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Synthesis of new cores and their use in the preparation of polyester dendrimers

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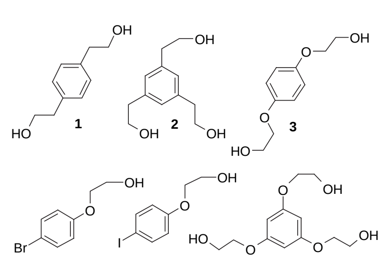
ABSTRACT

Six dendrimer and dendron cores terminated by hydroxyl groups that are neither phenolic nor cleavable by hydrogenolysis have been prepared in a consistent one-pot manner from terminal allyl groups by reduction of the product of reductive ozonolysis. Some of the terminal allyl derivatives are new and others have been prepared by new methods. The well-known *O*-benzylidene derivative of 2,2′-bis(hydroxymethyl)propanoic acid was shown to be the cis-stereoisomer. A new AB_3-type anhydride, tris(benzyloxymethyl)acetic anhydride has been prepared. It was demonstrated that these cores and dendrons could be assembled into first and second generation homo- and mixed polyester dendrimers.

1. Introduction

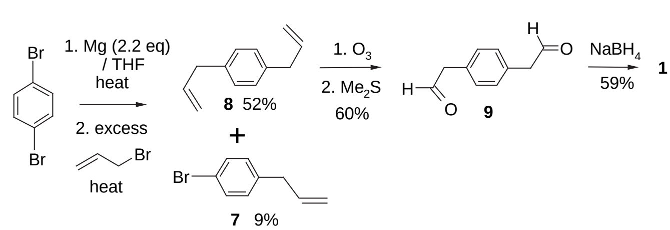
Polyester dendrimers have attracted interest[1–9] because they are non-toxic but are labile enough in vivo to release any biologically active units either covalently attached or encapsulated.[9–11] As part of a program to prepare glycodendrimers,[12] we desired aromatic cores with non-phenolic hydroxyl groups for ester stability that would not be cleaved under hydrogenolysis conditions. We selected the molecules **1**–**6** as synthetic targets. None of these cores have previously been used for the preparation of polyester dendrimers. Because these compounds all have terminal CH_2CH_2OH groups, we chose to employ one route for their synthesis that could be used for all: reduction of the products of reductive ozonolysis of allyl groups. This approach had not been used before to prepare any of these compounds and it proved to be convenient and high yielding. In addition, we demonstrate the use of some of these cores through the synthesis of second generation polyester dendrimers using both a well-known divalent dendron and a new dendron of the AB_3-type.



2. Results and discussion

2.1. Synthesis of new cores

1,4-Benzenediethanol (**1**) had been prepared previously by Clark and O'Reilly using the reaction of the Grignard reagent obtained from 1,4-dibromobenzene with ethylene oxide.[13] However, the yield reported was 52% and ethylene oxide, a toxic gas, is both expensive and inconvenient to handle on a laboratory scale. It has also been prepared in impure form by reduction of 1,4-phenylenediacetic acid, a relatively costly starting material with LAH.[14] Our initial approach via the diallyl derivative **8** is shown in Scheme 1. Steiger et al. reported the synthesis of **8** in 32% yield via coupling of the bis Grignard reagent of 1,4-dibromobenzene with allyl bromide.[15] In our hands, **8** was always accompanied by the monoadduct **7**, even after chromatography. Performing the reaction in two separate steps did not improve the yield; reaction of the mono Grignard reagent with allyl bromide gives **7**[16] in 63% yield in our hands and the yield for conversion of **7** to **8** under the same conditions was similar (59%).



Scheme 1. Initial synthesis of 1,4-benzenediethanol (**1**).

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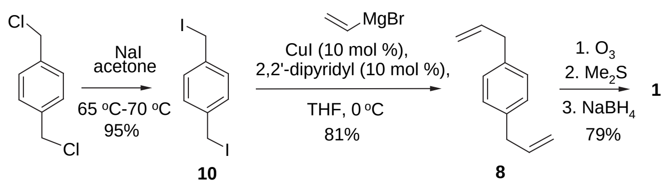
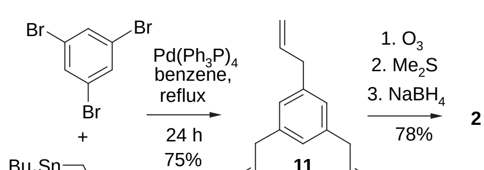
An alternative route to 1,4-diallylbenzene (**8**) proved to be cost effective and high yielding. The copper-catalyzed coupling of vinyl magnesium bromide with the known diiodide **10**[17] gave a good yield of the diallyl derivative **8** in 1 h at 0 °C. Compound **10** has also been made in excellent yield by performing Stille coupling of the bistriflate of hydroquinone with tributylallylstannane in the presence of $PdCl_2(PPh_3)_2$ (20 mol %) and LiCl.[18] Conversion to **1** via reductive ozonolysis followed by the same-pot reduction proceeded in good yield (Scheme 2).



Scheme 2. Improved synthesis of 1,4-benzenediethanol (**1**).

Two groups had reported the synthesis of 1,3,5-benzenetriethanol (**2**) by quite different methods. Cochrane et al.[19] prepared it by reduction of triethyl 1,3,5-benzenetriacetate.[20] The precursor 1,3,5-benzenetriacetic acid was made from 1,3,5-triacetylbenzene using the Kindler modification of the Willgerodt reaction[20] and 1,3,5-triacetylbenzene can be prepared by an acid-catalyzed trimerization of formyl acetone,[21] overall a four-step process. Bradshaw and Krakowiak used the same method but chose to reduce the precursor triacid in 45% yield.[22] An alternative one-pot synthesis of **2** gave a non-separated mixture of tris-(2-hydroxyethyl) benzenes using a cobalt-catalyzed trimerization of 3-butyn-1-ol but the starting material is expensive and the separation is impractical.[23] A reaction scheme analogous to Scheme 2 could not be followed because the required precursor, 1,3,5-tris(chloromethyl) benzene, is not commercially available. An attempt was made to prepare 1,3,5-triallylbenzene (**11**) from 1,3,5-tribromobenzene via the Grignard method but it gave unseparable mixtures of partially allylated derivatives along with the desired product.

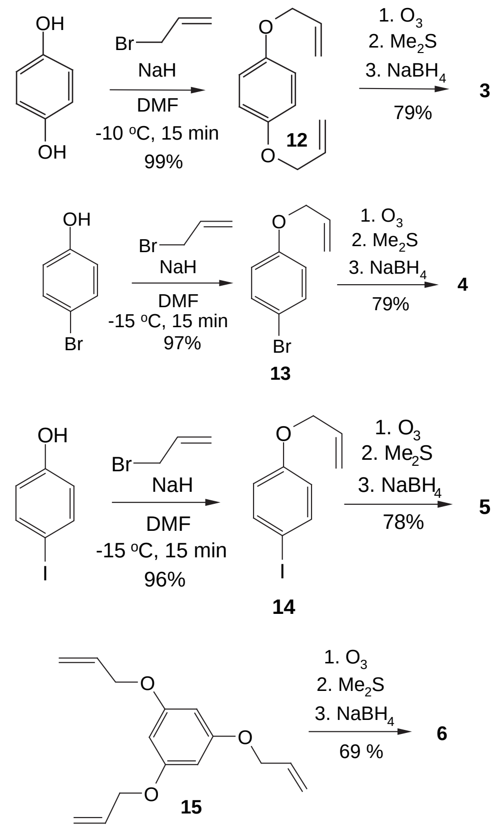
Allylation of aromatic halides with allyltributyltin[24] in the presence of tetrakis(triphenylphosphine)palladium(0) has been known for more than 30 years.[25] The triple version of this reaction worked well with 1,3,5-tribromobenzene on scales of <10 g as shown in Scheme 3. The product (**11**) was converted to the desired triol **2** as described above in the synthesis of **1**.



Scheme 3. The synthesis of 1,3,5-triallylbenzene (**11**) and 1,3,5-benzenetriethanol (**2**).

2-Hydroxyethoxy derivatives of aromatic compounds, such as **3**–**6**, have been made in a variety of ways. Compounds **3** and **4** were originally prepared by reaction of the sodium salts of the phenols with 2-chloroethanol[26] and 2-bromoethanol has also been used.[27] The patent literature contains numerous reports of the formation of **3** by reaction of the dianion with ethylene oxide. Compound **5** has been made by iodination of 2-hydroxyethoxybenzene.[28–30] Surprisingly, **6** has commonly been made from phloroglucinol by reaction with ethylene carbonate in DMF at 150 °C in the presence of tetrabutylammonium bromide.[31] Although this is a one-step reaction, it suffers from low yields, values of between 20 and 37% have been reported.[22,32–34] An alternative two-step approach involving displacement of methyl bromoacetate by phenoxide,[35] followed by reduction has also been used for **6**.[36]

The reduction of the products of reductive ozonolysis of allyl ethers yielded the remaining cores **3**,[37] **4**,[26,38] **5**,[39] and **6**,[22] in excellent yields (see Scheme 4). The required allyl ethers were obtained in 10–15 min at −10 to −15 °C by reaction of the phenoxide anions with allyl bromide in DMF.



Scheme 4. The synthesis of 2-hydroxyethoxy derivatives **3**–**6**.

2.2. Synthesis of dendrons

A number of research groups have synthesized and utilized **16**,[40–44] apparently as a single isomer, but its configuration has not been established as far as we are aware. Two stereoisomers of **16** are possible as shown in Fig. 1. ^1H NMR and ^{13}C NMR spectra of **16** showed that a single isomer had also been isolated here (Scheme 5), not the mixture of cis- and trans-isomers expected based on the free energy difference for the isomers of 5-carboxymethyl-2-isopropyl-5-methyl-1,3-dioxane.[45]

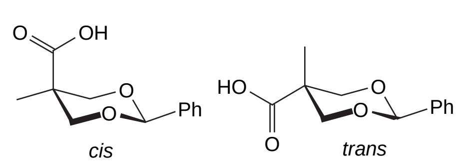
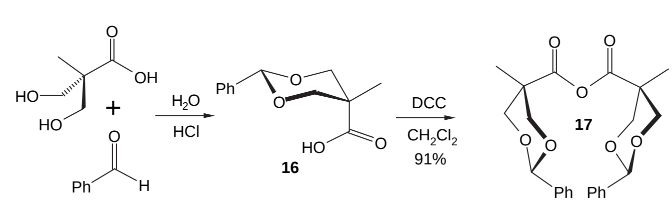


Fig. 1. cis- and trans-Isomers of 5-methyl-2-phenyl-1,3-dioxane-5-carboxylic acid (**16**).



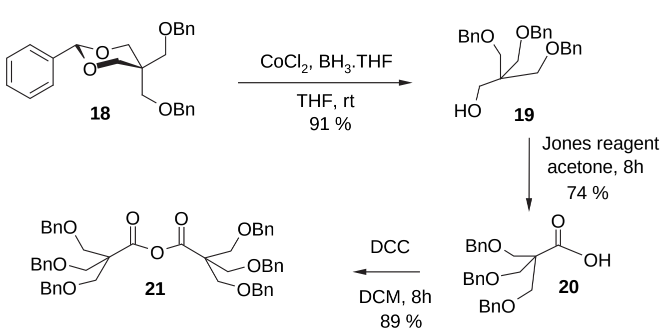
Scheme 5. Preparation of anhydride **17**.

Piasecki et al.[46–48] synthesized a series of 1,3-dioxanes bearing various long chain alkyl substituents at C-2 and a methyl group and a carboxyl group at C-5. The C-5 methyl protons in these compounds absorbed as singlets at 1.02 ppm. Eliel and Enanoza had noted that an axially-oriented $-CH_3$ at C-5 (chemical shifts ~1.5–1.6 ppm in 5-methyl-2-substituted-1,3-dioxanes) is deshielded by 0.5–0.6 ppm with respect to an equatorially-oriented $-CH_3$ (chemical shifts ~1 ppm).[45] In addition, in isomers with the $-CH_3$ and the C-2 group cis-, the chemical shift difference between the signals of the equatorial and axial protons at C-4,6 is negligible or small,[45] whereas in the trans-isomer it is large, about 1 ppm for those prepared by Piasecki et al.[47] For **16**, the methyl group absorbed at 1.11 ppm when the sample was run in chloroform-*d* or at 1.05 ppm when the sample was run in acetone-d_6. The chemical shift difference between the two protons on C-4,6 was 0.91 ppm in chloroform-*d* and 0.83 ppm in acetone-d_6. Based on these grounds, **16** is the cis-isomer (Fig. 1). Surprisingly, the sample of **16** prepared here and recrystallized from ethyl acetate had a different mp 149–151 °C than those previously reported, 185–187 °C from acetone,[42] and 197–198 °C from dichloromethane.[41] All three samples where mps were reported were clearly the same isomer because the two ^{1}H NMR-based criteria for isomer structure were the same: the reported chemical shifts of the methyl in the same solvent agreed within 0.02 ppm and the reported chemical shift differences between the equatorial and axial protons on C-4,6 were between 0.83 and 1.0 ppm in different solvents. The same isomer was also prepared in those papers where mps were not reported[40,43] as indicated by the two NMR criteria mentioned above. Presumably, different polymorphs are obtained under different recrystallization conditions.

Kaloustian et al. attributed the axial preference at C-5 of 1,3-dioxanes for positively charged groups, such as the trimethylammonium group, on the electrostatic attraction of the resultant C–O dipole and the $C-N^+$ dipole in this geometric arrangement and suggested that the small conformational effect of a carbonyl group at C-5 had a contribution from the same effect.[49] However, a similar favoring of the axial orientation for 5-fluoro derivatives must arise from the *gauche* effect,[50] where bonding interactions favor *gauche* arrangements and dipole–dipole repulsion disfavors them. Piasecki and Ruchała found that formation of the acetal in non-polar solvents, such as hexane gave mixtures whereas formation in polar solvents, such as acetonitrile gave only the cis-isomer,[48] consistent with the measured effects of solvent polarity on conformational equilibria and with decrease of through space dipole–dipole repulsion in polar solvents.[49] **16** was prepared here in a polar solvent, water, and only the cis-isomer was observed but preparations of **16** in non-polar solvents gave the same isomer [40–44] (see above).

Acid **16** was converted into the anhydride **17** as earlier,[43] using *N,N′*-dicyclohexylcarbodiimide (DCC) (Scheme 5).

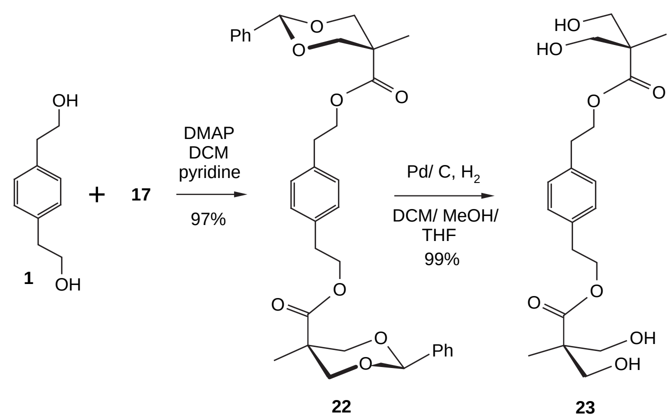
A symmetrical dendron **20** that could provide three branching points, that is, an AB_3 dendron, was prepared by selective reduction of known[51] di-*O*-benzyl-*O*-benzylidenepentaerythritol (**18**) to tri-*O*-benzylpentaerythritol (**19**) as shown in Scheme 6. This approach avoids the use of excess benzyl bromide required for the direct synthesis of **19** from pentaerythritol.[52,53] Jones oxidation of **19** gave carboxylic acid **20**, that was converted to crystalline anhydride **21** with DCC.



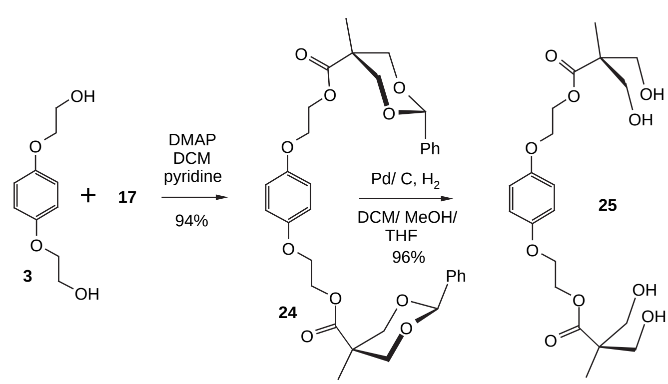
Scheme 6. Preparation of anhydride **21**.

2.3. Dendrimer synthesis

As shown in Schemes 7 and 8, cores **1** and **3** reacted with anhydride **17** in the presence of DMAP and pyridine to give protected first generation dendrimers **22** and **24** in excellent yield. Deprotection by hydrogenolysis also proceeded in excellent yield to give the deprotected first generation dendrimers **23** and **25**. The same two steps with **25** and **17** gave the deprotected second generation dendrimers **27** (Scheme 9).



Scheme 7. Preparation of first generation dendrimer **23**, a tetraol.

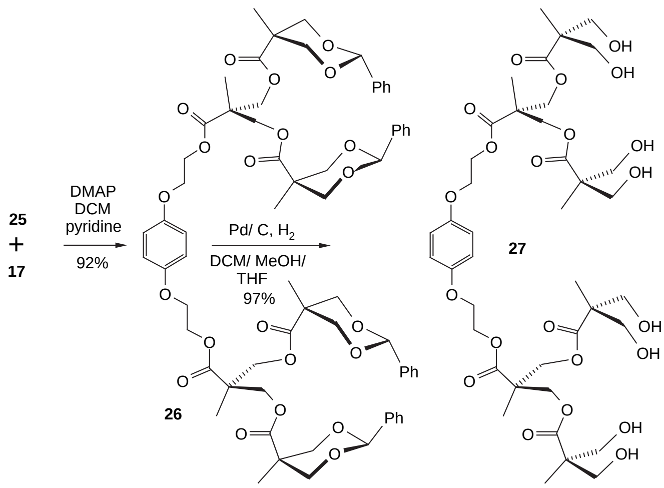


Scheme 8. Preparation of first generation dendrimer **25**, another tetraol.

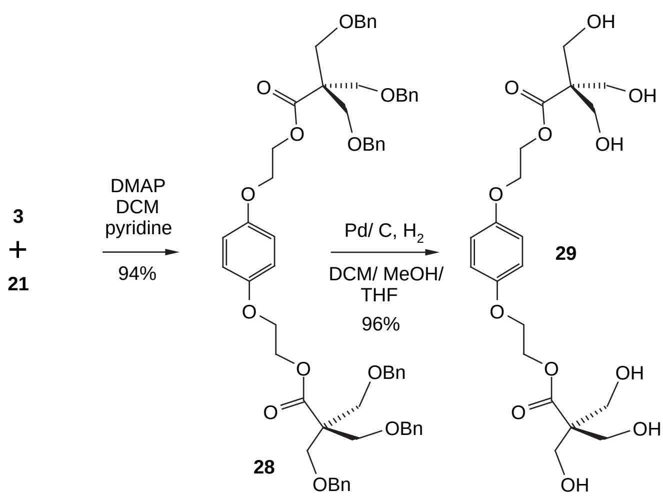
The AB_3 anhydride **21** reacted with core **3** under the standard conditions to give a protected first generation dendrimer in excellent yield. Hydrogenolysis of the six *O*-benzyl groups occurred on reaction overnight under the same conditions used for removal of the benzylidene acetals (Scheme 10). Reaction of the product hexaol **29** with anhydride **17**, followed by hydrogenolysis gave the second generation mixed polyester dendrimer **31**, again in excellent yield (Scheme 11).

3. Conclusions

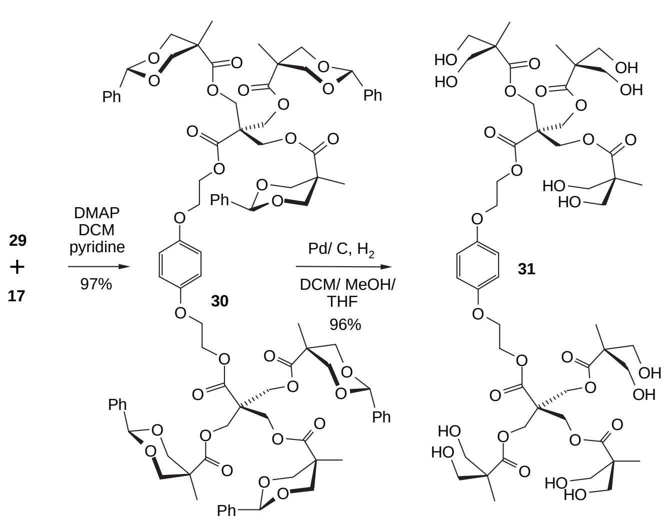
In Section 2.1 above, it was demonstrated that one-pot reductive ozonolysis of allyl derivatives followed by reduction with sodium borohydride is an efficient general procedure for the production of terminal CH_2CH_2OH groups. The allyl groups can be either *C*-allyl or *O*-allyl groups. The latter are readily accessible and a variety of



Scheme 9. Preparation of second generation dendrimer **27**, an octaol.



Scheme 10. Preparation of first generation dendrimer **29**, a hexaol.



Scheme 11. Preparation of second generation dendrimer **31**, a dodecaol.

strageties have been employed for the introduction of one to three *C*-allyl groups onto aromatic rings.

NMR parameters established that the configuration of the well-known *O*-benzylidene derivative of 2,2′-bis(hydroxymethyl)propanoic acid was cis. A new AB_3-type anhydride, tris(benzyloxymethyl)acetic anhydride (**21**) has been prepared. It was shown that the divalent diol cores **1** and **3** could be used with known anhydride **17** and new AB_3 anhydride **21** to produce homogeneous and heterogeneous second generation polyester dendrimers. Deprotection via hydrogenolysis proceeds readily with these products to give clean polyols.

4. Experimental section

4.1. General

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 500 NMR spectrometer operating at 500.13 and 125.7 MHz, respectively, using the solvent resonances as secondary standards. Coupling constant (*J*) values are reported in Hertz. High-resolution mass spectra were recorded on a Bruker Micro-TOF mass spectrometer using electrospray ionization except for **11**, whose HRMS were measured on a CEC 21–110B mass spectrometer using electron ionization (70 eV). Melting points were determined on a Fisher–John's melting point apparatus and are uncorrected. Acetone was refluxed over K_2CO_3 and distilled over molecular sieves. Dichloromethane was refluxed over calcium hydride and distilled onto molecular sieves. Benzene was refluxed over $CaCl_2$ and distilled over molecular sieves. Methanol was refluxed over calcium oxide and distilled over molecular sieves. Tetrahydrofuran was refluxed over $LiAlH_4$ and distilled over molecular sieves. Unless otherwise noted, non-aqueous reactions were carried out under a nitrogen atmosphere. Jones reagent (0.56 M) was prepared by dissolving sodium dichromate dihydrate ($Na_2Cr_2O_7 \cdot 2H_2O$, 300 g, 1.01 mol) in 1.5 L of water followed by slowly adding concd sulfuric acid (300 mL) to the cooled solution (0 °C). Compounds were located by spraying the TLC plate with a solution of 2% ceric ammonium sulfate in 0.5 M H_2SO_4, followed by heating on a hot plate until color developed. Solid compounds were purified on silica gel using flash column chromatography and specified eluents, or by crystallization. Liquids and oils were purified using flash column chromatography.

4.2. Synthesis of cores

*4.2.1. 1-Allyl-4-bromobenzene (**7**).* A stirred mixture of magnesium turnings (3.62 g, 0.149 mol) and dry THF (150 mL) in a two-neck round-bottomed flask was flushed with N_2 for 10 min then heated to 40 °C when two drops of 1,2-dibromoethane were added. 10% of a solution of 1,4-dibromobenzene (29.3 g, 0.124 mol) in THF (50 mL) was added and when the magnesium had started to react, the rest of this solution was added slowly over 1 h. Stirring was continued until magnesium turnings were completely consumed. The flask was cooled to 0 °C and a solution of allyl bromide (16.5 g, 0.136 mol) in dry THF (30 mL) was added slowly over 1 h. The mixture was refluxed for 12 h, then allowed to cool to rt. Water (60 mL) was carefully added and the mixture was extracted using diethyl ether (40 mL×3). The combined extracts were dried ($MgSO_4$), filtered, and concentrated. Purification using column chromatography (hexanes/EtOAc; 2: 1, R_f 0.44) afforded a colorless syrup (15.4 g, 63% yield). ^{1}H NMR and ^{13}C NMR data similar to lit.[54]

*4.2.2. 1,4-Diallylbenzene (**8**).* An oven-dried two-neck round-bottomed flask charged with **10** (48.0 g, 0.134 mol), CuI (2.55 g, 0.013 mol), and 2,2′-dipyridyl (2.10 g, 0.013 mol) was evacuated and flushed with N_2. Anhydrous THF (900 mL) was added and the stirred reaction mixture was cooled to 0 °C. A 1 M solution of vinyl magnesium bromide in THF (540 mL, 0.536 mol) was added quickly via cannula, and the reaction mixture was allowed to warm to rt. After 1 h, saturated NH_4Cl (200 mL) and 28% NH_3 (150 mL) were added and the mixture was stirred for 1 h at rt. The product was extracted with hexanes (100 mL×3) and the combined extracts were washed with brine (60 mL×2), dried ($MgSO_4$), filtered, and concentrated. Purification using column chromatography (hexanes, R_f 0.37) gave a colorless oily syrup (17.2 g, 81% yield); ^{1}H and ^{13}C NMR data similar to lit.[15,18]

*4.2.3. General method for one pot reductive ozonolysis and reduction: 1,4-benzenediethanol (**1**).* Ozone was bubbled through a solution of **8** (4.65 g, 29.4 mmol) maintained at −78 °C in a 1:1 mixture of methanol (100 mL) and dichloromethane (100 mL) until TLC confirmed the disappearance of the olefin. N_2 was then bubbled through the reaction mixture for 15 min. Excess dimethyl sulfide was added at −78 °C, and the reaction mixture was allowed to warm to rt with stirring, then concentrated under vacuum. The resulting syrup was dissolved in absolute ethanol (100 mL), and the solution was cooled to 0 °C. Excess $NaBH_4$ was added in portions with stirring, which was continued at rt for 20 h. Water (20 mL) was added and the solution was acidified to pH ∼6 (20% HCl), and the mixture filtered. Concentration under vacuum gave a thick oily residue, which was then dissolved in EtOAc (65 mL) and water (15 mL). The organic layer was collected, dried ($MgSO_4$), and concentrated. The product was obtained as a colorless solid and was purified by column chromatography (EtOAc, R_f 0.52) to give colorless crystals (3.86 g, 79% yield): mp 84–86 °C; lit.[13] mp 85 °C; ^{1}H NMR similar to lit.; $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 136.8 (qPhC), 129.4 (PhCH), 63.8 (CH_2O), 39.0 (CH_2Ph).

*4.2.4. 1,3,5-Triallylbenzene (**11**).* A sealed tube was charged with allyltributylstannane[24] (3.10 mL, 0.010 mol), 1,3,5-tribromobenzene (1.00 g, 0.003 mol), tetrakis(triphenylphosphine)palladium(0) (0.280 g, 7.50 mol %), dry benzene (5 mL), and a stirring bar. The reaction mixture was stirred under N_2 in the sealed tube at a bath temperature of 120 °C for 24 h. The tube was then allowed to cool to rt and the pressure was carefully released. Diethyl ether (15 mL) was added and the mixture was stirred for 15 min with saturated KF (10 mL). The organic layer was separated and stirred with 10% NH_4OH (10 mL) for 20 min. The organic layer was separated, washed with brine (10 mL), dried ($MgSO_4$), and concentrated to give crude triallylbenzene that was distilled (bp 125 °C/1.5 Torr) to give the pure product as a colorless syrup (0.47 g, 75% yield); ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 3.35 (d, J=6.5 Hz, 6H, 3CH_2 sp3), 5.08 (m, 6H, 3CH_2CH=CH_2), 5.96 (m, 3H, 3CH_2CH=CH_2), 6.87 (s, 3H, PhH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.3 (PhC), 137.6 (3CH_2CH=CH_2), 126.6 (PhC), 115.7 (3CH_2CH=CH_2), 40.2 (3CH_2 sp3). HR EIMS m/z calcd for $C_{15}H_{18}$ 198.1409; found 198.1419.

*4.2.5. 1,3,5-Benzenetriethanol (**2**).* Compound **2** was prepared from **11** (4.26 g, 0.022 mol) by the general method and purified by column chromatography (EtOAc, R_f 0.48) to give colorless crystals (3.52 g, 78% yield): mp 74–76 °C; lit.[19] mp 75 °C ^{1}H and ^{13}C NMR data similar to lit.[23]

*4.2.6. General method for forming allyl ethers: 1,4-diallyloxybenzene (**12**).* Allyl bromide (220 g, 1.82 mol) and anhydrous DMF (200 mL) were cooled to −10 °C and sodium hydride (60% oil dispersion, 17.6 g, 0.440 mol) was added. The resulting mixture was stirred for 10 min, and a solution of hydroquinone (20.0 g, 0.182 mol) in DMF (200 mL) was added dropwise over 30 min. The reaction mixture was stirred for 15 min after which TLC confirmed the disappearance of hydroquinone. The flask was allowed to warm to 0 °C and water (150 mL) was carefully added. The product was extracted with diethyl ether (250 mL) and the aqueous layer was extracted with ether (2×60 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated under vacuum. The product was obtained as a pale yellow oily liquid and crystallized from hexanes at −10 °C to give colorless crystals (34.2 g, 99% yield): mp 38–40 °C; lit.[55] mp 31.9–32.4 °C; ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 153.1 (PhC), 133.8 (CH=), 117.6 (=CH_2), 115.8 (PhC), 69.6 (CH_2); ^{1}H NMR similar to lit.[56]

*4.2.7. 1,4-Bis-(2-hydroxyethoxy)benzene (**3**).* Prepared from **12** (4.68 g, 0.025 mol) as for **1** and purified using column chromatography (EtOAc; R_f 0.51) to give the product as a colorless crystalline powder (3.87 g, 79% yield): mp 102–104 °C; lit.[37] mp 103–104 °C.

*4.2.8. 1-Allyloxy-4-bromobenzene (**13**).* Prepared from allyl bromide (70.0 g, 0.580 mol) in anhydrous DMF (200 mL), sodium hydride (60% oil dispersion, 5.60 g, 0.14 mol), and a solution of 4-bromophenol (20.0 g, 0.116 mol) in DMF (100 mL) as for **12**. The product was obtained as a colorless oily liquid after purification using column chromatography (24 g, 97% yield): (EtOAc/hexanes; 1:2, R_f 0.52); ^{1}H NMR and ^{13}C NMR spectra similar to lit.[57]

*4.2.9. 2-(4-Bromophenoxy)ethanol (**4**).* The general method for reductive ozonolysis and reduction with **13** (12.5 g, 0.058 mol) gave a product as a thick residue that was purified using column chromatography (EtOAc, R_f 0.31). The product solidified on cooling to give colorless crystals (10 g, 79% yield): mp 54–56 °C; lit.[26] mp 55 °C.

*4.2.10. 1-Allyloxy-4-iodobenzene (**14**).* The general method for allylation with allyl bromide (68.7 g, 0.568 mol) in DMF (240 mL), sodium hydride (60% oil dispersion, 5.45 g, 0.136 mol), and a solution of 4-iodophenol (25.0 g, 0.114 mol) in DMF (100 mL) gave, after purification using column chromatography (hexanes, R_f 0.43), **14** as a yellow oil (28.3 g, 96% yield); ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 4.49 (dt, J=5.0, 1.5 Hz, 2H, OCH_2), 5.33 (dq, J=10.5, 1.5 Hz, 1H, H_{cis}), 5.44 (dq, J=17.5, 1.5 Hz, 1H, H_{trans}), 6.05 (ddt, J=17.5, 10.5, 5 Hz, 1H, CH_2CH=CH_2), 6.69–6.72 (m, 2H, PhH), 7.55–7.58 (m, 2H, PhH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 158.3, 138.1 (PhC), 132.8 (vinyl CH) 117.8 (vinyl CH_2), 117.1 (PhCH), 83.0 (PhCI), 68.6 (CH_2 sp^3); HR EIMS m/z calcd for C_9H_9IO 259.9698; found 259.9690. Note that the ^{1}H NMR data are identical to those of Taskinen[58] but neither the ^{1}H NMR or ^{13}C NMR data match those for in the incomplete characterization of **14** provided by Qu et al.[59]

4.3. Synthesis of dendrons

*4.3.1. 5-Methyl-2-phenyl-1,3-dioxane-5-carboxylic acid (**16**).* 2,2-Bis(hydroxymethyl)propanoic acid (30.0 g, 0.224 mol) was dissolved in water (300 mL) in a 500 mL round-bottomed flask. Under vigorous stirring, concd HCl (3 mL) was added, and benzaldehyde (23.7 g, 0.224 mol) was added dropwise over a period of 2 h at 38 °C. When the addition was complete, stirring was continued overnight at 40 °C. The reaction mixture was allowed to cool to rt, and the precipitated solid product was collected using suction filtration, and was washed with water (2×50 mL), then crystallized (EtOAc) to give colorless needles (27 g, 54% yield): mp 149–151 °C; lit. mp 185–187 °C,[42] 197–198 °C;[41] ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 1.11 (s, 3H, CH_3), 3.71 (d, J=11.5 Hz, 2H, H-4$_{ax}$, H-6$_{ax}$), 4.62 (d, J=11.5 Hz, 2H, H-4$_{eq}$, H-6$_{eq}$), 5.49 (s, 1H, H-2), 7.32–7.37 (m, 3H, PhH), 7.44–7.48 (m, 2H, PhH), 10.6 (br, 1H, COOH); ^{1}H NMR (500.13 MHz, acetone-d_6) δ 1.05 (s, 3H, CH_3), 3.74 (d, J=11.5 Hz, 2H, H-4$_{ax}$, H-6$_{ax}$), 4.57 (d, J=11.5 Hz, 2H, H-4$_{eq}$, H-6$_{eq}$), 5.53 (s, 1H, H-2), 7.31–7.44 (m, 5H, PhH); ^{13}C NMR (125.7 MHz, acetone-d_6): δ 175.7 (C=O), 139.8, 129.4, 128.7, 127.1

(PhC), 102.1 (C-2), 74.0 (C-4, C-6), 42.6 (C-5), 18.2 (CH_3). HR ESI MS *m/z* calcd for $C_{12}H_{13}O_4$ 221.0819; found 221.0834.

*4.3.2. 5-Methyl-2-phenyl-1,3-dioxane-5-carboxylic anhydride (**17**).* Anhydride **17** was synthesized as previously described.[42] Carboxylic acid **16** (9.70 g, 43.7 mmol) and *N,N′*-dicylohexylcarbodiimide (DCC) (4.95 g, 23.9 mmol) afforded **17**, crystallized (EtOAc) to give colorless crystals (8.86 g, 91% yield): mp 152–154 °C; lit.[42] mp 151–153 °C.

*4.3.3. 5,5-Bis(benzyloxymethyl)-2-phenyl-1,3-dioxane (**18**).* Mono-*O*-benzylidinepentaerythritol[60] (0.740 g, 3.30 mmol), NaH (60%) (0.318 g, 7.95 mmol), and benzyl bromide (1.35 g, 7.89 mmol) were dissolved in dry DMF (15 mL) at 0 °C. The reaction flask was allowed to warm to rt with stirring for 12 h. Water (3 mL) and CH_2Cl_2 (20 mL) were added and the resulting mixture was stirred for 10 min. The organic layer was collected, washed with water (3×7 mL), dried ($MgSO_4$), filtered, and concentrated to give crude **18** as a colorless solid. Purification using column chromatography (hexanes/EtOAc; 5:1, R_f 0.45) gave **18** as a colorless crystalline solid (1.15 g, 86% yield): mp 79 °C; lit.[51] mp 72 °C; ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 3.46 (s, 2H, CH_{2eq}), 3.99 (s, 2H, CH_{2ax}), 4.03 (d, J=11.5 Hz, 2H, H-4_{ax}, H-6_{ax}), 4.31 (d, J=11.5 Hz, 2H, H-4_{eq}, H-6_{eq}), 4.58 (s, 2H, OCH_2Ph_{eq}), 4.70 (s, 2H, OCH_2Ph_{ax}), 5.54 (s, 1H, H-2), 7.38–7.50 (m, 13H, PhH), 7.57–7.59 (m, 2H, PhH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.7, 138.4, 138.3, 129.0, 128.4, 128.33, 128.30, 127.7, 127.52, 127.46, 126.2 (PhC), 101.8 (C-2), 73.4 (OCH_2Ph_{ax}), 73.3 (OCH_2Ph_{eq}), 70.3 (CH_{2ax}), 70.2 (C-4, C-6), 68.9 (CH_{2eq}), 39.0 (C-5). HR ESI MS *m/z* calcd for $C_{26}H_{28}NaO_4$ 427.1880; found 427.1852.

*4.3.4. 3-(Benzyloxy)-2,2-bis(benzyloxymethyl)propan-1-ol (**19**).* To a solution of benzylidene acetal (**18**) (2.00 g, 4.94 mmol) in anhydrous THF (10 mL) was added a 1 M solution of BH_3.THF complex (9.88 mL, 9.88 mmol) under nitrogen. Anhydrous $CoCl_2$ (1.28 g, 9.88 mmol) was added in one portion and the reaction mixture was stirred at rt for 20 min when TLC confirmed the disappearance of the starting material. The reaction mixture was diluted using EtOAc (40 mL) and filtered to remove undissolved $CoCl_2$. The blue solution was cooled to 0 °C and aqueous $NaBH_4$ solution was added dropwise with stirring until the blue color disappeared and there was formation of a black precipitate. The mixture was filtered and the organic layer was separated, washed with $NaHCO_3$ (1 M, 10 mL), water (10 mL), and dried ($MgSO_4$). Concentration followed by column chromatography (hexanes/EtOAc; 3:1, R_f 0.39) gave the product as a colorless syrup (1.83 g, 91% yield): ^{1}H and ^{13}C NMR spectra similar to lit.[52]

*4.3.5. 3-(Benzyloxy)-2,2-bis(benzyloxymethyl)propanoic acid (**20**).* Alcohol **19** (11.3 g, 28.0 mmol) was dissolved in acetone (120 mL) and the Jones reagent (0.56 M, 75 mL, 42 mmol) was added dropwise at 0 °C with stirring over a 1 h period. The ice-water bath was removed and stirring was continued for 8 h at rt. Acetone was removed under vacuum and water (120 mL) was added. The aqueous layer was extracted using diethyl ether (120 mL×3). The combined organic layers were washed with water (90 mL×3), dried ($MgSO_4$), and concentrated. Purification using column chromatography (hexanes/EtOAc; 3:1, R_f 0.27) gave the acid as a colorless solid (8.68 g, 74% yield). Purification was also achieved using crystallization (hexanes/EtOAc) in 61% yield: mp 94–95 °C; ^{1}H NMR (500.13 MHz, acetone-d_6) δ 3.77 (s, 6H, $3C_{quat}CH_2$ O), 4.53 (s, 6H, $3CH_2Ph$), 7.25–7.34 (m, 15H, PhH), 10.89 (br, 1H, OH); ^{13}C NMR (125.7 MHz, acetone-d_6) δ 173.9 (C=O), 139.5, 129.0, 128.14, 128.10 (PhC), 73.7 ($3CH_2Ph$), 68.8 ($3C_{quat}CH_2O$), 53.8 (C_{quat}). HR ESI MS *m/z* calcd for $C_{26}H_{27}O_5$ (M−H) 419.1864; found 419.1850.

*4.3.6. 3-(Benzyloxy)-2,2-bis(benzyloxymethyl)propanoic anhydride (**21**).* Carboxylic acid (**20**) (23.9 g, 56.8 mmol) and DCC (6.44 g, 31.1 mmol) were dissolved in dry CH_2Cl_2 (120 mL) and the mixture was stirred at rt for 8 h when TLC confirmed the disappearance of the acid. DCU by-product was filtered off and CH_2Cl_2 was removed under vacuum to give **21** as a colorless solid, purified using column chromatography (hexanes/EtOAc; 3:1; R_f 0.45) to give a colorless crystalline solid (20.8 g, 89% yield). Recrystallization (MeOH, −10 °C) gave colorless crystals: mp 69–70 °C; ^{1}H NMR (500.13 MHz, acetone-d_6) δ 3.70 (s, 12H, $6C_{quat}CH_2O$), 4.46 (s, 12H, $6CH_2Ph$), 7.24–7.32 (m, 30, PhH); ^{13}C NMR (125.7 MHz, acetone-d_6) δ 167.4 (C=O), 139.2, 129.1, 128.4, 128.3 (PhC), 73.9 (CH_2Ph), 68.1 ($C_{quat}CH_2O$), 55.8 ($C_{quat.}$). HR ESI MS *m/z* calcd for $C_{52}H_{54}NaO_9$ 845.3660; found 845.3651.

4.4. Dendrimer synthesis

4.4.1. General procedure for formation of dendritic esters. To an oven-dried round-bottomed flask equipped with a magnetic stir bar under nitrogen atmosphere, the benzylidene or benzyl protected anhydride, the hydroxyl-terminated dendrimer or core, and *N,N*-dimethyl-4-aminopyridine were dissolved in a 3:1 mixture of CH_2Cl_2/pyridine (v/v). The reaction mixture was stirred at rt for 4–12 h and diluted with water (~3 mL) in pyridine (3 mL). Stirring was continued overnight to quench the excess anhydride. The mixture was diluted with CH_2Cl_2 (150 mL) and washed with $NaHCO_3$ (1 M, 30 mL×3), 10% Na_2CO_3 (30 mL×3), brine (30 mL×2), water (30 mL), dried ($MgSO_4$), filtered, and concentrated. The crude solid was then purified using precipitation out of hexanes/EtOAc or column chromatography to give a colorless solid (92–97% yield). The $NaHCO_3$ layers were combined, acidified (pH=5–6), and the precipitated carboxylic acid by-product was recovered. However, a different work up procedure was used for the synthesis of dendrimer **30**.

4.4.2. General procedure for deprotection using hydrogenolysis. To an oven-dried round-bottomed flask equipped with a magnetic stir bar, the benzylidene or benzyl protected dendrimer was dissolved in a 1:2:1 mixture of CH_2Cl_2/MeOH/THF (v/v/v) and a catalytic amount of Pd/C was added. The flask was evacuated and back-filled with hydrogen three times. After stirring the mixture overnight under H_2 atmosphere, the catalyst was filtered off using Celite and this Celite was washed with MeOH. The filtrate was concentrated to dryness to afford the product as a colorless solid (96–99% yield).

*4.4.3. 1,4-Bis(2-((cis-5-methyl-r-2-phenyl-1,3-dioxan-5-yl)methanoyloxy)ethyl)benzene (**22**).* 1,4-Benzenediethanol (**1**, 0.630 g, 3.79 mmol), dry pyridine (11 mL), CH_2Cl_2 (33 mL), DMAP (0.203 g, 1.66 mmol), and the anhydride **17** (3.88 g, 9.09 mmol) were stirred at rt for 5 h under nitrogen. After work up and purification as described above, the product was obtained as colorless flakes (2.1 g, 97% yield): mp 138–140 °C; ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 0.95 (s, 6H, CH_3), 2.95 (t, J=7 Hz, 4H, $PhCH_2$), 3.62 (d, J=11.5 Hz, 4H, H-4_{ax}, H-6_{ax}), 4.38 (t, J=7 Hz, 4H, CH_2O), 4.63 (d, J=11.5 Hz, 4H, H-4_{eq}, H-6_{eq}), 5.44 (s, 2H, H-2), 7.13 (s, 4H, PhH), 7.32–7.34 (m, 6H, PhH), 7.42–7.46 (m, 4H, PhH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 173.9 (C=O), 137.9, 136, 129.1, 129, 128.2, 126.2 (PhC), 101.8 (C-2), 73.5 (C-4, C-6), 65.5 (CH_2O), 42.4 (C_{quat}), 34.7 ($PhCH_2$), 17.9 (CH_3). HR ESI MS *m/z* calcd for $C_{34}H_{38}NaO_8$ 597.2459; found 597.2413.

*4.4.4. 1,4-Bis-(2-(2,2′-bis(hydroxymethyl)propanoyloxy)ethyl)benzene (**23**).* Compound **22** (1.22 g, 2.12 mmol) dissolved in dry CH_2Cl_2 (15 mL), dry methanol (30 mL), and dry THF (15 mL) was deprotected as in the general method to afford hydroxyl-terminated **23** as a colorless crystalline solid (0.84 g, 99% yield): mp 118–120 °C; ^{1}H NMR (500.13 MHz, methanol-d_4) δ 1.09 (s, 6H,

CH_3), 2.92 (t, J=7 Hz, 4H, PhCH_2), 3.61 (AB q, $\Delta\nu_{AB}$=22.3 Hz, J_{AB}=10.5 Hz, 8H, CH_2OH), 4.27 (t, J=7 Hz, 4H, CH_2O), 7.19 (s, 4H, PhH); ^{13}C NMR (125.7 MHz, methanol-d_4) δ 176.6 (C═O), 137.7, 130.1 (PhC), 66.3 (CH_2O), 65.8 (CH_2OH), 51.5 (C_{quat}), 35.6 (PhCH_2), 17.3 (CH_3). HR EIMS m/z calcd for $C_{20}H_{30}NaO_8$ 421.1833; found 421.1830.

*4.4.5. 1,4-Bis(2-((cis-5-methyl-r-2-phenyl-1,3-dioxan-5-yl)methanoyloxy)ethoxy)benzene (**24**).* Compound **24** was synthesized as described above in the general dendritic ester procedure. 1,4-Bis-(2-hydroxyethoxy)benzene (**3**, 0.500 g, 2.52 mmol), dry pyridine (6 mL), CH_2Cl_2 (18 mL), DMAP (0.135 g, 1.11 mmol), and the anhydride **17** (2.58 g, 6.05 mmol) were stirred at rt for 4 h under nitrogen. After work up and purification as described above, the product was obtained as a colorless solid (1.48 g, 97% yield): mp 145 °C; ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 1.04 (s, 6H, CH_3), 3.65 (d, J=11.5 Hz, 4H, H-4$_{ax}$, H-6$_{ax}$), 4.16 (t, J=5 Hz, 4H, PhOCH_2O), 4.53 (t, J=5 Hz, 4H, OCH_2CH_2O), 4.68 (d, J=11.5 Hz, 4H, H-4$_{eq}$, H-6$_{eq}$), 5.45 (s, 2H, H-2), 6.81 (s, 4H, PhH), 7.28–7.44 (m, 10H, PhH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 174.1 (C═O), 153.2, 138, 129.1, 128.3, 126.4, 116.1 (PhC), 102 (C-2), 73.7 (C-4, C-6), 66.9 (OCH$_2$CH$_2$O), 63.6 (OCH$_2$$CH_2$O), 42.7 ($C_{quat}$), 18.0 ($CH_3$). HR ESI MS m/z calcd for $C_{34}H_{38}NaO_{10}$ 629.2357; found 629.2352.

*4.4.6. 1,4-Bis-(2-(2,2′-bis(hydroxymethyl)propanoyloxy)ethoxy)benzene (**25**).* Using the general procedure for deprotection described above, **24** (1.18 g, 1.95 mmol) dissolved in dry CH_2Cl_2 (15 mL), dry methanol (30 mL) and dry THF (15 mL) afforded hydroxyl-terminated **25** as a colorless solid (0.83 g, 99% yield): mp 155–156 °C; ^{1}H NMR (500.13 MHz, methanol-d_4) δ 1.16 (s, 6H, CH_3), 3.66 (AB q, $\Delta\nu_{AB}$=29.5 Hz, J_{AB}=11 Hz, 8H, CH_2OH), 4.16 (t, J=5 Hz, 4H, OCH_2-CH$_2$O), 4.40 (t, J=5 Hz, 4H, OCH$_2$CH_2O), 6.89 (s, 4H, PhH); ^{13}C NMR (125.7 MHz, methanol-d_4) δ 176.5 (C═O), 154.6, 116.9 (PhC), 67.9 (OCH$_2$CH$_2$O), 65.8 (CH_2OH), 64.3 (OCH$_2$$CH_2$O), 51.6 ($C_{quat}$), 17.3 ($CH_3$). HR ESI MS m/z calcd for $C_{20}H_{30}NaO_{10}$ 453.1731; found 453.1740.

*4.4.7. 1,4-(Bis-(2-(2,2′-bis(cis-5-methyl-r-2-phenyl-1,3-dioxan-5-yl)methanoyloxy-methyl)-propanoyloxy)ethoxy)benzene (**26**).* Compound **26** was synthesized as described above in the general dendritic ester procedure. Compound **25** (0.800 g, 1.86 mmol), dry pyridine (5 mL), CH_2Cl_2 (15 mL), DMAP (0.200 g, 1.64 mmol), and the anhydride **17** (3.80 g, 8.91 mmol) were stirred at rt for 10 h under nitrogen. After work up and purification as described above, the product was obtained as a colorless solid (2.13 g, 92% yield): mp 145 °C; ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 0.94 (s, 12H, 4CH_3), 1.28 (s, 6H, 2CH_3), 3.59 (d, J=11.5 Hz, 8H, H-4$_{ax}$, H-6$_{ax}$), 3.89 (t, J=5 Hz, 4H, OCH_2CH$_2$O), 4.27 (t, J=5 Hz, 4H, OCH$_2$CH_2O), 4.41 (AB q, $\Delta\nu_{AB}$=6 Hz, J_{AB}=11 Hz, 8H, 4CH_2OC═O), 4.58 (m, 8H, H-4$_{eq}$, H-6$_{eq}$), 5.42 (s, 4H, H-2), 6.69 (s, 4H, PhH), 7.28–7.42 (m, 20H, PhH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 173.4 (4C═O), 172.8 (2C═O), 153.0, 138, 129.0, 128.3, 126.3, 115.8 (PhC), 101.8 (C-2), 73.7, 73.6 (C-4, C-6), 66.3 (OCH$_2$CH$_2$O), 65.7 (4CH_2O), 63.8 (OCH$_2$$CH_2$O), 47.0 (2$C_{quat}$), 42.7 (4$C_{quat}$), 17.9 ($CH_3$). HR ESI MS m/z calcd for $C_{68}H_{78}Na_2O_{22}$ 1269.4877; found 1269.4866.

*4.4.8. 1,4-Bis-(2-(2,2′-bis(2,2′-bis(hydroxymethyl)propanoyloxy-methyl)propanoyloxy)-ethoxy)benzene (**27**).* Using the general procedure for deprotection described above, **26** (1.95 g, 1.56 mmol) dissolved in dry CH_2Cl_2 (15 mL), dry methanol (30 mL) and dry THF (15 mL) afforded **27** as a colorless solid (1.36 g, 97% yield): mp 155–156 °C; ^{1}H NMR (500.13 MHz, methanol-d_4) δ 1.12 (s, 12H, 4CH_3), 1.28 (s, 6H, CH_3), 3.62 (m, 16H, CH_2OH), 4.17 (br m, 4H, PhOCH_2CH$_2$), 4.27 (AB q, $\Delta\nu_{AB}$=19 Hz, J_{AB}=11 Hz, 8H, 4CH_2OC═O), 4.43 (br m, 4H, CH$_2$CH_2OC═O), 6.88 (s, 4H, PhH); ^{13}C NMR (125.7 MHz, methanol-d_4) δ 175.8 (4C═O), 174.4 (2C═O), 154.4, 116.9 (PhC), 67.6 (OCH$_2$CH$_2$O), 66.3 (4CH$_2$OC═O), 65.7 (CH_2OH), 65.0 (OCH$_2$$CH_2$O), 51.7 (4$C_{quat}$), 47.7 (2$C_{quat}$), 18.1 (2$CH_3$), 17.2 (4$CH_3$). HR ESI MS m/z calcd for $C_{40}H_{62}NaO_{22}$ 917.3625; found 917.3629.

*4.4.9. 1,4-Bis-(2-(2,2′,2″-tris(benzyloxymethyl)ethanoyloxy)ethoxy)benzene (**28**).* Compound **28** was synthesized as described above in the general dendritic ester procedure. The core moiety (**3**) (0.630 g, 3.18 mmol), dry pyridine (6 mL), CH_2Cl_2 (18 mL), DMAP (0.210 g, 1.72 mmol), and the anhydride **23** (6.15 g, 7.47 mmol) were stirred at rt for 12 h under nitrogen. After work up and purification as described above, the product was obtained as a colorless crystalline solid (hexanes/EtOAc; 3:1; R_f 0.35) (2.99 g, 94%): mp 70 °C; ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 3.71 (s, 12H, 6C_{quat}CH_2O), 4.01 (t, J=5 Hz, 4H, 2PhOCH_2), 4.42 (t, J=5 Hz, 4H, 2CH_2OC═O), 4.46 (s, 12H, 6CH_2 benzylic), 6.69 (s, 4H, PhH), 7.21–7.27 (m, 30H, PhH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 172.6 (C═O), 153.1, 138.5, 128.4, 127.52, 127.46, 115.8 (PhC), 73.3 (6CH_2 benzylic), 68.0 (6$C_{quat}$$C$O), 66.6 (2PhO$C$), 63.0 (2$C$OC═O), 53.9 ($C_{quat}$). HR ESI MS m/z calcd for $C_{62}H_{66}NaO_{12}$ 1025.4446; found 1025.4429.

*4.4.10. 1,4-Bis-(2-(2,2′,2″-tris(hydroxymethyl)ethanoyloxy)ethoxy)benzene (**29**).* Using the general procedure for deprotection described above, **28** (1.74 g, 1.73 mmol), dissolved in dry CH_2Cl_2 (15 mL), dry MeOH (30 mL), and dry THF (15 mL) afforded **29** as a colorless crystalline solid (0.77 g, 96% yield): mp 150–151 °C; ^{1}H NMR (500.13 MHz, methanol-d_4) δ 3.77 (s, 12H, 6CH_2O), 4.17 (t, J=5 Hz, 4H, 2PhOCH_2), 4.42 (t, J=5 Hz, 4H, 2CH_2OC═O), 6.90 (s, 4H, PhH); ^{13}C NMR (125.7 MHz, methanol-d_4) δ 175.4 (C═O), 154.7, 116.5 (PhC), 71.1 (2PhOC), 61.8 (2COC═O), 61.5 (6COH), 57.1 (C_{quat}). HR ESI MS m/z calcd for $C_{20}H_{30}NaO_{12}$ 485.1629; found 485.1656.

*4.4.11. 1,4-Bis-(2-(2,2′,2″-tris((cis-5-methyl-r-2-phenyl-1,3-dioxan-5-yl)methanoyloxy-methyl)ethanoyloxy)ethoxy)benzene (**30**).* Compound **30** was synthesized as described above in the general procedure for dendritic ester formation. Dendrimer **29** (0.550 g, 1.19 mmol), dry pyridine (4 mL), CH_2Cl_2 (12 mL), DMAP (0.262 g, 2.14 mmol), and the anhydride **17** (3.80 g, 8.91 mmol) were stirred at rt for 7 h under nitrogen. Water (4 mL) was added and the ester product precipitated immediately. The product was collected using suction filtration and was washed with methanol (3×5 mL) to afford a colorless crystalline solid (1.95 g, 97% yield): mp 183–185 °C; ^{1}H NMR (500.13 MHz, acetone-d_6/DMSO-d_6) δ 3.70 (d, J=11.5 Hz, 12H, 6H-4$_{ax}$, 6H-6$_{ax}$), 3.93 (t, J=4.5 Hz, 4H, 2PhOCH_2), 4.27 (t, J=4.5 Hz, 4H, 2CH_2OC═O), 4.44 (d, J=11.5 Hz, 12H, 6H-4$_{eq}$, 6H-6$_{eq}$), 4.47 (s, 12H, 2Cquat(CH_2)$_3$), 5.50 (s, 6H, H-2), 6.73 (s, 4H, PhH), 7.30–7.38 (m, 30H, PhH); ^{13}C NMR (125.7 MHz, acetone-d_6/DMSO-d_6) δ 173.4 (6C═O), 170.5 (2C═O), 153.2, 138.9, 129.1, 128.4, 126.7, 116.0 (PhC), 101.5 (6C-2), 73.2 (6C-4, 6C-6), 66.4 (2PhOC), 64.4 (2CH$_2$OC═O), 62.0 (2C_{quat}(CH$_2$)$_3$), 51.4 (2C_{quat}), 42.9 (6C-5), 17.5 (6CH_3). HR ESI MS m/z calcd for $C_{92}H_{102}Na_2O_{30}$ 866.3120; found 866. 3048.

*4.4.12. 1,4-Bis-(2-(2,2′,2″-tris(2,2′-bis(hydroxymethyl)propanoyloxy-methyl)ethanoyloxy)-ethoxy)benzene (**31**).* Using the general procedure for deprotection described above, **30** (1.50 g, 0.889 mmol), dissolved in dry CH_2Cl_2 (30 mL), dry MeOH (15 mL), and dry THF (15 mL) afforded **31** as a colorless crystalline solid (0.99 g, 96% yield): mp 151–152 °C; ^{1}H NMR (500.13 MHz, DMSO-d_6) δ 3.38–3.46 (m, 24H, 12CH_2OH), 4.12 (t, J=5 Hz, 4H, 2PhOCH_2), 4.23 (s, 12H, 2C_{quat}(CH_2)$_3$), 4.37 (t, J=5 Hz, 4H, 2CH_2OC═O), 4.67 (t, J=5.5 Hz, 12H, 12OH), 6.87 (s, 4H, PhH); ^{13}C NMR (125.7 MHz, DMSO-d_6) δ 174.0 (6C═O), 170.2 (2C═O), 152.5, 115.6 (PhC), 65.9

(2PhO*C*H_2), 63.8 (2*C*H_2OC=O), 63.6 (12*C*H_2OH), 61.1 (2Cquat(*C*H_2)3), 50.4 (6*C*CH_2OH), 50.3 (2C_{quat}), 16.7 (6CH_3). HR ESI MS *m*/*z* calcd for $C_{50}H_{78}NaO_{30}$ 1181.4470; found 1181.4470.

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Supplementary data

[1]H and [13]C{[1]H} NMR spectra for all new compounds and compounds prepared by new methods. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2010.10.018.

References and notes

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