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Alternative convergent and accelerated double-stage convergent approaches towards functionalized dendritic polyethers

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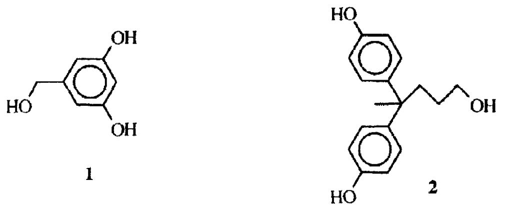
Abstract: Alternative convergent synthesis strategies for the preparation of dendritic macromolecules, using either mesylate activation or the Mitsunobu reaction, are described. The synthesis can be further accelerated by using a double stage convergent approach. Two t-butyldiphenylsilyl protected synthons **3** and **5** were prepared in excellent yields and used in a one-pot synthesis of higher generation polyether dendrons. Additionally these synthons were used to prepare dendrons with functional groups at the periphery.

Keywords: dendrimers; Mitsunobu reactions; ethers

Introduction

The convergent synthesis of dendritic polyethers, based on the AB_2 monomer 3,5-dihydroxybenzyl alcohol **1**, has been developed by Hawker and Fréchet[1] and was successfully used by his[2] and other groups[3] to construct monodisperse macromolecules. The drawbacks of the method, however are that (1) the growth of the dendritic wedges is time-consuming and (2) the increasing steric hindrance, which occurs at the focal functional group with increasing dendron size, may inhibit its anchoring to a monomer or central core. Fréchet *et al.*[4] circumvented these problems by using hypercores constructed from 4,4'-bis(4-hydroxyphenyl)pentanol **2**. During the convergent growth the phenol functions at the periphery were protected with benzyl groups. The latter were removed by catalytic hydrogenolysis after the dendrons had been attached to a central polyfunctional molecule. These hypercores were then alkylated with polyether benzylic bromides derived from the monomer **1** to give dendrimers with nominal molecular weights up to 84 219. The dendrimers thus obtained possessed a two-layered structure.



Scheme 1

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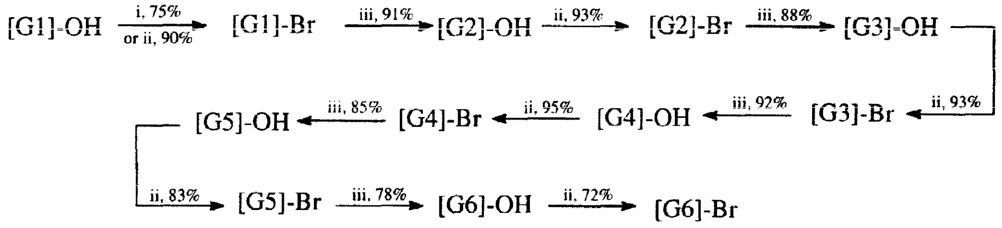
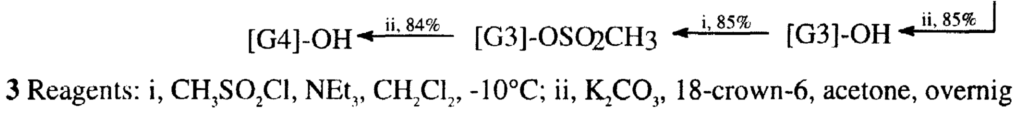
Results

The convergent dendrimer synthesis described by Hawker and Fréchet is based on the reaction of two equivalents of a benzylic bromide and one equivalent of the 3,5-dihydroxybenzyl alcohol **1** monomer. The first generation benzylic alcohol[5] can be easily prepared in large amounts through a coupling reaction of two equivalents of benzyl bromide to one equivalent of methyl 3,5-dihydroxybenzoate **3**, followed by a $LiAlH_4$ reduction step. Transformation of this [G1]-OH to the corresponding bromide activates the [G1]-Br dendron for coupling to a new monomer **1** and formation of [G2]-OH. Dendrons of generations one to six were obtained by this procedure in high yields[1] (Scheme 2). In our hands, preparation of large quantities of [G1]-Br proved to be cumbersome as the PBr_3 bromination often gives traces of HBr which may partially cleave the desired product. An alternative way to prepare [G1]-Br consists of using PPh_3/CBr_4 as in the preparation of the higher generation bromides. This method gave [G1]-Br as a pure product in high and reproducible yields. Disadvantages of this procedure are the high cost and the column chromatographic purification necessary for the purification of [G1]-Br. In spite of these disadvantages we prefer this method to prepare [G1]-Br.



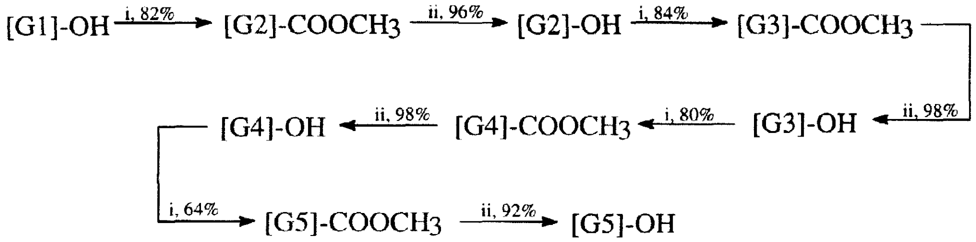
Scheme 2[1] Reagents: i, PBr_3, toluene; ii, CBr_4, PPh_3, THF; iii, K_2CO_3, 18-crown-6, acetone, 48h

The reported yields of the [Gn]-Br are not always easy to reproduce and great care is necessary, especially with the higher generation bromides. Therefore, we prepared mesylates as an alternative to bromides from the corresponding benzylic alcohols [Gn]-OH using methanesulphonyl chloride in the presence of an excess of NEt_3. The reaction has to be carried out at −10°C to avoid the formation of chloride byproducts. The advantage of "the mesylate route" compared to the reported[1] "bromide route" is that crystallization of the G1 and G2 mesylates is possible in a reproducible way and therefore chromatographic purification can be avoided. This makes the synthesis easily adaptable to prepare large amounts of the third generation [G3]-OH. An extra benefit is the higher reactivity of the mesylates. The reaction times of the Williamson ether synthesis could be reduced from 48 hours to overnight reflux with comparable yields to the method of Hawker and Fréchet. (Scheme 3).



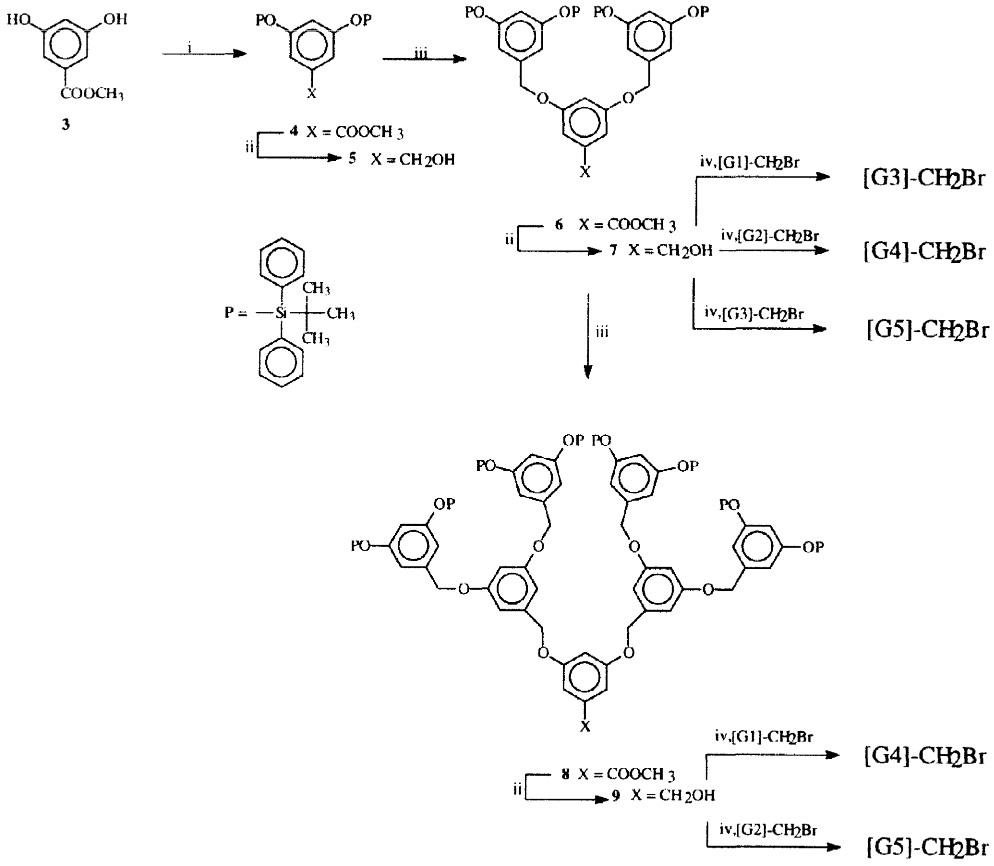
Scheme 3 Reagents: i, CH_3SO_2Cl, NEt_3, CH_2Cl_2, -10°C; ii, K_2CO_3, 18-crown-6, acetone, overnight reflux

A second alternative method to speed up the dendron growth ("the benzoate route") uses the Mitsunobu coupling reaction of phenols and benzylic alcohols. Admittedly, the yields under Mitsunobu conditions (diethyl azodicarboxylate and PPh_3)[6] are generally lower than those for the Williamson ether synthesis, but the reaction conditions change again from 48 hours reflux to overnight stirring at room temperature. After the Mitsunobu reaction, a $LiAlH_4$ reduction step is required to obtain the corresponding higher generation alcohol (Scheme 4). This step proceeds fast and reproducibly in very high yields. Another advantage is that carbon alkylation as observed by Fréchet *et al.* in their coupling of the [Gn]-Br to the 3,5-dihydroxybenzyl alcohol will not occur. Moreover, the benzoates are much more stable than the benzyl bromides and mesylates and can be kept indefinitely at room temperature. Either the mesylate or benzoate convergent route have been employed several times with reproducible yields in our laboratories.

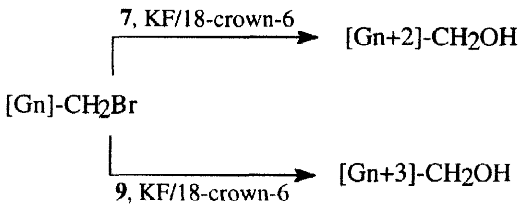


Scheme 4 Reagents: i, $EtO_2CN{=}NCO_2Et$, PPh_3; ii, $LiAlH_4$, THF

A third approach which accelerates the synthesis of the dendrons even more is based on the replacement of the AB_2 monomer 3,5-dihydroxybenzyl alcohol **1** by a AB_4 trimer or AB_8 heptamer[7]. Thus, an increase of two generations can be made by alkylation of the AB_4 trimer and an increase of three generations by alkylation of an AB_8 heptamer. This two-front convergent synthesis starts from methyl 3,5-dihydroxybenzoate **3** by protecting the phenol functions with t-butyldiphenylsilyl groups. This group was chosen both for its stability and its smooth and selective removal with the fluoride ion. The bis(t-butyldiphenylsilyl) protected ester **4** was reduced with $LiAlH_4$ to the protected alcohol **5**, which was isolated as a white crystalline solid. The t-butyldimethylsilyl protecting group, which was checked as an alternative, is less suitable since it was partially removed in the $LiAlH_4$ reduction step of our synthesis. Coupling of **5** with the precursor **3** under Mitsunobu conditions afforded the trimer ester **6** which was reduced ($LiAlH_4$) to the protected AB_4 trimer alcohol **7**. This sequence can be repeated to give the AB_8 heptamer alcohol **9** (Scheme 5). With the synthons **7** and **9** at hand, higher generation dendrons can now be easily prepared in a one-pot reaction by simultaneous deprotection and alkylation. This approach is illustrated by reacting the alcohol **7** overnight with KF/18-crown-6 and Fréchet's benzylic bromides [Gn]-Br of the first (n=1), second (n=2) and third (n=3) generation, which yielded dendritic wedges [Gn+2]-OH of the third (92%), fourth (90%) and fifth (82%) generation respectively; thus increasing the generation number by two units in each case (Scheme 5 and Scheme 6). Similar transformations were achieved with the heptamer alcohol **9**, where the higher dendrons [G4]-OH (82%) and [G5]-OH (83%) were obtained directly from Fréchet's benzylic bromides of the first and second generation; here an increase of three generations is made in each case (Scheme 5 and Scheme 6). The sixth generation dendrons could not be prepared in this way since the Mitsunobu reaction is more sensitive to steric hindrance than the Williamson ether synthesis. The protection/deprotection strategy outlined above represents a simple accelerated method for the synthesis of polyether dendrons as compared with the classical approach, where two separate steps are required for each generation growth.



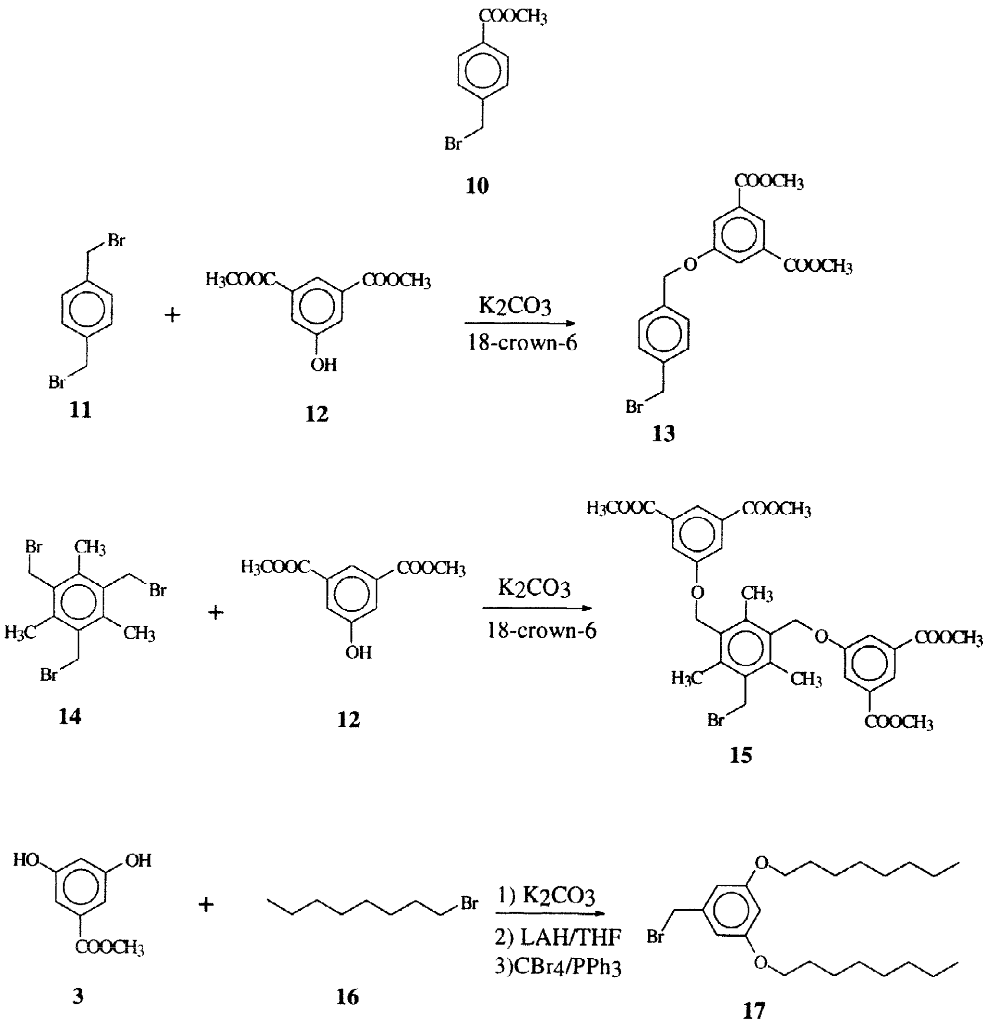
Scheme 5 Reagents: i, t-BuPh$_2$SiCl, imidazole, DMF; ii, LiAlH$_4$, THF; iii, EtO$_2$CN=NCO$_2$Et, PPh$_3$, THF; iv, KF, 18-crown-6, acetone, overnight reflux



Gn = generation number (n = 1, 2, 3, ...)

Scheme 6

An advantage of the double stage convergent approach[7] is the fact that the periphery of the dendrons can be varied at a later stage of the synthesis. As a first example it was interesting to functionalize the periphery with ester functions.[8,9] To this end, we used three different ester synthons in combination with the trimer **7**. We prefer the trimer **7** over the heptamer **9** because of its shorter synthesis, and the easier chromatographic separations involved. The first synthon, which was also used by Fréchet *et al.*[9] had one ester per reactive site, the commercial methyl 4-(bromomethyl)benzoate **10** (Scheme 7).

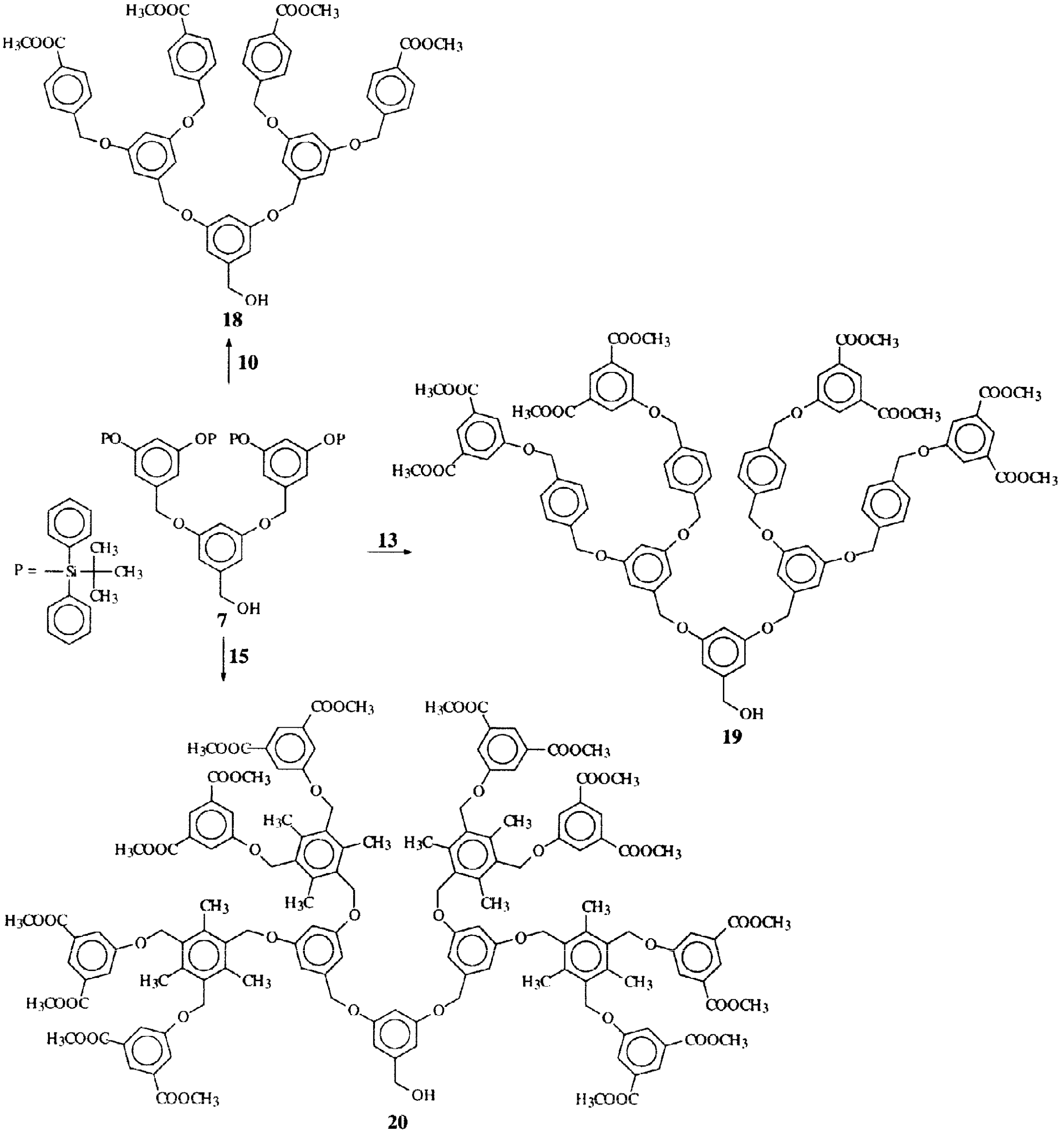


Scheme 7

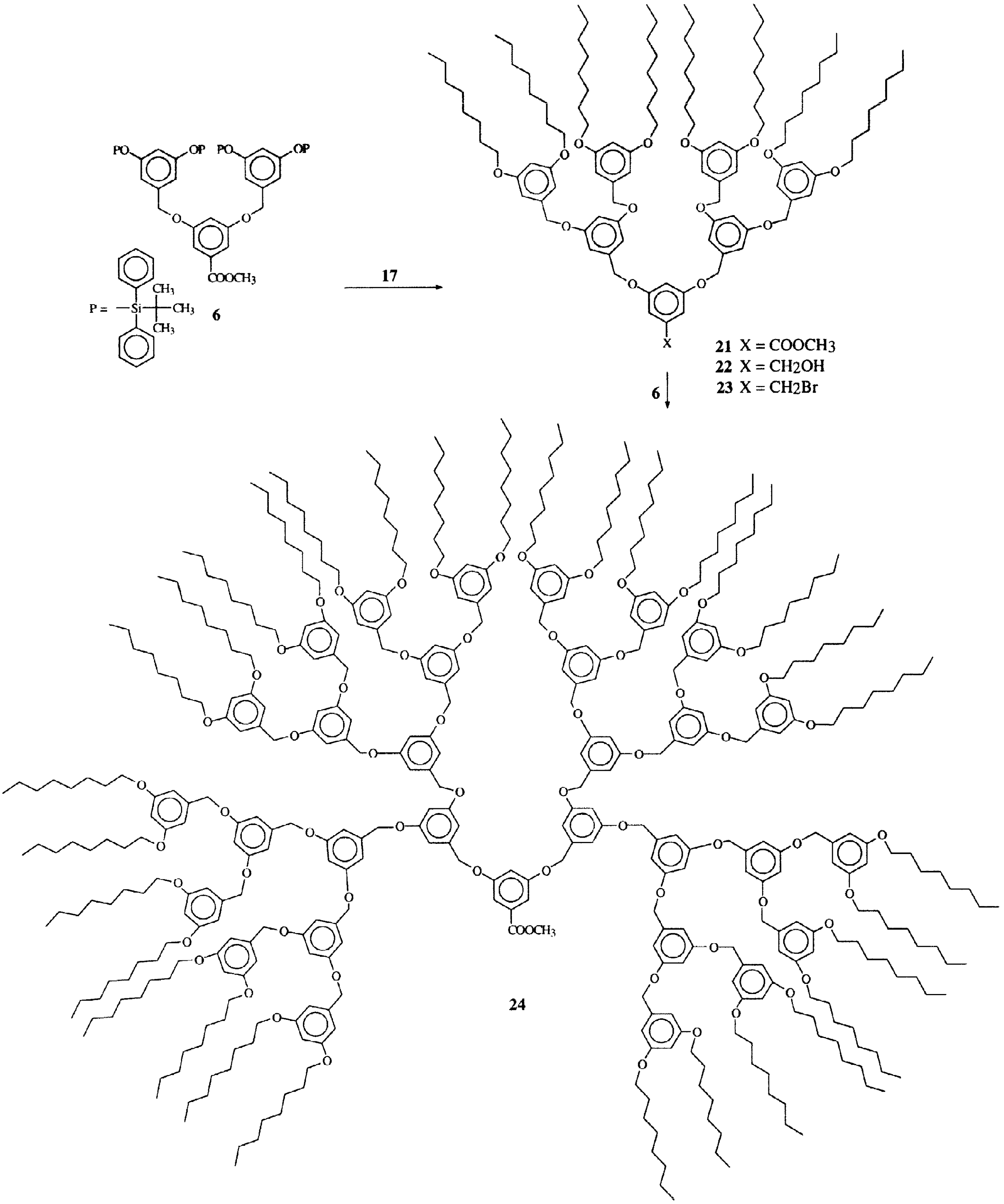
In a one step deprotection/alkylation reaction a second generation ester functionalized dendron **18** was obtained in high yield (94%) (Scheme 8). A better mass balance is obtained starting from ester synthons **13** and **15** having respectively two and four ester functions per reactive site. To synthesize the diester **13**, 1,4-bis(bromomethyl)benzene **11** was reacted with one equivalent dimethyl 5-hydroxyisophthalate **12** in the presence of K_2CO_3 and 18-crown-6. This reaction gave the benzylic bromide **13** (Scheme 7) which was coupled to the trimer **7** to give a second generation ester functionalized benzylic alcohol **19** (Scheme 8). Finally a tetraester **15** was prepared in fair yield using the readily available[10] 1,3,5-tris(bromomethyl)-2,4,6-

trimethylbenzene **14** and dimethyl 5-hydroxyisophthalate **12**. This afforded the benzylic bromide **15** (Scheme 7) which was attached to the trimer. The resulting dendron of the second generation **20** had already a molecular mass of 2688 as confirmed by ESMS (Scheme 8).

Another interesting example is the synthesis of dendrons with long alkyl tails in the periphery. These compounds were already communicated by Shen *et al.*[11] in 1997 using the convergent growth approach as introduced by Fréchet[1]. We prepared **17** using the Shen procedure[11] and carried out the coupling reaction with trimer **6** to obtain **21** in excellent yield (87%). After reduction and bromination of this compound we reacted it once more with the trimer to obtain a fifth generation dendron **24** with 32 octyl groups in the periphery (68%). This reaction sequence demonstrates very convincingly the effectiveness of this accelerated growth of high generation dendrons.



Scheme 8


PO
OP
PO
OP
O
O
COOCH3
P = —Si—CH3 CH3 CH3
6
17
X
21 X = COOCH3
22 X = CH2OH
23 X = CH2Br
6
COOCH3
24

Scheme 9

Experimental

Mp's were determined using a Reichert Thermovar apparatus. IR spectra were recorded with a Perkin-Elmer spectrometer and NMR spectra on a Bruker AMX-400 spectrometer. Mass spectra were obtained on a Kratos Concept 1H instrument with FAB ionization in a matrix of 3-mercapto-1,2-propanediol (for **5**) or 3-nitrobenzyl alcohol (for **7**), on a Hewlett Packard type MS Engine n° 5989A in EI (250°C) (for [G1]-OSO_2CH_3, [G2]-OSO_2CH_3, **13** and **15**) and ESI Micromass Quattro II ES+ with MeOH/CCl_4 (1:9) – NH_4OAc (0.1M in MeOH), core 120V with infusion pump (for [G3]-OSO_2CH_3, **19**, **20**, **22**, **23** and **24**).

The solvents dimethylformamide (DMF) and acetone were dried on molecular sieves 4 Å, and tetrahydrofuran (THF) was freshly distilled from sodium metal in a nitrogen atmosphere.

Synthesis of the [G1]-Br using CBr_4

To a stirred solution of [G1]-OH (5.4 g, 16.9 mmol) and CBr_4 (16.8 g, 50.8 mmol) in dry THF (50 ml) was added PPh_3 (13.3 g, 50.8 mmol) portionwise while cooling on an ice bath. After the addition was completed, the mixture was stirred for another hour at room temperature under a nitrogen atmosphere, poured into water (200 ml), extracted with dichloromethane (3 x 100 ml), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel using dichloromethane as the eluent giving [G1]-Br as a white powder (5.8 g, 90%); mp (n-hexane) 92.9-93.2°C (Lit.[5] 92-93°C)

^1H, ^{13}C NMR and MS spectra were identical to the ones reported.

General procedure for the synthesis of the mesylates exemplified for [G1]-OSO_2CH_3

To a mixture of [G1]-OH (4.8 g, 15 mmol) and NEt_3 (7.6 g, 75 mmol) in dry dichloromethane (50 ml) methanesulphonyl chloride (6.9 g, 60 mmol) was added in 15 min. at -10°C under a nitrogen atmosphere. After stirring for 1h at -10°C the reaction mixture was poured into a mixture of crushed ice (100 ml) and concentrated HCl (10 ml). The dichloromethane layer was separated, washed with saturated $NaHCO_3$ solution (100 ml), dried ($MgSO_4$) and evaporated. The crude material was crystallized from diethyl ether to yield [G1]-OSO_2CH_3 (5.2 g, 87%); mp 81.5-81.8°C; ν_{max} (KBr)/cm^{-1} 1607s, 1455s, 1380m, 1352s, 1323s, 1171s and 1154s; δ_H ($CDCl_3$, 400 MHz) 2.83 (s, 3H, SO_2CH_3), 5.05 (s, 4H, CH_2O), 5.15 (s, 2H, CH_2OSO_2), 6.63 (s, 3H, C_6H_3), 7.5-7.3 (m, 10H, C_6H_5); δ_C ($CDCl_3$) 38.4 (CH_3), 70.2 (CH_2O), 71.4 (CH_2OSO_2), 103.0, 107.6, 135.5 and 160.2, (Ar C-4, C-2, C-1 and C-3), 127.5, 128.1, 128.6, and 136.5 (Ph C-2, C-4, C-3 and C-1); MS (EI, m/z) 398 (M+.).

[G2]-OSO_2CH_3 was obtained using the general procedure from [G2]-OH (3.9 g, 5.3 mmol), NEt_3 (2.7 g, 26.7 mmol) and methanesulphonyl chloride (2.5 g, 21.7 mmol) in dry dichloromethane (50 ml). The crude material was crystallized from diethyl ether to yield [G2]-OSO_2CH_3 (3.8 g, 87%) as a white powder, mp 128.7-128.9°C; ν_{max} (KBr)/cm^{-1} 1598s, 1450m, 1375m, 1352m, 1163s; δ_H ($CDCl_3$, 400 MHz) 2.82 (s, 3H, CH_3), 4.97 (s, 4H,

CH_2O), 5.03 (s, 8H, CH_2O); 5.13 (s, 2H, CH_2OSO_2), 6.57 (t, 2H, J 2.2, 4-H 2nd gen. Ar), 6.59 (t, 1H, J 2, 2/6-H 1st gen. Ar), 6.60 (d, 2H, J 2, 4-H, 1st gen. Ar), 6.66 (d, 4H, J 2.2, 2/6-H, 2nd gen. Ar), 7.5-7.3 (m, 20H, Ph); δ_C ($CDCl_3$) 38.4 (CH_3), 70.0 and 70.2 (CH_2O), 71.3 (CH_2OSO_2), 103.0, 107.7, 135.6 and 160.2, (1st gen. Ar C-4, C-2, C-1 and C-3), 101.7, 106.4, 138.9 and 160.1 (2nd gen. Ar C-4, C-2, C-1 and C-3), 127.5, 128.0, 128.6, and 136.7 (Ph C-2, C-4, C-3 and C-1); MS (EI, m/z) 822 (M+.).

[G3]-OSO_2CH_3 was obtained using the general procedure from [G3]-OH (1.2 g, 0.75 mmol), NEt_3 (0.4 g, 3.5 mmol) and methanesulphonyl chloride (0.4 g, 3.1 mmol) in dry dichloromethane (20 ml). The crude material was chromatographed on silica gel with dichloromethane as the eluent to yield [G3]-OSO_2CH_3 (1.0 g, 85%) as a colorless oil; ν_{max} (KBr)/cm^{-1} 1596s, 1449m, 1372m, 1350m, 1161s; δ_H ($CDCl_3$, 400 MHz) 2.72 (s, 3H, CH_3), 4.89 (s, 12H, CH_2O), 4.94 (s, 16H, CH_2O), 5.03 (s, 2H, CH_2OSO_2), 6.7-6.5 (m, 21H, Ar), 7.5-7.3 (m, 40H, Ph); δ_C ($CDCl_3$) 38.0 (CH_3), 69.8 and 69.9 (CH_2O), 71.2 (CH_2OSO_2), 101.7, 106.4, 138.9 and 160.1 (1st gen. and 2nd gen. Ar C-4, C-2, C-1 and C-3), 101.5, 107.5, 138.9 and 160.0 (1st gen. and 2nd gen. Ar C-4, C-2, C-1 and C-3), 127.4, 127.9, 128.4, and 136.7 (Ph C-2, C-4, C-3 and C-1); MS (ES+, m/z) 1672.

General procedure for the synthesis of the higher dendritic polyethers, using mesylates exemplified for [G2]-OH.

A mixture of [G1]-OSO_2CH_3 (7g, 17.6 mmol), 3,5-dihydroxybenzyl alcohol (0.82 g, 5.9 mmol), K_2CO_3 (4.9 g, 35 mmol) and 18-crown-6 (100 mg, 0.38 mmol) in dry acetone (70 ml) was refluxed overnight under a nitrogen atmosphere. The reaction mixture was poured into water (300 ml) and extracted with dichloromethane (3 x 150 ml). The combined extracts were dried ($MgSO_4$), evaporated and the residue chromatographed on silica gel with dichloromethane/diethyl ether (20:1) as the eluent to give [G2]-OH (11.4 g, 87%); mp (toluene / n-hexane) 110.7-111.2°C (lit[1]. 110-111°C).

^1H, ^{13}C NMR and MS spectra were identical to the ones reported[1].

[G3]-OH was obtained using the general procedure from [G2]-OSO_2CH_3 (2.5 g, 3.1 mmol), 3,5-dihydroxybenzyl alcohol (0.14 g, 1.0 mmol), K_2CO_3 (0.85 g, 6.2 mmol) and 18-crown-6 (100 mg, 0.38 mmol) in dry acetone (40 ml). The residue was chromatographed on silica gel with dichloromethane/diethyl ether (25:1) as the eluent to give [G3]-OH as a colorless glass (4.2 g, 85%).

^1H, ^{13}C NMR and MS spectra were identical to the ones reported[1].

[G4]-OH was obtained using the general procedure from [G3]-OSO_2CH_3 (1.5 g, 0.9 mmol), 3,5-dihydroxybenzyl alcohol (0.042 g, 0.3 mmol), K_2CO_3 (0.85 g, 6.1 mmol) and 18-crown-6 (100 mg, 0.38 mmol) in dry acetone (40 ml). The residue was chromatographed on silica gel with dichloromethane/diethyl ether (25:1) as the eluent to give [G4]-OH as a colorless glass (2.5 g, 84%).

^1H, ^{13}C NMR and MS spectra were identical to the ones reported[1].

General procedure for the synthesis of the higher dendritic polyethers, using Mitsunobu conditions exemplified for [G2]-OH.

A mixture of [G1]-OH (8.9 g, 27.8 mmol), methyl 3,5-dihydroxybenzoate **3** (2.1 g, 12.7 mmol), diethyl azodicarboxylate (5.5 g, 31.7 mmol) and triphenylphosphine (8.3 g, 31.7 mmol) in dry THF (150 ml) was stirred overnight at room temperature. After removal of the solvent, the residue was chromatographed on silica gel with dichloromethane as the eluent to give [G2]-$COOCH_3$ **6** as a colorless oil (8.0 g, 82%); ν_{max} (KBr)/cm^{-1} 3066m, 2931m, 2322m, 1730m, 1589s, 1539s; δ_H ($CDCl_3$, 400 MHz) 3.89 (s, 3H, CH_3), 4.99 (s, 4H, CH_2O), 5.02 (s, 8H, $PhCH_2$), 6.57 (t, 2H, J 2, H-4 2nd gen. Ar), 6.67 (d, 4H, J 2, H-2/6 2nd gen. Ar), 6.76 (t, 1H, J 2, H-4 1st gen. Ar), 7.2-7.5 (m, 22H, Ph and H-2/6 1st gen Ar); δ_C ($CDCl_3$) 52.2 (CH_3), 70.1 (CH_2O), 101.7, 106.4, 138.8 and 160.2 (2nd gen. Ar C-4, C-2, C-1 and C-3), 107.1, 108.4, 132.0 and 159.7 (1st gen. Ar C-4, C-2, C-1 and C-3), 127.5, 128.0, 128.6 and 136.7 (Ph C-2, C-4, C-3 and C-1), 166.7 ($\underline{C}OOCH_3$).

A solution of [G2]-$COOCH_3$ **6** (13.6 g, 17.6 mmol) in dry THF (150 ml) was added dropwise to a suspension of $LiAlH_4$ (1.0 g, 26 mmol) in THF (20 ml). After refluxing for 1 h, the solution was treated with aqueous NaOH (1 M, 10 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give [G2]-OH **7** as a white solid (12.5 g, 96%); mp (toluene / n-hexane) 110.8-111.0°C (lit[1]. 110-111°C).

[G3]-OH

A mixture of [G2]-OH (17.2 g, 23.1 mmol), methyl 3,5-dihydroxybenzoate **3** (1.8 g, 10.5 mmol), diethyl azodicarboxylate (4.6 g, 26.3 mmol) and triphenylphosphine (6.9 g, 26.3 mmol) in dry THF (150 ml) was stirred overnight at room temperature. After removal of the solvent, the residue was chromatographed on silica gel with dichloromethane as the eluent to give [G3]-$COOCH_3$ **6** as a white solid (14.3 g, 84%); ν_{max} (KBr)/cm^{-1} 3068m, 3033m, 2930m, 2872m, 2320m, 1724m, 1591s, 1544s; δ_H ($CDCl_3$, 400 MHz) 3.85 (s, 3H, CH_3), 4.93 (s, 8H, CH_2O), 4.95 (s, 4H, CH_2O), 4.98 (s, 16H, $PhCH_2$), 6.55 (m, 6H, H-4 Ar), 6.6-6.7 (m, 12H, H-2/6 Ar), 6.77 (t, 1H, J 2.2, H-4 Ar), 7.2-7.4 (m, 42H, H-2/6 Ar and Ph); δ_C ($CDCl_3$) 52.2 (CH_3), 69.9 and 70.0 (CH_2O), 101.6, 106.3, 138.8 and 160.0 (2nd gen. Ar C-4, C-2, C-1 and C-3), 101.6, 106.4, 139.1 and 160.1 (3rd gen. Ar C-4, C-2, C-1 and C-3), 107.1, 108.4, 132.0 and 159.6 (1st gen. Ar C-4, C-2, C-1 and C-3), 127.5, 127.9, 128.5 and 136.7 (Ph C-2, C-4, C-3 and C-1), 166.6 ($\underline{C}OOCH_3$).

A solution of [G3]-$COOCH_3$ **6** (13.6 g, 8.4 mmol) in dry THF (150 ml) was added dropwise to a suspension of $LiAlH_4$ (0.48 g, 12.6 mmol) in THF (20 ml). After refluxing for 1 h, the solution was treated with aqueous NaOH (1 M, 10 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give [G3]-OH **7** as a colorless glass (13.1 g, 98%).

[G4]-OH

A mixture of [G3]-OH (13.1 g, 8.2 mmol), methyl 3,5-dihydroxybenzoate **3** (0.55 g, 3.3 mmol), diethyl azodicarboxylate (1.4 g, 8.3 mmol) and triphenylphosphine (2.2 g, 8.3 mmol) in dry THF (150 ml) was stirred overnight at room temperature. After removal of the solvent, the residue was chromatographed on silica gel with dichloromethane as the eluent to give [G4]-COOCH$_3$ **6** as a white solid (8.8 g, 80%); ν_{max} (KBr)/cm^{-1} 3065m, 2929m, 2320m, 1734m, 1590s, 1541s; δ_H (CDCl$_3$, 400 MHz) 3.82 (s, 3H, CH$_3$), 4.91 (s, 30H, CH$_2$O), 4.96 (s, 32H, PhCH$_2$), 6.45-6.65 (m, 14H, Ar), 7.26-7.38 (m, 80H, Ph); δ_C (CDCl$_3$) 52.2 (CH$_3$), 69.9 and 70.0 (CH$_2$O), 101.5, 101.6 and 107.1 (Ar C-4), 106.3, 106.4 and 108.4 (Ar C-2), 127.5, 128.0, 128.5 and 136.7 (Ph C-2, C-4, C-3 and C-1), 132.0, 138.9 and 139.2 (Ar C-1), 159.6, 160.0, and 160.1 (Ar C-3), 166.7 ($\underline{C}$OOCH$_3$).

A solution of [G4]-COOCH$_3$ **6** (15.0 g, 4.5 mmol) in dry THF (150 ml) was added dropwise to a suspension of LiAlH$_4$ (0.26 g, 6.8 mmol) in THF (20 ml). After refluxing for 1 h, the solution was treated with aqueous NaOH (1 M, 10 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give [G4]-OH **7** as a colorless glass (14.5 g, 98%).

[G5]-OH

A mixture of [G4]-OH (14.5 g, 4.4 mmol), methyl 3,5-dihydroxybenzoate **3** (0.34 g, 2.0 mmol), diethyl azodicarboxylate (0.87 g, 5.0 mmol) and triphenylphosphine (1.3 g, 0.5 mmol) in dry THF (150 ml) was stirred overnight at room temperature. After removal of the solvent, the residue was chromatographed on silica gel with dichloromethane as the eluent to give [G5]-COOCH$_3$ **6** as a white solid (8.6 g, 64%); ν_{max} (KBr)/cm^{-1} 3064m, 2930m, 2290m, 1745m, 1590s, 1558s; δ_H (CDCl$_3$, 400 MHz) 3.80 (s, 3H, CH3), 4.90 (s, 60 H, CH$_2$O), 4.96 (s, 64 H, PhC$\underline{H}_2$), 6.45-6.65 (m, 93 H, Ar), 7.2-7.4 (m, 160 H, Ph); δ_C (CDCl$_3$) 52.2 (CH3), 69.9 and 70.0 (CH$_2$O), 101.5 (Ar C-4), 106.3 (Ar C-2), 139.2 and 139.3 (Ar C-1), 160.0 and 160.1 (Ar C-3), 127.5, 127.9, 128.5 and 136.7 (Ph C-2, C-4, C-3 and C-1).

A solution of [G5]-COOCH$_3$ **6** (10.6 g, 16 mmol) in dry THF (150 ml) was added dropwise to a suspension of LiAlH$_4$ (0.091 g, 2.4 mmol) in THF (20 ml). After refluxing for 1 h, the solution was treated with aqueous NaOH (1 M, 10 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give [G5]-OH **7** as a colorless glass (9.8 g, 92%).

^{1}H, ^{13}C NMR and MS spectra were identical to the ones reported[1].

3,5-Bis(t-butyldiphenylsilyloxy)benzyl alcohol 5.

A solution of compound **3** (8.4 g, 50 mmol), imidazole (8.5 g, 125 mmol) and t-butyldiphenylsilyl chloride (30.25 g, 110 mmol) in dry DMF (100 ml) was stirred at room temperature for 24 h. The reaction mixture was poured into water (300 ml), extracted with diethyl ether (3 x 200 ml), and the combined extracts were dried ($MgSO_4$) and evaporated. The resulting oil **4** was dissolved in dry THF (100 ml) and added dropwise to a suspension of $LiAlH_4$ (2.5 g, 60 mmol) in THF (50 ml). After reflux for 1 h, the solution was treated with aqueous NaOH (1 M, 15 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give the protected benzyl alcohol **5** as a white crystalline solid (26.7 g, 87%), mp 105.0-105.7°C; ν_{max} (KBr)/cm^{-1} 3583m, 3494w, 3070m, 3051m, 2959s, 2928s, 2890m, 2856s and 1599vs; δ_H ($CDCl_3$, 400 MHz) 0.99 (s, 18 H, t-Bu), 1.23 (t, 1 H, J 6, OH), 4.31 (d, 2 H, J 6, CH_2O), 6.10 (t, 1 H, J 2, 4-H Ar), 6.31 (d, 2 H, J 2, 2/6-H Ar), 7.26 (m, 8 H, 3/5-H Ph), 7.35 (m, 4 H, 4-H Ph) and 7.53 (d, 8 H, J 8, 2/6-H Ph); δ_C ($CDCl_3$) 19.4 and 26.5 (t-Bu), 65.0 (CH_2O), 110.7, 111.5, 142.6 and 156.3 (Ar C-4, C-2, C-1 and C-3), 127.6, 129.7, 132.7 and 135.4 (Ph C-3, C-4, C-1 and C-2); m/z (FAB) 617 $(M+H)^+$ (Found : C, 75.8; H, 7.2. $C_{39}H_{44}O_3Si_2$ requires : C, 75.93; H, 7.19%).

3,5-Bis(3,5-bis(t-butyldiphenylsilyloxy)benzyloxy)benzyl alcohol 7.

A mixture of the monomer alcohol **5** (17.16 g, 27.9 mmol), methyl 3,5-dihydroxybenzoate **3** (2.13 g, 12.7 mmol), diethyl azodicarboxylate (5.52 g, 31.7 mmol) and triphenylphosphine (8.32 g, 31.7 mmol) in dry THF (150 ml) was stirred overnight at room temperature. After removal of the solvent, the residue was chromatographed on silica gel with dichloromethane/light petroleum (5:1) as the eluent to give the trimer ester **6** as a colorless oil (14.7 g, 85%); ν_{max} (CCl_4)/cm^{-1} 3078m, 3053m, 2961s, 2932s, 2860s, 1718s (C=O), 1590s and 1544s; δ_H ($CDCl_3$, 400 MHz) 0.99 (s, 36H, t-Bu), 3.89 (s, 3H, CH_3O), 4.68 (s, 4H, CH_2O), 6.15 (t, 2H, J 2, 4-H 2nd gen. Ar), 6.40 (t + d, 5H, J 2, 4-H 1st gen. + 2/6-H 2nd gen. Ar), 7.07 (d, 2H, J 2, 2/6-H 1st gen. Ar), 7.23 (br t, 16H, J 7.5, 3/5-H Ph), 7.34 (tt, 8H, J 7.5 and 1.5, 4-H Ph) and 7.54 (dd, 16H, J 7.5 and 1.5, 2/6-H Ph); δ_C ($CDCl_3$) 19.4 and 26.5 (t-Bu), 52.1 (CH_3O), 69.6 (CH_2O), 106.9, 108.2, 131.6 and 159.5 (1st gen. Ar C-4, C-2, C-1 and C-3), 111.1, 111.8, 138.1 and 156.4 (2nd gen. Ar C-4, C-2, C-1 and C-3), 127.6, 129.7, 132.7 and 135.4 (Ph C-3, C-4, C-1 and C-2) and 166.8 (C=O).

A solution of the trimer ester **6** (13.6 g, 10 mmol) in dry THF (50 ml) was added dropwise to a suspension of $LiAlH_4$ (0.57 g, 15 mmol) in THF (20 ml). After reflux for 1 h, the solution was treated with aqueous NaOH (1 M, 10 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give the trimeric alcohol **7** as a colorless oil (12.6 g, 94%) (white foam after extensive drying); ν_{max} (CCl_4)/cm^{-1} 3053w, 2960m, 2932m, 2860m, and 1544s; δ_H ($CDCl_3$, 400 MHz) 0.99 (36 H, s, t-Bu), 1.50 (br s, 1H, OH), 4.52 (br s, 2H, $C\underline{H}_2OH$), 4.65 (s, 4H, CH_2O), 6.14 (t, 2H, J 2, 4-H 2nd gen. Ar), 6.19 (t, 1H, J 2, 4-H 1st gen. Ar), 6.38 (d, 2H, J 2, 2/6-H 1st gen. Ar), 6.41 (d, 4H, J 2, 2/6-H 2nd gen. Ar), 7.23 (br t, 16H, J 7.5, 3/5-H Ph), 7.33 (tt, 8H, J 7.5 and 1.5, 4-H Ph) and 7.54 (dd, 16H, J 7.5 and 1.5, 2/6-H Ph); δ_C ($CDCl_3$) 19.4 and 26.5 (t-Bu), 65.3 (CH_2OH), 69.4 (CH_2O), 101.1, 105.5, 143.0 and 159.8 (1st gen. Ar C-4, C-2, C-1 and C-3), 111.0, 111.8, 138.5 and 156.3 (2nd gen. Ar C-4, C-2, C-1 and C-3), 127.6, 129.7, 132.7 and 135.4 (Ph C-3, C-4, C-1 and C-2); m/z (FAB) 1337 $(M-H)^-$ (Found : C, 76.1; H, 7.1. $C_{85}H_{92}O_7Si_4$ requires : C, 76.30; H, 6.93%).

3,5-Bis(3,5-bis(3,5-bis(t-butyldiphenylsilyloxy)benzyloxy)benzyloxy)benzyl alcohol 9.

A mixture of the trimer alcohol **7** (5.7 g, 4.27 mmol), methyl 3,5-dihydroxybenzoate **3** (326 mg, 1.94 mmol), diethyl azodicarboxylate (844 mg, 4.85 mmol) and triphenylphosphine (1.27 g, 4.85 mmol) in dry THF (50 ml) was stirred overnight at room temperature. After removal of the solvent, the residue was chromatographed on silica gel with dichloromethane/light petroleum (3:1) as the eluent to give the heptamer ester **8** as a colorless oil (4.3 g, 79%); ν_{max} (CCl_4) 3072w, 2959m, 2932m, 2860m, 1725w (C=O), 1590s and 1544s; δ_H ($CDCl_3$, 400 MHz) 0.99 (s, 72H, t-Bu), 3.89 (s, 3H, CH_3O), 4.65 (s, 8H, CH_2O), 4.90 (s, 4H, CH_2O), 6.15 (t, 4H, J 2, 4-H 3th gen. Ar), 6.22 (t, 2H, J 2, 4-H 2nd gen. Ar), 6.42 (d, 8H, J 2, 2/6-H 3th gen. Ar), 6.47 (d, 4H, J 2, 2/6-H 2nd gen. Ar), 6.82 (t, 1H, J 2, 4-H 1st gen. Ar), 7.23 (t, 32H, J 7.5, 3/5-H Ph), 7.31 (m, 18H, 2/6-H 1st gen. Ar + 4-H Ph) and 7.54 (d, 32H, J 7.5, 2/6-H Ph); δ_C ($CDCl_3$) 19.4 and 26.5 (t-Bu), 52.2 (CH_3O), 69.5 and 70.3 (CH_2O), 107.1, 108.3, 132.1 and 159.85 (1st gen. Ar C-4, C-2, C-1 and C-3), 101.5, 106.5, 138.3 and 159.9 (2nd gen. Ar C-4, C-2, C-1 and C-3), 111.0, 111.9, 138.4 and 156.4 (3th gen. Ar C-4, C-2, C-1 and C-3), 127.6, 129.7, 132.7 and 135.4 (Ph C-3, C-4, C-1 and C-2) and 166.7 (C=O).

A solution of the heptamer ester **8** (800 mg, 0.285 mmol) in dry THF (50 ml) was added dropwise to a suspension of $LiAlH_4$ (20 mg, 0.53 mmol) in THF (10 ml). After reflux for 1 h, the solution was treated with aqueous NaOH (1 M, 5 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give the heptamer alcohol **9** as a colorless glass (714 mg, 90%); ν_{max} (CCl_4)/cm^{-1} 3610w (OH), 3071w, 2960m, 2932m, 2859m and 1593s; δ_H ($CDCl_3$, 400 MHz) 0.99 (s, 72H, t-Bu), 1.60 (t, 1H, J 6, OH), 4.62 (d, 2H, J 6, $C\underline{H}_2OH$), 4.65 (s, 8H, CH_2O), 4.88 (s, 4H, CH_2O), 6.14 (t, 4H, J 2, 4-H 3th gen. Ar), 6.21 (t, 2H, J 2, 4-H 2nd gen. Ar), 6.41 (d, 8H, J 2, 2/6-H 3th gen. Ar), 6.47 (d, 4H, J 2, 2/6-H 2nd gen. Ar), 6.55 (t, 1H, J 2 4-H 1st gen. Ar), 6.61 (d, 2H, J 2, 2/6-H 1st gen. Ar), 7.23 (br t, 32H, J 7.5, 3/5-H Ph), 7.32 (br t, 16H, J 7.5, 4-H Ph) and 7.54 (br d, 32H, J 7.5, 2/6-H Ph); δ_C ($CDCl_3$) 19.4 and 26.5 (t-Bu), 65.3 (CH_2OH), 69.5 and 70.0 (CH_2O), 101.1, 105.6, 143.4 and 160.2 (1st gen. Ar C-4, C-2, C-1 and C-3), 101.3, 106.3, 138.7 and 159.9 (2nd gen. Ar C-4, C-2, C-1 and C-3), 111.0, 111.9, 138.4, 156.3 (3th gen. Ar C-4, C-2, C-1 and C-3), 127.6, 129.7, 132.7 and 135.4 (Ph C-3, C-4, C-1 and C-2) (Found : C, 76.3; H, 7.0. $C_{177}H_{188}O_{15}Si_8$ requires C, 76.47; H, 6.82%).

General procedure for the synthesis of the higher dendritic polyethers, exemplified for [G5]-OH.

A solution of the heptamer **9** (650 mg, 0.234 mmol), 1.1 equiv of Fréchet's [G2]-CH_2Br[1] (1.65 g, 2.04 mmol), KF (270 mg, 4.65 mmol) and 18-crown-6 (100 mg, 0.38 mmol) in dry acetone (50 ml) was refluxed for 24 h under a nitrogen atmosphere. The reaction mixture was poured into water (200 ml) and extracted with dichloromethane (3 x 100 ml). The combined extracts were dried ($MgSO_4$), evaporated, and the residue chromatographed on silica gel with dichloromethane/diethyl ether (60:1) as the eluent to give the dendron [G5]-OH as a colorless oil (1.28 g, 83%); δ_H ($CDCl_3$, 400 MHz) 1.65 (t, 1H, J 6, OH), 4.39 (d, 2H, J 6, $\underline{C}H_2OH$), 4.84

(s, 60H, CH$_2$O), 4.91 (s, 64H, PhC$\underline{H}_2$), 6.45-6.65 (m, 93H, Ar), 7.2-7.4 (m, 160H, Ph); δ_C (CDCl$_3$) 65.0 (CH$_2$OH), 69.9 and 70.0 (CH$_2$O), 101.5 (Ar C-4), 106.3 (Ar C-2), 139.2 and 139.3 (Ar C-1), 160.0 and 160.1 (Ar C-3), 127.5, 127.9, 128.5 and 136.7 (Ph C-2, C-4, C-3 and C-1).

3,5-Bis(3,5-bis(4-methoxycarbonylphenyl)benzyloxy)benzyl alcohol 18[9]

A mixture of the trimeric alcohol **7** (0.37 mmol, 500 mg), methyl 4-(bromomethyl)benzoate **10** (1.65 mmol, 377 mg), KF (3.7 mmol, 215 mg) and 18-crown-6 (0.10 g, 0.38 mmol) in dry acetone (30 ml) was refluxed overnight under a nitrogen atmosphere. The reaction mixture was poured into water (100 ml) and extracted with dichloromethane (3 x 50 ml). The combined extracts were dried (MgSO$_4$), evaporated and the residue chromatographed on silica gel with dichloromethane / diethyl ether (10:1) as the eluent to give compound **18**[9] as a white powder (340 mg, 94%); mp (dichloromethane / n-hexane) 117.9 - 118.3°C; ν_{max}(KBr)/cm^{-1} 3450 (br), 2950 (m), 1724 (s), 1592 (s), 1438 (s), 1368 (m), 1275 (s), 1162 (s), 1107 (s); δ_H (CDCl$_3$, 400 MHz) 2.23 (t, 1H, -OH, J=5.5 Hz), 3.90 (s, 12H, -COOCH$_3$), 4.58 (d, 2H, -CH$_2$OH, J=5.5 Hz), 4.93 (s, 4H, -CH$_2$O-), 5.05 (s, 8H, -CH$_2$O-), 6.44 (t, 1H, 1st gen. C$_6$H$_3$ H-4, J=2.2 Hz), 6.51 (t, 2H, 2nd gen. C$_6$H$_3$ H-4, J=2.2 Hz), 6.55 (d, 2H, 1st gen. C$_6$H$_3$ H-2 and 6, J=2.2 Hz), 6.63 (d, 4H, 2nd gen. C$_6$H$_3$ H-2 and 6, J=2.2 Hz), 7.43 (d, 8H, C$_6$H$_4$ H-3 and 5, J=8.2 Hz), 8.01 (d, 8H, C$_6$H$_4$ H-2 and 6, J=8.2 Hz); δ_C (CDCl$_3$) 52.1 (COOCH$_3$), 65.0 (-CH$_2$OH), 69.3 and 69.6 (-CH$_2$O-), 101.1, 105.6, 143.6 and 159.82 (1st gen. Ar C-4, C-2, C-1 and C-3), 101.5, 106.3, 139.5 and 159.76 (2nd gen. Ar C-4, C-2, C-1 and C-3), 126.9 (C$_6$H$_4$, C-2), 129.6 (C$_6$H$_4$ ipso C-COOCH$_3$), 129.8 (C$_6$H$_4$, C-3), 141.9 (C$_6$H$_4$ ipso C-CH$_2$O-), 166.8 (-$\underline{C}$OOCH$_3$).

4-(3,5-Bis(methoxycarbonyl)phenoxymethyl)benzyl bromide 13.

A mixture of 1,4-bis(bromomethyl)benzene **11** (5.7 mmol, 1.5 g), dimethyl 5-hydroxyisophthalate **12** (5.7 mmol, 1.19 g), K$_2$CO$_3$ (8.55 mmol, 1.18 g) and 18-crown-6 (0.10 g, 0.38 mmol) in dry acetone (50 ml) was refluxed for 24h under a nitrogen atmosphere. The reaction mixture was poured into water (200 ml) and extracted with dichloromethane (3 x 100 ml). The combined extracts were dried (MgSO$_4$), evaporated and the residue chromatographed on silica gel with dichloromethane / n-hexane (2:1) as the eluent to give compound **13** as a white powder (1.09 g, 49%); mp (CH$_2$Cl$_2$/acetone) 111.7-112.2°C; ν_{max}(KBr)/cm^{-1} 2952m, 2362w, 1719s, 1598s, 1455s, 1434s, 1339s, 1255s, 1118s, 1056s; δ_H (CDCl$_3$, 400 MHz) 3.94 (s, 6H, COOCH$_3$), 4.50 (s, 2H, CH$_2$Br), 5.14 (s, 2H, CH$_2$O), 7.43 (s, 4H, Ar H 1/4), 7.82 (d, 2H, J=1.4Hz, Ar H-2/6), 8.30 (t, 1H, J=1.4Hz, Ar H-4); δ_C (CDCl$_3$) 33.0 (CH$_2$Br), 52.4 (COO$\underline{C}$H$_3$), 70.0 (CH$_2$O), 120.1 (Ar C-2), 123.3 (Ar C-4), 127.9 (Ar C-3), 129.4 (Ar C-2), 131.9 (Ar C-1), 136.4 (Ar C-1), 137.8 (Ar C-4), 158.6 (Ar C-3), 166.0 ($\underline{C}$OOCH$_3$); MS(EI, m/z) 392/394; (Found : C, 54.7; H, 4.3. C$_{177}$H$_{188}$O$_{15}$Si$_8$ requires C, 54.98; H, 4.36%).

3,5-Bis(3,5-bis(4-(3,5-bis(methoxycarbonyl)phenoxymethyl)benzyloxy) benzyloxy)benzyl alcohol 19.

A mixture of the trimer alcohol **7** (0.37 mmol, 500 mg), compound **13** (1.65 mmol, 648 mg), KF (3.7 mmol, 215 mg) and 18-crown-6 (0.10 g, 0.38 mmol) in dry acetone (30 ml) was refluxed overnight under a nitrogen atmosphere. The reaction mixture was poured into water (100 ml) and extracted with dichloromethane (3 x 50 ml). The combined extracts were dried (MgSO$_4$), evaporated and the residue chromatographed on silica gel with dichloromethane / diethyl ether (10:1) as the eluent to give compound **19** as a colorless oil (520 mg, 86%); ν_{max}(KBr)/cm^{-1} 3530m (OH), 2952s, 2872m, 1722s (COOCH$_3$), 1594s, 1456s, 1339s, 1313s, 1243s, 1159s, 1042s; δ_H (CDCl$_3$, 400 MHz) 2.02 (t, 1H, J=5.84Hz CH$_2$OH), 3.92 (s, 24H, COOCH$_3$), 4.61 (d, 2H, J=5.84Hz CH$_2$O), 4.96 (s, 4H, CH$_2$O), 5.03 (s, 8H, CH$_2$O), 5.12 (s, 8H, CH$_2$O), 6.50 (t, 1H, J=2.28Hz 1st gen. Ar H-4), 6.55 (t, 2H, J=2.24Hz 2nd gen. Ar H-4), 6.60 (d, 2H, J=2.2Hz 1st gen. Ar H-2/6), 6.66 (d, 4H, J=2.16Hz 2nd gen. Ar H-2/6), 7.43 (s, 16H, Ar H-2/3), 7.81 (d, 8H, J=1.44Hz Ar, H-2/6), 8.27 (t, 4H, J=1.44Hz Ar H-4); δ_C (CDCl$_3$) 52.3 (COO$\underline{C}$H$_3$), 65.1 (CH$_2$OH), 69.8 (CH$_2$O), 69.9 (CH$_2$O), 70.2 (CH$_2$O), 101.3, 105.8, 143.6 and 160.0 (1ste gen. Ar C-4, C-2, C-1 and C-3), 101.6, 106.4, 139.4 and 160.1 (2nd gen. Ar C-4, C-2, C-1 and C-3), 120.1 (Ar C-2,6), 123.2 (Ar C-4), 127.73 (Ar C-3,5), 127.74 (Ar C-2,6), 131.9 (Ar C-1), 135.9 (Ar-CH$_2$O), 136.9 (Ar CH$_2$O), 158.7 (Ar C-3), 166.0 ($\underline{C}$OOCH$_3$); MS (ES+, M+NH$_4^+$) 1651 (for 1633 calc.); (Found : C, 68.3; H, 5.3. C$_{177}$H$_{188}$O$_{15}$Si$_8$ requires C, 68.37; H, 5.18%).

3,5-Bis(3,5-bis(methoxycarbonyl)phenoxymethyl)-2,4,6-trimethylbenzyl bromide 15.

A mixture of 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene **14**^{10} (1.50 g, 3.76 mmol), dimethyl 5-hydroxyisophthalate **12** (1.58 g, 7.52 mmol), K$_2$CO$_3$ (1.56 g, 11.28 mmol,) and 18-crown-6 (0.10 g, 0.38 mmol) in dry acetone (50 ml) was refluxed for 24h under a nitrogen atmosphere. The reaction mixture was poured into water (200 ml) and extracted with dichloromethane (3 x 100 ml). The combined extracts were dried (MgSO$_4$), evaporated and the residue chromatographed on silica gel with dichloromethane / diethyl ether (25:1) as the eluent to give compound **15** as a white powder (920 mg, 37%); mp 189.9-190.2°C; ν_{max}(KBr)/cm^{-1} 3085m, 2998m, 2952s, 2844m, 1738s (COOCH$_3$), 1594s, 1457s, 1430s, 1337s, 1260s, 1118s; δ_H (CDCl$_3$, 400 MHz) 2.43 (s, 3H, CH$_3$), 2.48 (s, 6H, CH$_3$), 3.95 (s, 12H, COOCH$_3$), 4.65 (s, 2H, CH$_2$Br), 5.18 (s, 4H, CH$_2$O), 7.87 (s, 4H, C$_6$H$_3$ H-2 and 6), 8.33 (s, 2H, C$_6$H$_3$ H-4); δ_C (CDCl$_3$) 15.7 (CH$_3$), 16.0 (CH$_3$), 30.2 (CH$_2$Br), 52.4 (COO$\underline{C}$H$_3$), 65.5 (CH$_2$O), 119.9 (C$_6$H$_3$ C-2 and 6), 123.3 (C$_6$H$_3$ C-4), 131.3 (ipso C-CH$_2$O), 131.9 (ipso C-COOCH$_3$), 133.1 (ipso C-CH$_2$Br), 138.9 (ipso C-CH$_3$), 139.3 (ipso C-CH$_3$), 159.0 (ipso C-OCH$_2$), 166.1 (ipso $\underline{C}$OOCH$_3$); MS (EI, m/z) 656/658; (Found : C, 58.2; H, 5.2. C$_{177}$H$_{188}$O$_{15}$Si$_8$ requires C, 58.46; H, 5.06%).

3,5-Bis(3,5-bis(3,5-bis(3,5-bis(methoxycarbonyl)phenoxymethyl)-2,4,6-trimethylbenzyloxy) benzyloxy)benzyl alcohol 20.

A mixture of the trimer alcohol **7** (0.299 mmol, 400 mg), compound **15** (1.32 mmol, 866 mg), KF (2.99 mmol, 173 mg) and 18-crown-6 (0.10 g, 0.38 mmol) in dry acetone (50 ml) was refluxed overnight under a nitrogen atmosphere. The reaction mixture was poured into water (200 ml) and extracted with dichloromethane (3 x 100 ml). The combined extracts were dried ($MgSO_4$), evaporated and the residue chromatographed on silica gel with dichloromethane / diethyl ether (10:1) as the eluent to give compound **20** as a white powder (550 mg, 68%); mp (dichloromethane / n-hexane) 143.8-144.0°C; ν_{max}(KBr)/cm^{-1} 3530m (OH), 2953m, 2362m, 2340w, 1722s ($COOCH_3$), 1593s, 1456s, 1434s, 1338s, 1312s, 1242s, 1152s, 1118s; δ_H ($CDCl_3$, 400 MHz) 1.83 (t, 1H, OH, J=5.92 Hz), 2.45 (s, 12H, CH_3), 2.46 (s, 24H, CH_3), 3.93 (s, 48H, $COOCH_3$), 4.64 (d, 2H, CH_2OH, J=5.92 Hz), 5.02 (s, 4H, CH_2O), 5.11 (s, 8H, CH_2O), 5.19 (s, 16H, CH_2O), 6.59 (t, 1H, Ar 1st gen. Ar H-4, J=2.24 Hz), 6.66 (d, 4H, Ar 2nd gen. Ar H-4 and 1st gen. Ar H-2 and 6, J=2.04 Hz), 6.76 (d, 4H, Ar 2nd gen. H-2 and 6, J=2.04 Hz), 7.86 (d, 16H, Ar H-2/6, J=1.4 Hz), 8.31 (t, 8H, Ar H-4, J=1.4 Hz); δ_C ($CDCl_3$) 15.91 (CH_3), 15.94 (CH_3), 52.3 ($COOCH_3$), 65.0 (CH_2OH), 65.2 (1st gen. CH_2O), 65.6 (2nd gen. CH_2O), 70.1 (CH_2O), 101.0, 106.0, 143.5 and 160.1 (1st gen. Ar C-4, 2, 1 and 3), 101.2, 106.2, 139.4 and 160.5 (2nd gen. Ar C-4, 2, 1 and 3), 119.8 (Ar C-2/6), 123.2 (Ar C-4), 131.2 and 131.8 (ipso C-CH_3), 131.9 (ipso C-$COOCH_3$), 139.3 and 139.5 (ipso C-CH_2O), 159.1 (ipso C-OCH_2), 166.0 ($\underline{C}$-$COOCH_3$); MS (ES+, M+NH_4^+) 2706; (Found : C, 66.4; H, 5.4. $C_{177}H_{188}O_{15}Si_8$ requires C, 66.51; H, 5.54%).

Third generation ester 21.

A mixture of the trimer ester **6** (2.6 mmol, 3.6 g), compound **17**[11] (11.7 mmol, 5.0 g), KF (16.0 mmol, 925 mg) and 18-crown-6 (0.10 g, 0.38 mmol) in dry acetone (100 ml) was refluxed overnight under a nitrogen atmosphere. The reaction mixture was poured into water (200 ml) and extracted with dichloromethane (3 x 100 ml). The combined extracts were dried ($MgSO_4$), evaporated and the residue chromatographed on silica gel with dichloromethane / n-hexane (2:1) as the eluent to give compound **21** as a colorless oil (4.0 g, 87%); ν_{max}(CCl_4)/cm^{-1} 2914m, 1725s ($COOCH_3$), 1588s, 1458s, 1322s; δ_H ($CDCl_3$, 400 MHz) 0.88 (t, 24H, CH_3, J=7Hz), 1.29-1.78 (m, 96H, CH_2), 3.90 (m, 19H, $COOCH_3$ and CH_2O), 4.94 (s, 8H, CH_2O), 4.99 (s, 4H, CH_2O), 6.40 (t, 4H, Ar 3rd gen. Ar H-4, J=2 Hz), 6.55 (d, 8H, Ar 3rd gen. Ar H-4, , J=2 Hz), 6.57 (t, 2H, Ar 2nd gen. H-4, , J=2 Hz), 6.67 (d, 4H, Ar 2nd gen. Ar H-4, J=2Hz), 6.79 (t, 1H, 1st gen. Ar H-4, J=2Hz), 7.28 (d, 2H, 1st gen. Ar H-2/6, J=2Hz); δ_C ($CDCl_3$) 14.0 (CH_3), 22.6, 26.0, 26.9, 29.19, 29.23, 29.3, 31.8 (CH_2), 52.1 ($COOCH_3$), 68.0 (2nd and 3rd gen. CH_2O), 70.1 (1st gen. CH_2O), 107.1, 108.4, 138.8 and 159.7 (1st gen Ar C-4, 2, 1 and 3), 101.7, 106.4, 138.8 and 160.2 (2nd gen Ar C-4, 2, 1 and 3), 100.8, 105.7, 138.9 and 160.5 (3rd gen Ar C-4, 2, 1 and 3), 132.0 (ipso $\underline{C}$-$COOCH_3$), 166.6 ($\underline{C}OOCH_3$); MS (ES+, M+NH_4^+) 1816.

Third generation alcohol 22.

A solution of **21** (2.0 g, 1.1 mmol) in dry THF (50 ml) was added dropwise to a suspension of $LiAlH_4$ (0.05 g, 1.32 mmol) in THF (20 ml). After reflux for 1 h, the solution was treated with aqueous NaOH (1 M, 3 ml), filtered and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give the compound **22** as a colorless oil (1.91 g, 98%); ν_{max}(CCl_4)/cm^{-1} 3500w (OH), 2929m, 2857s, 1596s, 1551s, 1456s, 1378s, 1296s, 1253s, 1169s; δ_H ($CDCl_3$, 400 MHz) 0.88 (t, 24H, CH_3, J=7Hz), 1.31-1.75 (m, 96H, CH_2), 1.85 (br s, 1H, OH), 3.90 (m, 16H, CH_2O, J=6.5Hz), 4.61 (br s, 2H, CH_2OH), 4.94 (s, 8H, CH_2O), 4.96 (s, 4H, CH_2O), 6.39 (t, 4H, Ar 3rd gen. Ar H-4, J=2 Hz), 6.52 (t, 1H, Ar 1st gen. H-4, , J=2 Hz), 6.54 (d, 8H, Ar 3rd gen. Ar H-4, , J=2 Hz), 6.55 (t, 2H, 2nd gen. Ar H-4, J=2Hz), 6.59 (d, 2H, Ar 1st gen. Ar H-4, J=2Hz), 6.66 (d, 4H, 2nd gen. Ar H-2/6, J=2Hz); δ_C ($CDCl_3$) 14.0 (CH_3), 22.6, 26.0, 26.9, 29.20, 29.24, 29.3, 29.8, 31.8 (CH_2), 65.2 (CH_2OH), 68.1 (3rd gen. CH_2O), 70.0 (1st gen. CH_2O), 70.2 (2nd gen. CH_2O), 101.2, 105.7, 143.5 and 160.07 (1st gen Ar C-4, 2, 1 and 3), 101.6, 106.3, 139.2 and 160.14 (2nd gen Ar C-4, 2, 1 and 3), 100.9, 105.7, 138.9 and 160.5 (3rd gen Ar C-4, 2, 1 and 3); MS (ES+, M+NH_4^+) 1788.

Third generation bromide 23.

To a stirred solution of **22** (2.0 g, 1.1 mmol) and CBr_4 (748 mg, 2.3 mmol) in dry THF (20 ml) was added PPh_3 (592 mg, 2.3 mmol) portionwise on an ice bath. After the complete addition the mixture was stirred for another hour at room temperature under a nitrogen atmosphere, poured into water (100 ml), extracted with dichloromethane (3 x 50 ml), dried ($MgSO_4$) and evaporated. The residu was chromatographed on silica gel using dichloromethane as the eluent giving compound **23** as a colorless oil (1.79 g, 89%); ν_{max}(CCl_4)/cm^{-1} 2932m, 2856s, 2253s, 1610s, 1551s, 1456s, 1378s, 1307s; δ_H ($CDCl_3$, 400 MHz) 0.88 (t, 24H, CH_3, J=7Hz), 1.31-1.75 (m, 96H, CH_2), 3.92 (t, 16H, CH_2O, J=6.5Hz), 4.39 (s, 2H, CH_2Br), 4.94 (s, 8H, CH_2O), 4.95 (s, 4H, CH_2O), 6.40 (d, 4H, Ar 2nd gen. Ar H-2/6, J=2 Hz), 6.53 (t, 1H, 1st gen. Ar H-4, J=2Hz), 6.55 (d, 8H, Ar 3rd gen. Ar H-2/6, , J=2 Hz), 6.56 (t, 2H, 2nd Ar gen. H-4, , J=2 Hz), 6.62 (d, 2H, Ar 1st gen. Ar H-2/6, J=2Hz), 6.65 (d, 4H, 2nd gen. Ar H-2/6, J=2Hz); δ_C ($CDCl_3$) 14.0 (CH_3), 22.6, 26.0, 26.9, 29.20, 29.24, 29.3, 29.8, 31.8 (CH_2), 65.2 (CH_2OH), 68.1 (3rd gen. CH_2O), 70.0 (1st gen. CH_2O), 70.2 (2nd gen. CH_2O), 101.2, 105.7, 143.5 and 160.07 (1st gen Ar C-4, 2, 1 and 3), 101.6, 106.3, 139.2 and 160.14 (2nd gen Ar C-4, 2, 1 and 3), 100.9, 105.7, 138.9 and 160.5 (3rd gen Ar C-4, 2, 1 and 3); MS (ES+, M+NH_4^+) 1851/1853.

Fifth generation ester 24.

A mixture of the trimer ester **6** (0.074 mmol, 101 mg), compound **23** (0.033 mmol, 600 mg), KF (0.74 mmol, 43 mg) and 18-crown-6 (0.010 g, 0.038 mmol) in dry acetone (10 ml) was refluxed overnight under a nitrogen atmosphere. The reaction mixture was poured into water (50 ml) and extracted with dichloromethane (3 x 50 ml). The combined extracts were dried ($MgSO_4$), evaporated and the residue chromatographed on silica gel with dichloromethane / n-hexane (2:1) as the eluent to give compound **24** as a colorless oil (373 mg, 68%);

mp 143.8-144.0°C; $\nu_{max}(CCl_4)/cm^{-1}$ 2930m, 2856s, 1592s, 1551s, 1456s, 1378s; δ_H ($CDCl_3$, 400 MHz) 0.87 (t, 96H, CH_3, J=7Hz), 1.27-1.73 (m, 320H, CH_2), 3.90 (m, 67H, $COOCH_3$ and CH_2O), 4.91, 4.92, 4.93 and 4.94 (4 x s, 60H, CH_2O), 6.38 (m, 20H, 2nd gen. Ar H-2/6 and 5th gen. Ar H-4), 6.53 (m, 49H, 1st gen. Ar H-4, 4th gen. Ar H-2/6 and 5th gen. Ar H-2/6), 6.66 (m, 22H, 1st gen. Ar H-4, 3rd gen. Ar H-2/4/6 and 4th gen. H-4), 7.28 (d, 2H, 1st gen. Ar H-2/6, , J=2 Hz); δ_C ($CDCl_3$) 14.0 (CH_3), 22.6, 26.0, 26.7, 29.2, 29.25, 29.34 and 31.8 (CH_2), 52.1 ($COO\underline{C}H_3$), 68.0-70.1 (CH_2O), 100.9, 101.6, 105.7, 106.4, 132.0 (ipso C-$COOCH_3$), 138.9, 139.1, 139.2, 159.7, 160.2, 160.5, 166.2 ($\underline{C}OOCH_3$); MS (ES+, M/4) 1856.

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References.

1. C. Hawker and J.M.J. Fréchet, *J. Chem. Soc., Chem. Commun.*, **1990**, 1010; C.J. Hawker and J.M.J. Fréchet, *J. Am. Chem. Soc.*, **1990**, 112, 7638.
2. See for instance : K.L. Wooley, C.J. Hawker and J.M.J. Fréchet, *J. Chem. Soc., Perkin Trans. 1*, **1991**, 1059; C.J. Hawker, K.L. Wooley and J.M.J. Fréchet, *ibid.*, **1993**, 1287; K.L. Wooley, C.J. Hawker, J.M.J. Fréchet, F. Wudl, G. Srdanov, S. Shi, C. Li and M. Kao, *J. Am. Chem. Soc.*, **1993**, 115, 9836; K.L. Wooley, C.J. Hawker and J.M.J. Fréchet, *ibid.*, **1993**, 115, 11496; C.J. Hawker, K.L. Wooley and J.M.J. Fréchet, *J. Chem. Soc., Chem. Commun.*, **1994**, 925.
3. See for instance : D. Seebach, J.M. Lapierre, K. Skobridis and G. Greiveldinger, *Angew. Chem. Int. Ed. Engl.*, **1994**, 33, 440; D. Seebach, J.M. Lapierre, G. Greiveldinger and K. Skobridis, *Helv. Chim. Acta*, **1994**, 77, 1673; G. L'abbé, B. Haelterman and W. Dehaen, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 2203; G. Ferguson, J.F. Gallagher, M.A. McKervey and E. Madigan, *ibid.*, **1996**, 599; C. Bolm, N. Derrien and A. Seger, *Synlett*, **1996**, 387; R. Sadamoto, N. Tomioka and T. Aida, *J. Am. Chem. Soc.*, **1996**, 118, 3978; G.M. Stewart and M.A. Fox, *ibid.*, **1996**, 118, 4354.
4. K.L. Wooley, C.J. Hawker and J.M.J. Fréchet, *J. Am.Chem. Soc.*, **1991**, 113, 4252.
5. E. Reimann, *Chem. Ber.*, **1969**, 102, 2881.
6. O. Mitsunobu, *Synthesis*, **1981**, 1.
7. Part of this work was reported as a communication: G. L'abbé, B. Forier and W. Dehaen, *J.Chem.Soc. Chem Commun.*, **1996**, 2143.
8. J.W. Leon, M. Kawa, J.M.J. Fréchet, *J.Am.Chem.Soc.*, **1996**, 118, 8847.
9. C.J. Hawker, K.L. Wooley and J.M.J. Fréchet, *J. Chem. Soc. Perkin Trans. 1*, **1993**, 1287.
10. J. Zavada, M. Pankova, P. Holy, M. Tichy, *Synthesis*, 1994, 1132 ; A.W. van der Made, R.H. van der Made, *J. Org. Chem.*, **1993**, 58, 1262.
11. Z. Bo, X. Zhang, X. Yi, M. Yang, J. Shen, Y. Rehn and S. Xi, *Polymer Bulletin*, **1997**, 38, 257.