^{Ar}-3) ppm. IR (neat): ν̄ = 2924 (s), 2854 (s), 1597 (s), 1458 (s), 1381 (m), 1342 (w), 1327 (w), 1296 (w), 1165 (s), 1057 (m), 903 (w), 833 (w), 679 (w), 640 (w), 594 (w) cm⁻¹. EI-MS: *m/z* = 336 [M]⁺. C₂₁H₃₆O₃ (336.5): calcd. C 74.95, H 10.78; found C 75.20, H 10.58.

Compound 13: LiAlH₄ (1.71 g, 45.0 mmol) in Et₂O (500 mL) was cooled to 0 °C, and **9** (18.0 g, 35.7 mmol) was added slowly over a period of 1 h. The reaction mixture was heated under reflux for 5 h and then stirred at room temperature overnight. NaOH (11 mL, 1 M) was added until a white precipitate formed. The solid was filtered through Celite and washed thoroughly with Et₂O and water. Purification was as for **10**, and compound **13** was isolated as a white solid (16.0 g, 33.5 mmol, 94%). M.p. 41 °C. ¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.9 Hz, 6 H, Me), 1.20–1.38 (m, 32 H, CH₂), 1.39–1.48 (m, 4 H, CH₂), 1.62 (br. s, 1 H, OH), 1.76 (quint, *J* = 7.0 Hz, 4 H, OCH₂CH₂), 3.93 (t, *J* = 6.6 Hz, 4 H, OCH₂), 4.61 (s, 2 H, CH₂OH), 6.37 (t, *J* = 2.3 Hz, 1 H, 4-H^{Ar}), 6.50 (d, *J* = 2.3 Hz, 2 H, 2-H^{Ar}) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.5 (Me), 23.1 (CH₂), 26.5 (CH₂), 29.7 (CH₂), 29.8 (2CH₂), 30.0 (3CH₂), 30.1 (CH₂), 32.3 (CH₂), 65.9 (CH₂OH), 68.5 (OCH₂), 100.9 (C^{Ar}-4), 105.4 (C^{Ar}-2), 143.6 (C^{Ar}-1), 160.9 (C^{Ar}-3) ppm. IR (neat): ν̄ = 3510 (br. w), 2916 (s), 2854 (m), 1589 (m), 1466 (m), 1396 (w), 1312 (m), 1165 (m), 1011 (m), 833 (m), 710 (m) cm⁻¹. MALDI MS: *m/z* = 476 [M]⁺. C₃₁H₅₆O₃ (476.8): calcd. C 78.09, H 11.84; found C 78.02, H 11.65.

Compound 18: A solution of **10** (230 mg, 0.91 mmol) in CH₂Cl₂ (10 mL) was cooled to –10 °C, and NEt₃ (1.0 mL, 7.1 mmol) was added. Methanesulfonyl chloride (0.40 mL, 5.2 mmol) was added slowly over a period of 15 min. The reaction mixture was stirred at –10 °C for 1 h, after which it was poured into a mixture of concentrated HCl (3 mL) and crushed ice and extracted with CH₂Cl₂. The organic layer was washed with a saturated solution of NaHCO₃, dried with Na₂SO₄, and the solvent removed to yield a brown oil. Crude **14** was used immediately without purification. Compound **14** (289 mg), 18-crown-6 (25.7 mg, 0.0972 mmol) and K₂CO₃ (269 mg, 1.94 mmol) were added to a solution of **4** (250 mg, 0.49 mmol) in acetone (15 mL). The reaction mixture was heated under reflux for 48 h, after which time water was added. The organic layer was extracted with CH₂Cl₂, dried with MgSO₄, and solvent removed. Column chromatography (SiO₂; ethyl acetate/hexane, 1:3) yielded **18** as a yellow oil (300 mg, 0.40 mmol, 82%). ¹H NMR (500 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.5 Hz, 6 H, Me), 0.97 (t, *J* = 7.0 Hz, 6 H, Me), 1.23–1.39 [m, 16 H, (CH₂)₄Me(octyl)], 1.40–1.54 [m, 8 H, OCH₂CH₂CH₂(octyl + butyl)], 1.76 [m, 8 H, OCH₂CH₂(octyl + butyl)], 3.90 (s, 3 H, OMe), 3.94 [m, 8 H, OCH₂(octyl + butyl)], 4.98 [s, 4 H, CH₂O(ringA)], 6.40 (t, *J* = 2.0 Hz, 2 H, 4-H^{B+C}), 6.55 (d, *J* = 2.0 Hz, 4 H, 2-H^{B+C}), 6.79 (t, *J* = 2.5 Hz, 1 H, 4-H^A), 7.27 (d, *J* = 2.5 Hz, 2 H, 2,6-H^A) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 13.9 (Me), 14.2 (Me), 19.3 (CH₂), 22.7 (CH₂), 26.1 (CH₂), 29.3 (CH₂), 29.4 (CH₂), 31.0 (CH₂), 31.3 (CH₂), 31.9 (CH₂), 52.5 (OMe), 67.8 (OCH₂CH₂), 68.1 (OCH₂CH₂), 70.5 [CH₂O(ringA)], 100.9 (C^{B+C}-4), 105.7 (C^{B+C}-2), 107.2 (C^A-4), 108.3 (C^A-2,6), 132.2 (C^A-1), 138.8 (C^{B+C}-1), 159.9 (C^A-3), 160.7 (C^{B+C}-3), 167.0 (C=O) ppm. IR (neat): ν̄ = 2932 (m), 2878 (m), 1728 (m), 1597 (s), 1450 (s), 1373 (m), 1342 (m), 1319 (m), 1296 (m), 1234 (w), 1165 (s), 949 (w), 833 (w), 771 (w), 679 (w), 640 (w), 617 (w) cm⁻¹. MALDI-MS: *m/z* = 788 [M + K]⁺. C₄₆H₆₈O₈ (749.0): calcd. C 73.65, H 9.15; found C 73.70, H 9.17.

Compound 19: NEt_3 (1.0 mL, 7.1 mmol) was added to a solution of **11** (280 mg, 0.908 mmol) in CH_2Cl_2 (10 mL) previously cooled to -10°C . Methanesulfonyl chloride (0.40 mL, 5.2 mmol) was added slowly over a period of 15 min. The reaction mixture was stirred at -10°C for 1 h, after which time it was poured into a mixture of concentrated HCl (3 mL) and crushed ice and extracted with CH_2Cl_2 . The organic layer was washed with a saturated solution of NaHCO_3 , dried with Na_2SO_4 , and the solvent removed to yield **15** as a brown oil. This crude product was used immediately without further purification. Compound **15** (352 mg), 18-crown-6 (25.7 mg, 0.0972 mmol), and K_2CO_3 (269 mg, 1.94 mmol) were added to a solution of **4** (250 mg, 0.486 mmol) in acetone (15 mL). The reaction mixture was heated at reflux for 48 h, after which time water was added. The organic layer was extracted with CH_2Cl_2 , dried with MgSO_4 , and the solvent removed. Column chromatography (SiO_2 ; ethyl acetate/hexane, 1:3) yielded **19** as a yellow oil (360 mg, 0.447 mmol, 92%) ^1H NMR (500 MHz, CDCl_3): δ = 0.89 [m, 12 H, Me(octyl + hexyl)], 1.23–1.35 [m, 24 H, (CH_2)(octyl + hexyl)], 1.44 [m, 8 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$ (octyl + hexyl)], 1.76 [m, 8 H, OCH_2CH_2 (octyl + hexyl)], 3.89 (s, 3 H, OMe), 3.96 [m, 4 H, OCH_2 (octyl/hexyl)], 3.93 [m, 4 H, OCH_2 (octyl/hexyl)], 4.98 [s, 4 H, $\text{CH}_2\text{O}(\text{ringA})$], 6.40 (t, J = 2.0 Hz, 2 H, 4- $\text{H}^{\text{B+C}}$), 6.55 (d, J = 2.0 Hz, 4 H, 2- $\text{H}^{\text{B+C}}$), 6.79 (t, J = 2.5 Hz, 1 H, 4- H^{A}), 7.28 (d, J = 2.5 Hz, 2 H, 2,6- H^{A}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.25 (Me), 14.3 (Me), 22.8 (CH_2), 22.9 (CH_2), 25.9 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 26.3 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 29.4 (CH_2), 29.5 (2CH_2), 29.6 (CH_2), 31.8 (CH_2), 32.0 (CH_2), 52.5 (OMe), 68.3 [OCH_2 (octyl + hexyl)], 70.5 [$\text{CH}_2\text{O}(\text{ringA})$], 101.1 ($\text{C}^{\text{B+C-4}}$), 105.9 ($\text{C}^{\text{B+C-2}}$), 107.4 ($\text{C}^{\text{A-4}}$), 108.5 ($\text{C}^{\text{A-2,6}}$), 132.2 (C^{A1}), 138.8 ($\text{C}^{\text{B+C-1}}$), 159.9 ($\text{C}^{\text{A-3}}$), 160.7 ($\text{C}^{\text{B+C-3}}$), 167.0 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu}$ = 2955 (m), 2929 (s), 2871 (w), 2857 (m), 1726 (m), 1597 (s), 1464 (m), 1455 (m), 1447 (m), 1435 (w), 1386 (w), 1349 (w), 1325 (w), 1300 (m), 1231 (w), 1166 (s), 1056 (w), 630 (w) cm^{-1} . EI-MS: m/z = 804 [$\text{M}]^+$. $\text{C}_{50}\text{H}_{76}\text{O}_8$ (805.1): calcd. C 74.59, H 9.51; found C 74.58, H 9.62.

Compound 20: A solution of **12** (330 mg, 0.98 mmol) in CH_2Cl_2 (10 mL) was cooled to -10°C , and NEt_3 (1.0 mL, 7.1 mmol) was added. Methanesulfonyl chloride (0.40 mL, 5.2 mmol) was added slowly over a period of 15 min, and the reaction mixture was then stirred at -10°C for 1 h. The mixture was then poured into a mixture of concentrated HCl (3 mL) and crushed ice and extracted with CH_2Cl_2 . The organic layer was washed with a saturated solution of NaHCO_3 , dried with Na_2SO_4 , and the solvent removed to yield **16** as a brown oil. The crude product was used immediately without further purification. Compound **16** (362 mg), 18-crown-6 (25.7 mg, 0.0972 mmol) and K_2CO_3 (269 mg, 1.94 mmol) were added to a solution of **4** (250 mg, 0.49 mmol) in acetone (15 mL). The reaction mixture was heated at reflux for 72 h, after which time water was added. The organic layer was extracted with CH_2Cl_2 , dried with MgSO_4 , and the solvent removed. Column chromatography (SiO_2 ; ethyl acetate/hexane, 1:3) yielded **20** as a yellow oil (350 mg, 0.420 mmol, 86%) ^1H NMR (500 MHz, CDCl_3): δ = 0.88 [m, 12 H, Me(octyl + heptyl)], 1.23–1.36 [m, 28 H, (CH_2)(octyl + heptyl)], 1.44 [m, 8 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$ (octyl + heptyl)], 1.76 [m, 8 H, OCH_2CH_2 (octyl + heptyl)], 3.90 (s, 3 H, OMe), 3.93 [m, 8 H, OCH_2 (octyl + heptyl)], 4.98 [s, 4 H, $\text{CH}_2\text{O}(\text{ringA})$], 6.41 (t, J = 2.0 Hz, 2 H, 4- $\text{H}^{\text{B+C}}$), 6.55 (d, J = 2.0 Hz, 4 H, 2- $\text{H}^{\text{B+C}}$), 6.79 (t, J = 2.0 Hz, 1 H, 4- H^{A}), 7.28 (d, J = 2 Hz, 2 H, 2,6- H^{A}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.16 (Me), 14.17 (Me), 22.65 (CH_2), 22.7 (CH_2), 26.05 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 26.1 ($\text{OCH}_2\text{CH}_2\text{CH}_2$), 29.1 (CH_2), 29.3 (3CH_2), 29.4 (CH_2), 31.83 (CH_2), 31.86 (CH_2), 52.5 (OMe), 68.3 [OCH_2 (octyl + heptyl)], 70.5 [$\text{CH}_2\text{O}(\text{ringA})$], 101.1 ($\text{C}^{\text{B+C-4}}$), 105.9 ($\text{C}^{\text{B+C-2}}$), 107.4 ($\text{C}^{\text{A-4}}$), 108.5 ($\text{C}^{\text{A-2,6}}$), 132.2 ($\text{C}^{\text{A-1}}$), 138.8 ($\text{C}^{\text{B+C-1}}$), 160.0 ($\text{C}^{\text{A-3}}$), 160.7 ($\text{C}^{\text{B+C-3}}$), 167.0 ($\text{C}=\text{O}$)

ppm. IR (neat): $\tilde{\nu}$ = 2923 (m), 2854 (m), 1720 (m), 1597 (s), 1450 (m), 1373 (w), 1342 (w), 1319 (w), 1296 (m), 1234 (w), 1165 (s), 1049 (m), 833 (m), 771 (w), 717 (w), 679 (w), 633 (w), 548 (w) cm^{-1} . EI-MS: m/z = 832 [$\text{M}]^+$. $\text{C}_{52}\text{H}_{80}\text{O}_8$ (833.2): calcd. C 74.96, H 9.68; found C 74.61, H 9.58.

Compound 21: NEt_3 (22 mL, 0.16 mol) was added to a solution of **13** (15.0 g, 0.314 mol) in CH_2Cl_2 (100 mL), previously cooled to -10°C . Methanesulfonyl chloride (9.7 mL, 0.13 mol) was added slowly over a period of 20 min, and then the reaction mixture was stirred at -10°C for 1 h. The mixture was filtered, the filtrate poured into a mixture of concentrated HCl (20 mL) and crushed ice, and extracted with CH_2Cl_2 . The organic layer was washed with a saturated solution of NaHCO_3 , dried with Na_2SO_4 , and the solvent removed. Compound **17** was isolated as a yellow solid which was pure by NMR spectroscopy. **17:** ^1H NMR (400 MHz, CDCl_3): δ = 0.88 (t, J = 6.9 Hz, 6 H, Me), 1.18–1.38 [m, 32 H, (CH_2)₈], 1.39–1.49 (m, 4 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.76 (quint, J = 7.0 Hz, 4 H, OCH_2CH_2), 2.92 (s, 3 H, SMe), 3.92 (t, J = 6.6 Hz, 4 H, OCH_2CH_2), 5.15 (s, 2 H, CH_2OS), 6.45 (t, J = 2.2 Hz, 1 H, 4- H^{A}), 6.52 (d, J = 2.2 Hz, 2 H, 2- H^{A}) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 14.5 (Me), 23.1 (CH_2), 26.4 (CH_2), 29.6 (CH_2), 29.8 (2CH_2), 30.0 (3CH_2), 30.1 (CH_2), 32.3 (CH_2), 38.8 (SO_2CH_3), 68.6 (OCH_2), 72.0 (CH_2OS), 102.5 ($\text{C}^{\text{Ar-4}}$), 107.3 ($\text{C}^{\text{Ar-2}}$), 135.6 ($\text{C}^{\text{Ar-1}}$), 161.1 ($\text{C}^{\text{Ar-3}}$) ppm. IR (neat): $\tilde{\nu}$ = 2916 (s), 2847 (w), 2600 (s), 2492 (s), 1605 (w), 1474 (s), 1396 (m), 1342 (m), 1173 (s), 1034 (s), 972 (w), 926 (w), 849 (m), 810 (m), 648 (m) cm^{-1} . Compound **17** (404 mg), 18-crown-6 (25.7 mg, 0.0972 mmol), K_2CO_3 (269 mg, 1.94 mmol) were added to a solution of **4** (250 mg, 0.486 mmol) in acetone (15 mL) cm^{-1} . The reaction mixture was heated at reflux for 48 h. Water was then added and the organic layer extracted with CH_2Cl_2 , dried with MgSO_4 , and the solvent removed. Column chromatography (SiO_2 ; ethyl acetate/hexane, 1:3) gave **21** as a white/yellow sticky solid (420 mg, 0.431 mmol, 89%) ^1H NMR (500 MHz, CDCl_3): δ = 0.88 [m, 12 H, Me(octyl + dodecyl)], 1.22–1.38 [m, 48 H, (CH_2)(octyl + dodecyl)], 1.44 [m, 8 H, $\text{OCH}_2\text{CH}_2\text{CH}_2$ (octyl + dodecyl)], 1.77 [m, 8 H, OCH_2CH_2 (octyl + dodecyl)], 3.90 (s, 3 H, OMe), 3.93 [t, J = 6.0 Hz, 8 H, OCH_2 (octyl + dodecyl)], 4.98 [s, 4 H, $\text{CH}_2\text{O}(\text{ringA})$], 6.41 (t, J = 2.2 Hz, 2 H, 4- $\text{H}^{\text{B+C}}$), 6.55 (d, J = 2.0 Hz, 4 H, 2- $\text{H}^{\text{B+C}}$), 6.79 (t, J = 2.2 Hz, 1 H, 4- H^{A}), 7.28 (d, J = 2.0 Hz, 2 H, 2,6- H^{A}) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 14.37 (Me), 14.39 (Me), 22.94 (CH_2), 22.90 (CH_2), 26.3 [$\text{OCH}_2\text{CH}_2\text{CH}_2$ (octyl + dodecyl)], 29.47 [OCH_2CH_2 (octyl + dodecyl)], 29.48 (CH_2), 29.60 (2CH_2), 29.64 (CH_2), 29.82 (CH_2), 29.85 (CH_2), 29.88 (CH_2), 29.91 (CH_2), 32.0 (CH_2), 32.1 (CH_2), 52.5 (OMe), 68.3 [OCH_2 (octyl + dodecyl)], 70.5 [$\text{CH}_2\text{O}(\text{ringA})$], 101.0 ($\text{C}^{\text{B+C-4}}$), 105.9 ($\text{C}^{\text{B+C-2}}$), 107.3 ($\text{C}^{\text{A-4}}$), 108.5 ($\text{C}^{\text{A-2,6}}$), 132.1 ($\text{C}^{\text{A-1}}$), 138.7 ($\text{C}^{\text{B+C-1}}$), 159.9 ($\text{C}^{\text{A-3}}$), 160.7 ($\text{C}^{\text{B+C-3}}$), 167.0 ($\text{C}=\text{O}$) ppm. IR (neat): $\tilde{\nu}$ = 2956 (m), 2919 (s), 2871 (m), 2852 (m), 1719 (m), 1595 (s), 1464 (m), 1438 (m), 1392 (w), 1369 (m), 1349 (m), 1337 (w), 1301 (m), 1239 (w), 1172 (s), 1146 (m), 1103 (w), 1056 (m), 836 (w), 829 (w), 761 (w), 683 (w), 668 (w) cm^{-1} . EI-MS: m/z = 973 [$\text{M}]^+$. $\text{C}_{62}\text{H}_{100}\text{O}_8$ (973.5): calcd. C 76.50, H 10.35; found C 76.41, H 10.29.

Acknowledgments

We thank the Swiss National Science Foundation, in part under program NRP 47, the Swiss National Center of Competence in Research in Nanoscale Science, and the University of Basel for financial support. We also thank Marc Häusler for helpful discussion.

- [1] *Topics in Current Chemistry* (Dendrimers) (Ed.: F. Vögtle), Springer-Verlag, Berlin, **1998**, vol. 197.
- [2] *Topics in Current Chemistry* (Dendrimers II) (Ed.: F. Vögtle), Springer-Verlag, Berlin, **2000**, vol. 210.
- [3] *Topics in Current Chemistry* (Dendrimers III) (Ed.: F. Vögtle), Springer-Verlag, Berlin, **2001**, vol. 212.
- [4] *Topics in Current Chemistry* (Dendrimers IV) (Ed.: F. Vögtle), Springer-Verlag, Berlin, **2001**, vol. 217.
- [5] *Topics in Current Chemistry* (Dendrimers V) (Eds.: C. A. Schalley, F. Vögtle), Springer-Verlag, Berlin, **2003**, vol. 228.
- [6] C. J. Hawker, J. M. J. Fréchet, *J. Am. Chem. Soc.* **1990**, *112*, 7638–7647.
- [7] C. J. Hawker, J. M. J. Fréchet, *J. Chem. Soc., Chem. Commun.* **1990**, 1010–1013.
- [8] S. K. Grayson, J. M. J. Fréchet, *Chem. Rev.* **2001**, *101*, 3819–3867.
- [9] I. Widmer, U. Hubler, M. Stöhr, L. Merz, H.-J. Güntherodt, B. A. Hermann, P. Samorí, J. P. Rabe, P. B. Rheiner, G. Greiveldinger, P. Murer, *Helv. Chim. Acta* **2002**, *85*, 4255–4263.
- [10] E. C. Constable, B. A. Hermann, C. E. Housecroft, L. Merz, L. J. Scherer, *Chem. Commun.* **2004**, 928–929.
- [11] L. J. Scherer, L. Merz, E. C. Constable, C. E. Housecroft, M. Neuburger, B. A. Hermann, *J. Am. Chem. Soc.* **2005**, *127*, 4033–4041.
- [12] L. Merz, H.-J. Güntherodt, L. J. Scherer, E. C. Constable, C. E. Housecroft, M. Neuburger, B. A. Hermann, *Chem. Eur. J.* **2005**, *11*, 2307–2318.
- [13] B. A. Hermann, L. J. Scherer, E. C. Constable, C. E. Housecroft, *Adv. Funct. Mater.* **2006**, *16*, 221–235.
- [14] E. C. Constable, M. Häusler, B. A. Hermann, C. E. Housecroft, M. Neuburger, S. Schaffner, L. J. Scherer, *CrystEngComm* **2007**, *9*, 176–180.
- [15] P. B. Rheiner, D. Seebach, *Chem. Eur. J.* **1999**, *5*, 3221–3226.
- [16] G. W. Gokel, H. D. Durst, *Synthesis* **1976**, 168–184.
- [17] S. A. DiBiase, G. W. Gokel, *J. Org. Chem.* **1978**, *43*, 447–452.
- [18] T. Ritter, K. Stanek, I. Larrosa, E. M. Carreira, *Org. Lett.* **2004**, *6*, 1513–1514.
- [19] J. Zhu, R. Beugelmans, S. Bourdet, J. Chastanet, G. Roussi, *J. Org. Chem.* **1995**, *60*, 6389–6396.

Received: February 4, 2008
Published Online: April 4, 2008