## 151. Synthesis of Chiral Starburst Dendrimers from PHB-Derived Triols as Central Cores

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Chiral triols 1-3 ('tris(hydroxymethyl)methane' derivatives), prepared from (*R*)-3-hydroxybutanoic acid and aldehydes, are used as center pieces of dendrimers. The triols may be employed as such or after attachment of spacers containing alkyl or aryl moieties (see 5 and 7). The branches combined with the original or elongated triols are those first reported by *Fréchet* (9–12, benzyl ethers of 3,5-dihydroxybenzyl alcohol and bromide). In this way, 1st-, 2nd-, and 3rd-generation chiral dendrimers without (13–15), or with aliphatic (16–18) or aromatic (19–21) spacers are prepared. The molecular weights range from 447 to 2716 Dalton. Two of the chiral triols, *i.e.*, 2 and 3, are used as center pieces for chiral dendrimers containing 6 NH<sub>2</sub>, or 6 and 12 NO<sub>2</sub> groups on the periphery (22–27), with 3,5-dinitrobenzoyl chloride as the branching unit. All compounds thus synthesized are of course monodisperse and are fully characterized. In some cases, the optical activity of the dendrimers indicates that conformationally chiral substructures might be present. The NH<sub>2</sub>- and NO<sub>2</sub>-substituted compounds avidly clathrate smaller molecules; they are sorbents exchanging host molecules through the gas phase.

**Introduction.** – Starburst dendrimers<sup>4</sup>) are macromolecules of unique molecular weight (ideally, a dendrimer has no molecular-weight dispersion, although only convergent synthetic approaches permit the synthesis of high-generation dendrimers without defaults). Dendrimers are emerging as intriguing nonnatural target molecules of organic synthesis.

There are many speculations about the properties of such dendritic molecular architectures. What is the shape of a dendrimer containing a chiral central core (see A)? Will it be optically active? Will the core create internal chiral cavities to accomodate guest molecules – enantioselectively? To collect information about such questions, we have started a program to synthesize various types of chiral dendrimers. As part of our efforts in this area, we have been working on the synthesis of chiral dendritic molecules containing enantiomerically pure trifunctional building blocks [2] as center pieces.

Previously, we have developed [3] an efficient method for the synthesis of chiral triols of type **D** from the dioxanone **C** (which is easily accessible from the biopolymer PHB (**B**) [4]). The triols **D** can be used as central core units themselves, or they can be further

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<sup>&</sup>lt;sup>4</sup>) For excellent review articles and highlights on starburst dendrimers, see [1].



elaborated to give building blocks of type E [2], in which the distance between the functional groups is increased so that steric hindrance during the attachment of branches is decreased.

Prior to our first preliminary account [5], there was only one report [6a] on the synthesis of chiral starburst dendrimer by *Newkome* and coworkers. These authors attached tryptophan units at carboxylic-acid groups on the surface of a tetrabranched dendrimer, thus presenting a chiral surface but not a chiral dendritic structure<sup>5</sup>)<sup>6</sup>). Here we wish to report a full account of our work on the synthesis of 1st-, 2nd-, and 3rd-generation chiral dendrimers (*Tomalia* definition [1]), using PHB-derived central core units.

Syntheses of the Dendrimers 13–27. – The center pieces in our dendrimer synthesis are the triols 1–3, prepared as described previously [2] [3]. The choice of 1 as the center piece for nearly all of our work so far was based on the following reasons: i) ease of preparation<sup>7</sup>), ii) ease of handling as a solid<sup>8</sup>), and iii) the *t*-Bu group acts as a marker in the

<sup>&</sup>lt;sup>5</sup>) There are reports [7–10] on 1- and 2-directional cascade molecules based on lysine [7] [9], oligonucleotides [8], and biphenylacetate [10]. These molecules are not starburst dendrimers, although they possess a dendritic structure.

<sup>&</sup>lt;sup>6</sup>) Independent work by *Hak-Fun Chow* and his colleagues on chiral dendrimers from an achiral trifunctional core and branching unit, with the tartaric-acid-derived 2,2-dimethyl-1,3-dioxolane-4,5-dimethanol as chiral linker has just appeared [11a]. Even more recent is a report by *Mitchell et al.* about dendritic molecules built of glutamic-acid units [11b].

<sup>&</sup>lt;sup>7</sup>) For a one-pot procedure for the preparation of 1 from the dioxanone C in 76% yield, see *Exper. Part.* 

<sup>&</sup>lt;sup>8</sup>) Weighing and manipulating a solid rather than a viscous oil proved to be especially advantageous, when high accuracy and strict anhydrous conditions were required for the step combining three large branches (mol. wt. up to 808 Da in the present work) to the triol **1** (mol. wt. 174 Da).



<sup>1</sup>H-NMR spectra<sup>9</sup>). A disadvantage is of course the steric hindrance imposed by the *t*-Bu group, upon the neighboring OH group.

In addition to triol 1, we prepared two new elongated triols: compound 5 with aliphatic spacers (obtained by hydroboration of the allyl ether 4) and compound 7 with aromatic spacers (by reduction of the triester 6; see *Scheme 1*). The triols 5 and 7 provide



<sup>&</sup>lt;sup>9</sup>) The <sup>1</sup>H-NMR signal of the *t*-Bu group is in the high-field window of most <sup>1</sup>H-NMR spectra, it is always a *singlet*; its 9 protons can be used for integration comparison; by-products and products of incomplete conversions can be readily detected.

center pieces with an increased distance between the three functional groups involved in the coupling step<sup>10</sup>)<sup>11</sup>). It was demonstrated that this factor plays an important role in the accessibility of high-generation dendrimers [12].

Following *Fréchet*'s strategy [13], the chiral dendrimers were built in a convergent manner by coupling dendritic branches (dendrons) to the chiral center pieces. The preparation of the *Fréchet* dendrons 10 and 12 was readily achieved according to the published procedure (*Scheme 2*), except that the purification steps were modified (see



*Exper. Part*). Thus, commercial methyl 3,5-dihydroxybenzoate was *O*-benzylated ( $\rightarrow$ 8), reduced ( $\rightarrow$ 9), and converted to the benzyl bromide 10, which, in turn, was used to benzylate the phenolic OH groups of 3,5-dihydroxybenzyl alcohol ( $\rightarrow$ 11). Treatment of 11 with CBr<sub>4</sub>/PPh<sub>3</sub> gave bromide 12. The total yield of branched benzyl bromides 10 and 12 from dihydroxybenzoate was 59 and 37%, respectively.

Coupling of the center pieces with the benzyl bromides was achieved by treating a triol 1, 5, or 7 with excess NaH (9 equiv.) in refluxing THF and then adding an excess of the corresponding benzyl bromide. The dendrimers 13-15 from the non-elongated triol 1 and those from the elongated triols 5 ( $\rightarrow 16-18$ ) and 7 ( $\rightarrow 19-21$ ) were thus obtained in

Table 1. Yields, Optical Activities, Molecular Weights, and Molecular Rotations of Chiral Dendrimers of Generation 1 (13, 16, and 19), 2 (14, 17, and 20), and 3 (15, 18, and 21). These dendrimers were obtained by benzylation of the triols 1, 5, and 7 with benzyl bromides.

Triol	Benzylbromide	Product	Yield [%]	$[\alpha]_{D}^{r.t.}$ (c in CHCl <sub>3</sub> )	Mol. wt. [Da]	$[\Phi]_{\rm D}^{\rm r.t.}$
1	BnBr	13	82	+10.7 (2.7)	447	+48
1	10	14	93	+4.3(4.0)	1083	+46
1	12	15	85	+3.7(2.5)	2357	+87
5	BnBr	16	80	-0.8(1.1)	620	-5
5	10	17	33	-1.5 (1.0)	1258	14
5	12	18	75	-0.2 (1.6)	2531	5
7	BnBr	19	58	+12.2(1.4)	807	+98
7	10	20	50	+7.0(1.5)	1149	+101
7	12	21	55	+3.8 (1.7)	2716	+103

<sup>&</sup>lt;sup>10</sup>) In a stretched-out molecular model of **1**, **5**, and **7**, the distances between the OH groups are *ca*. **4**, 11, and 16 Å, respectively.

<sup>&</sup>lt;sup>11</sup>) Similar compounds derived from triol **2** were described in our previous paper [2].

good-to-excellent yields (see *Table 1*). The yields refer to samples which were purified by flash chromatography. All compounds **13–21** gave correct elemental analyses and the expected spectroscopic data (<sup>1</sup>H- and <sup>13</sup>C-NMR, IR, EI- or FAB-MS, UV/VIS, and CD spectra). Most compounds in this series are colorless or slightly yellow oils, or honey-like or glassy materials which retain solvents tenaciously. Thus the samples sometimes had to be kept under high vacuum at elevated temperatures for longer periods of time to be freed of solvent. The largest dendrimer **21** has a molecular weight of 2716 Da.









The synthesis of dendrimers 22–27 containing an ester linkage to the chiral core and amide bonds at the branching points was achieved *via* a divergent<sup>12</sup>) approach, by constructing the 2nd generation on the dendritic molecule of 1st generation [1]. We used, as center pieces, triol 2 and the more hindered triol 3. The preparation of the hexanitro and hexaamino derivatives 22–24 was described in our previous paper [2]. Reduction  $(Pt/H_2)$  of the 6 NO<sub>2</sub> groups of triester 23 to NH<sub>2</sub> groups gave the hexaamino derivative 25 with a diphenylmethyl group on the center piece. Acylation of the 6 NH<sub>2</sub> groups of 24 and 25 with 3,5-dinitrobenzoyl chloride yielded the dodecanitro-dendrimers 26 and 27 (83 and 92%, resp., after purification). The compounds 24–27 were characterized as clathrates with solvent molecules (*vide infra*).

**Properties of the Dendrimers 13–27.** – Inspection of the  $[\alpha]_D$  values in *Table 1* shows that in the series of dendrimers with no (13–15) and with aromatic spacer (19–21), the optical activity at the sodium D-line decreases as the generation number increases. In the series with aliphatic spacer (16–18), there is hardly any optical activity at all ( $[\alpha]_D^{r.t} = -0.2$  to -1.5; the chiral center pieces, triol 1 and elongated triol 5 have  $[\alpha]_D^{r.t.} = +12.6$  and -14.2, resp.)<sup>13</sup>). In the absence of chiral substructures which might contribute to the optical activity, we expect that attachment of achiral branches to a chiral center piece leads to a kind of dilution effect. This is indeed the case in the series 19–21 with aromatic spacer (see the almost constant values of the molar rotations  $[\Phi]_D^{r.t.}$  in *Table 1*). With compounds 13–15 containing no spacer, there is an anomaly in that the value of the molar rotation doubles on going from generation 2 (14) to generation 3 (15), with more than

<sup>&</sup>lt;sup>12</sup>) In natural-product synthesis, this strategy is normally called a linear as compared to a convergent approach [14]. The dendrimer specialists use the terms divergent and convergent [1] [12] [13].

<sup>&</sup>lt;sup>13</sup>) Interestingly, the sign of optical rotation reverses on going from the tris(allylic ether) 4 ( $[\alpha]_D^{\text{ct.}} = +10.8$ ) to the triol 5!

doubling the molecular weight. The dendrimers 16-18 with aliphatic elongation of the center piece do not even show significant optical activity at shorter wavelenghts: the CD spectra measured in MeCN are just horizontal lines from 400 to *ca.* 220 nm, with a steep incline at shorter wavelength.

The signals from the benzylic CH<sub>2</sub> groups in the <sup>1</sup>H- and <sup>13</sup>C-NMR spectra of the three series of dendrimers **13–15**, **16–18**, and **19–21** can be taken as a measure for the degree of dissimilarity of their environments: on going from the center to the outer parts of the molecules, the heterotopic CH<sub>2</sub> H-atoms and the corresponding C-atoms become isochronous because of the similarity of their time-averaged local environments. Constitutional heterotopicity and diastereotopicity show up best near the chiral center piece. Except for the proximity, the conformational flexibility of the molecular fragment between the chiral core and the particular set of benzylic CH<sub>2</sub> groups influences the degree of anisochrony of the corresponding H-atoms. This is evident from the 300-MHz <sup>1</sup>H-NMR spectra of the 3rd-generation dendrimers **18**, **21**, and **15** shown in the *Figure* 



Figure. Benzylic region of the 300-MHz <sup>1</sup>H-NMR spectra of the 3rd-generation dendrimers 18, 21, and 15. The labelling of signals or groups of signals refers to the sets of CH<sub>2</sub> groups in the corresponding formulae (see text). On going from the 12 outermost ( $\blacksquare$ ) to the 6 intermediate ( $\odot$ ), and then the 3 (18, 15) or 9 (21) innermost ( $\blacktriangle$ ) CH<sub>2</sub> groups, the <sup>1</sup>H-NMR signals move upfield and their multiplicity increases.

(benzylic region). There are essentially 3 *singlets* for the 3 sets of 12, 6, and 3 CH<sub>2</sub> groups in **18**, the dendrimer with a floppy aliphatic spacer group. In the <sup>1</sup>H-NMR spectrum of **21**, the dendrimer with aromatic spacers, the outer 12 and the intermediate 6 CH<sub>2</sub> groups give rise to *singlet* signals, while the inner 9 (including those of the spacer unit) appear as a wide-spread *multiplet*. The dendrimer **15**, in which the branches are directly coupled with the non-elongated triol **1** shows no *singlets* for any of the sets of analogous benzylic H-atoms. In the <sup>13</sup>C-NMR spectra, a similar pattern of the signals from the benzylic C-atoms is observed.

The optical properties of the dendrimers with 6 (22 and 23) and 12 (26 and 27)  $NO_2$  groups and of the corresponding synthetic intermediate hexaamines (24 and 25) are given in *Table 2*. It is remarkable that here a dramatic change of the optical activity is observed

 Table 2. Optical Activities and Molecular Rotations of the Chiral Nitro-Substituted Dendrimers 22, 23, 26, and 27

 and of the Synthetic Intermediates 24 and 25

	R	x	$[\alpha]_{D}^{r.t.}(c, solvent)$	Mol. wt. [Da]	[ <b>\$</b> ] <sup>r.t.</sup> -124
22	i-Pr	NO <sub>2</sub>	-16.7 (3.0, acetone)		
26	i-Pr	$NO_2$	+9.0 (1.0, dioxane)	1729	+155
23	Ph <sub>2</sub> CH	$NO_2$	-95.3 (2.3, acetone)	868	-827
27	$Ph_2CH$	$NO_2$	-15.2 (2.4, dioxane)	1853	-282
24	i-Pr	$\overline{NH_{2}}$	0 (1.7, acetone)	564	0
25	Ph <sub>2</sub> CH	$\overline{NH_2}$	-69.5 (1.1, acetone)	688	-446

on going from the 1st to the 2nd generation, both with the i-Pr-substituted ( $[\Phi]_{D}^{rL}$  from -124 to +155) and the Ph<sub>2</sub>CH-substituted ( $[\Phi]_{D}^{rL}$  from -827 to -282) center piece. This indicates that we now have considerable contributions to the optical activity from conformationally chiral chromophors in the periphery of the molecules. Unfortunately, we have so far not been able to isolate crystals of one of the NO<sub>2</sub>-substituted dendrimers in a quality suitable for X-ray analysis<sup>14</sup>) to learn details of its structure.

The NO<sub>2</sub>- and NH<sub>2</sub>-substituted compounds **24–27** were found to have a strong tendency to form clathrates with other molecules [15]. Thus, recrystallization of the hexaamines **24** and **25** from dioxane yielded the corresponding clathrates [**24**  $\cdot$  C<sub>4</sub>H<sub>8</sub>O<sub>2</sub>] and [**25**  $\cdot$  C<sub>4</sub>H<sub>8</sub>O<sub>2</sub>], respectively. The dodecanitrodendrimers **26** and **27**, when recrystallized from a mixture of MeOH/AcOEt, also gave inclusion compounds, [2 **26**  $\cdot$  AcOEt  $\cdot$  8 H<sub>2</sub>O] and [**27**  $\cdot$  2 AcOEt  $\cdot$  2 H<sub>2</sub>O], respectively. These are the first examples of host-guest complexes with the host having a dendritic structure. Inclusion complexes accomplished directly *via* solid-host/gaseous-guest interaction are rare. Such an interaction was used with some simple host compounds in the enantioselective sorption of organic guest molecules [16]. The dendrimer **27**, containing 11 benzene rings, 3 ester, 6 amide, and 12 NO<sub>2</sub> groups, also proved to be a sorbent for organic-solvent vapors, forming complexes with, *e.g.*, AcOEt, MeCN, and acetone, which can replace each other in intact crystals through the gas phase! We are currently testing whether this sorption process is enantioselective.

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<sup>&</sup>lt;sup>14</sup>) The configuration of 3 as shown in the formula was recently confirmed by an X-ray crystal-structure analysis (unpublished results by *Alois Boog* and *Florian N. M. Kühnle*, ETH-Zürich, 1994).

## **Experimental Part**

General. Solvents used were Fluka puriss. grade, except for THF which was distilled over K/benzophenone. Commercially available reagents were used as received without any further purification. The preparation of 2 is described in [3] and that of 3 and 22–24 in [2]. Thin-layer chromatography (TLC): glass-plated TLC silica gel 60  $F_{254}$  (Merck). Flash chromatography (FC): silica gel 60 (Merck) 40–60 µm. M.p.: Büchi 510; uncorrected. Optical rotations: Perkin-Elmer-241 polarimeter; in 1-dm cells. IR: Perkin-Elmer-983 or Perkin-Elmer-297 spectrometer; in cm<sup>-1</sup>. NMR: Bruker-AMX400, Varian-XL-300, Bruker-WM-300, or Varian-Gemini-200 spectrometer; in CDCl<sub>3</sub>, unless mentioned otherwise; chemical shifts  $\delta$  in ppm downfield from internal SiMe<sub>4</sub>, coupling constants J in Hz. MS: Hitachi-Perkin-Elmer RMU-6M; m/z relative intensities (in %) in parentheses. Microanalyses were performed by Mikroanalytisches Laboratorium der ETH-Zürich. Abbreviations: THF (tetrahydrofuran), LDA (lithium diisopropylamide) h.v. (high vacuum).

(2R,3S,4R)-3-(Hydroxymethyl)-5,5-dimethylhexane-2,4-diol (1). An ice-cold soln. of (i-Pr)<sub>2</sub>NH (7.43 ml, 53 mmol, 1.14 equiv.) in THF (115 ml) was treated with BuLi (41 ml, 53 mmol, 1.5M in hexane, 1.14 equiv.), kept at 0° for 15 min, and then cooled to  $-78^{\circ}$ . To this soln. of LDA was added dioxanone C (8.0 g, 46.5 mmol) in THF (50 ml) at such a rate that the temp. never exceeded  $-75^{\circ}$ ; after 45 min at this temp., a soln. of pivalaldehyde (7.2 ml, 64 mmol) in THF (ca. 50 ml) was added, again such that the temp. did not rise above  $-75^{\circ}$ . The reaction mixture was maintained at  $-78^{\circ}$  for 4 h. Then AcCl (6.7 ml, 93 mmol, 2 equiv.) was added, the mixture allowed to reach r.t., and pyridine (18.8 ml, 232.5 mmol, 5 equiv.) added. After 9 h of stirring, the mixture was washed with 10% HCl, soln. (3 × 100 ml), H<sub>2</sub>O (100 ml), and sat. aq. NaCl soln. (20 ml) at 0°. The mixture was dried (MgSO<sub>4</sub>) and evaporated under vacuum and h.v. The residue in Et<sub>2</sub>O (300 ml) at 0°. The mixture was stirred under reflux for 4 h. After cooling to 0° H<sub>2</sub>O (8.83 ml), 15% NaOH soln. (8.83 ml), and H<sub>2</sub>O (26.5 ml) were added consecutively, and the resulting mixture was stirred vigorously, until a white precipitate was formed. Addition of MgSO<sub>4</sub>, filtration, and evaporation yielded a colorless liquid. FC (Et<sub>2</sub>O), subsequent evaporation and drying under h.v. gave 6.17 g (76%) of pure 1. White solid. For physical data, see [3].

*Bis(allyl)* (2' R,3' S,4' R)-3'-*f* (*Allyloxy)methyl]-5',5'-dimethylhexane-2',4'-diyl Diether* (4). To a suspension of NaH (2.45 g, 0.10 mol, 9 equiv.) in THF (50 ml) was added 1 (2.00 g, 11.35 mmol) in THF (50 ml), and the mixture was stirred under reflux for 30 min. Then allyl bromide (8.6 ml, 0.10 mol, 9 equiv.) was introduced and the mixture stirred under reflux for 4 h, then quenched with H<sub>2</sub>O (100 ml), extracted with Et<sub>2</sub>O (3 × 150 ml). The combined org. extract was dried (MgSO<sub>4</sub>) and evaporated and the crude product distilled ('Kugelrohr' apparatus, 100°/0.1 Torr): 2.99 g (89%) of pure 4. [ $\alpha$ ]<sub>D</sub><sup>tL</sup> = +10.8 (*c* = 1.69, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3079*m*, 3014*m*, 2960*s*, 1996 (br.), 1844*w*, 1646*m*, 1465*s*, 1424*m*, 1407*m*, 1394*m*, 1377*m*, 1363*s*, 1333*m*, 1288*m*, 1245*m*, 1196*m*, 1097*s*, 995*s*, 920*s*, 777*w*. <sup>1</sup>H-NMR (300 MHz): 0.92 (*s*, *t*-Bu); 1.21 (*d*, *J* = 6.45, 3 H−C(1')); 2.17 (*dddd*, *J* = 8.86, 3.62, 3.62, 1.85, H−C(2')); 3.66 (*dd*, *AB*, *J* = 10.16, 3.66, 1 H, CH<sub>2</sub>−C(3')); 3.87-4.15 (*m*, 3 CH<sub>2</sub>=CHCH<sub>2</sub>); 5.05-5.29 (*m*, 3 CH<sub>2</sub>=CHCH<sub>2</sub>); 5.81-5.97 (*m*, 3 CH<sub>2</sub>=CHCH<sub>2</sub>). <sup>13</sup>C-NMR (75 MHz): 16.41; 26.32; 37.29; 44.41; 68.14; 69.82; 71.93; 73.32; 76.04; 86.27; 115.08; 116.12; 116.25; 135.38; 135.53; 135.78. MS: 297 ( < 1, [*M* + 1]<sup>+</sup>), 281 ( < 1), 255 ( < 1), 239 (10), 183 (7), 167 ( < 1), 153 (4), 139 (2), 127 (49), 111 (7), 97 (100), 85 (52), 69 (9), 55 (15), 43 (24), 41 (68). Anal. calc. for C<sub>18</sub>H<sub>32</sub>O<sub>3</sub>: C 72.93, H 10.88; found: C 72.98, H 10.84.

3.3' -{{(2" R, 3" S, 4" R) - 3" - [(3-Hydroxypropyloxy)methyl] - 5", 5" - dimethylhexane -2", 4" - diyl}bis(oxy)}bis-(propanol) (5). To a soln. of **4** (2.4 g, 8.1 mmol) in THF (50 ml) was added 1M BH<sub>3</sub> · THF (5.1 ml, 5.1 mmol). The mixture was kept at r.t. for 1 h (TLC monitoring (hexanes/Et<sub>2</sub>O 10:1)), then H<sub>2</sub>O (6.2 ml) added, followed by 15% NaOH soln. (8.1 ml) in one portion and 30% H<sub>2</sub>O<sub>2</sub> soln. (8.1 ml) at such a rate that the temp. never exceeded 50°. The mixture was stirred at r.t. for 3 h and then diluted with Et<sub>2</sub>O (200 ml) and H<sub>2</sub>O (100 ml), the aq. phase saturated with NaCl and extracted with Et<sub>2</sub>O (2 × 100 ml), and the combined org. extract dried (MgSO<sub>4</sub>) and evaporated. FC (Et<sub>2</sub>O/MeOH 19:1) gave 0.931 (33%) of pure 5.  $[\alpha]_D^{E1} = -14.2$  (c = 1.13, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3437m, 3007m, 2956s, 2870m, 1478m, 1425m, 1365m, 1262m, 1070s, 1009m. <sup>1</sup>H-NMR (300 MHz): 0.91 (s, t-Bu); 1.25 (d, J = 6.32, 3 H-C(1")); 1.75–1.90 (m, 3 CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH); 1.95 (m, H-C(3")); 2.91 (m, H-C(4")); 3.04–3.18 (br. m, 2 OH); 3.35–3.65 (m, 3 CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, CH<sub>2</sub>-C(3")); 3.67–3.81 (m, 3 CH<sub>2</sub>CH<sub>2</sub>OH); 3.83–3.92 (m, H-C(2")). <sup>13</sup>C-NMR (75 MHz): 17.12; 26.22; 32.17; 32.47; 32.82; 37.00; 45.71; 61.02; 61.77; 62.15; 68.30; 68.55; 69.65; 72.41; 78.42; 88.15. MS: 351 (< 1, [M + 1]<sup>+</sup>), 301 (< 1), 293 (1), 275 (< 1), 235 (< 1), 217 (3), 199 (1), 185 (1), 171 (4), 157 (2), 145 (17), 129 (6), 115 (100), 103 (40), 87 (48), 71 (13), 59 (66), 45 (15), 31 (19). Anal. calc. for C<sub>18</sub>H<sub>38</sub>O<sub>6</sub>: C 61.68, H 10.93; found: C 61.56, H 11.22.

methyl)benzoic acid (4.9 g, 23 mmol, 4 equiv.) in THF (35 ml), the mixture was stirred under reflux for 1 week. The reaction was quenched with H<sub>2</sub>O (20 ml) and 10% HCl soln. (ca. 20 ml; until pH 1-2). Then Et<sub>2</sub>O (100 ml) was added, the aq. phase extracted with Et2O (2×), the combined org. extract dried (MgSO4) and evaporated, and the residue dissolved in Et<sub>2</sub>O (100 ml) and treated with diazomethane/Et<sub>2</sub>O until the yellow color persisted. The mixture was stirred for 1 h and then carefully evaporated. FC (hexane/Et<sub>2</sub>O 1:1) gave 1.98 g (56%) of pure 6.  $[\alpha]_{D}^{r,l} = +18.9$  (c = 2.13, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3539w, 3008w, 2955m, 2869w, 1718s, 1614m, 1577w, 1437m, 1437m, 1614m, 1577w, 1614m, 1577w, 1614m, 1577w, 1614m, 1577w, 1437m, 1614m, 1577w, 1614m, 1614m, 1577w, 1614m, 1577w, 1614m, 1577w, 1614m, 1577w, 1614m, 1614m, 1577w, 1614m, 1614m, 1577w, 1614m, 15770w, 1614m, 15770w, 16140m, 16140m, 16140m, 1614m, 16140m, 16140m, 16140 1416w, 1364w, 1283s, 1176m, 1105s, 1020m, 968w. <sup>1</sup>H-NMR (300 MHz): 0.96 (s, t-Bu); 1.30 (d, J = 6.40, 3H-C(1''); 2.31 (dddd, J = 8.22, 4.11, 4.11, 1.86, H-C(3''); 3.21 (d, J = 1.93, H-C(4''); 3.57 (dd, AB, J = 9.91, 1.25,8.27, 1 H, CH<sub>2</sub>-C(3")); 3.74 (qd, J = 6.42, 3.80, H-C(2")); 3.79 (dd, AB, J = 9.96, 3.60, 1 H, CH<sub>2</sub>-C(3")); 3.91 (s, MeO); 3.91 (s, MeO); 3.92 (s, MeO); 4.45-4.54 (m, 4 benzyl. H); 4.66 (d, J = 9.18, 1 benzyl. H); 4.70 (d, J = 9.02, 1 benzyl. H); 7.25 (d, J = 8.53, 2 arom. H); 7.34 (d, J = 8.49, 2 arom. H); 7.40 (d, J = 8.52, 2 arom. H); 7.93–8.03 (m, 6 arom. H). <sup>13</sup>C-NMR (75 MHz): 16.64; 26.32; 37.45; 45.12; 52.06; 68.37; 70.31; 72.58; 73.42; 76.87; 86.93; 126.38; 127.12; 127.25; 129.52; 129.65; 144.08; 144.24; 144.73; 166.94; 167.02. MS: 621 ( < 1, *M*<sup>+</sup>), 602 ( < 1), 589 (2), 563 (1), 487 (1), 471 (1), 431 (1), 397 (1), 383 (1), 297 (3), 283 (1), 261 (1), 235 (3), 221 (4), 205 (5), 165 (5), 149 (100), 135 (4), 121 (8), 105 (3), 90 (5), 57 (4). Anal. calc. for C<sub>36</sub>H<sub>44</sub>O<sub>9</sub>: C 69.66, H 7.14; found: C 69.84, H 7.15.

4,4'-{{(2" R,3" S,4" R)-3"-{ $I_{-}(Hydroxymethyl)phenyl}methoxymethyl}-5",5"-dimethylhexane-2",4"-diyl}bis-(oxymethylene)}bis(benzenemethanol) (7). To a suspension of LiAlH<sub>4</sub> (0.70 g, 18 mmol) in Et<sub>2</sub>O (15 ml) was added$ **6** $(1.98 g, 3.19 mmol) in Et<sub>2</sub>O (20 ml). The mixture was stirred under reflux for 5 h, then cooled to 0°, and quenched by the successive addition of H<sub>2</sub>O (0.7 ml), 15% NaOH soln. (0.7 ml), and H<sub>2</sub>O (2.1 ml) under vigorously stirring. The solid formed was removed and the filtrate dried (MgSO<sub>4</sub>) and evaporated: colorless oil. FC (Et<sub>2</sub>O/MeOH 19:1) gave 1.37 g (83%) of pure 7. [<math>\alpha$ ][ $_{D}^{rL}$  = +19.2 (c = 1.43, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3602w, 3392w (br.), 3053w, 3007m, 2956m, 2873m, 1514w, 1467w, 1421w, 1380m, 1364m, 1262w, 1098s, 1017m. <sup>1</sup>H-NMR (300 MHz): 0.95 (s, t-Bu); 1.27 (d, J = 6.40, 3 H–C(1")); 2.12–2.20 (br., 3 OH); 2.22–2.30 (m, H–C(3")); 3.18 (d, J = 1.90, H–C(4")); 3.74 (d, AB, J = 10.00, 8.42, 1 H, CH<sub>2</sub>–C(3")); 3.70 (d, d, J = 6.75, 37.42; 44.93; 65.09; 68.14; 70.44; 72.81; 73.77; 76.34; 86.75; 126.83; 126.89; 127.12; 127.82; 127.96; 138.28; 138.42; 139.03; 139.58; 139.97. FAB-MS: 537 (4,  $M^+$ ), 518 (<1), 415 (<1), 399 (2), 277 (3), 261 (3), 241 (7), 223 (10), 211 (6), 175 (6), 154 (15), 137 (18), 121 (100), 105 (32), 91 (37), 77 (28). Anal. calc. for C<sub>33</sub>H<sub>44</sub>O<sub>6</sub>: C 73.85, H 8.26; found: C 73.62, H 8.20.

On the Preparation of the Branch Intermediates 8–12. The modifications of the purification steps in the procedures describing the preparation of the Fréchet dendrons were as follows: Ester 8 was recrystallized from  $Et_2O$ /pentane 2:1. The benzyl alcohol 9 was obtained in a nearly pure form after workup and not further purified. The crude benzyl bromide 10 was simply stirred in  $Et_2O/CH_2Cl_2$  and filtered off, affording pure 10. The latter was coupled with 3,5-dihydroxybenzyl alcohol and the resulting 11 purified by FC ( $CH_2Cl_2$ ; yield 51%). Bromination of 11 was achieved with  $CBr_4/PPh_3$ ; the crude bromide was stirred in  $Et_2O$  to give pure 12 in 88% yield.

On the Nomenclature of the Dendrimers Used. The nomenclature used to describe the dendrimers 13–21 and 25–27 in a short form refers to the one proposed by *Tomalia* and coworkers [1] and *Fréchet* and coworkers [13]. An alternative would be the nomenclature published by *Newkome* and coworkers [6b]. We used the following abbreviations: [G-1] = generation 1 [G-2] = generation 2 [G-3] = generation 3; [C] = center piece 1, without spacer; [C<sub>c</sub>] = center piece 5, with aliphatic spacer (c = chain); [C<sub>a</sub>] = center piece 7, with aromatic spacer (a = aromatic).

 $[G-1]_{3}-[C]$  (= Bis(benzyl) (2' R,3' S,4' R)-3'-[(Benzyloxy)methyl]-5',5'-dimethylhexane-2',4'-diyl Diether; 13). To NaH (724 mg, 30.2 mmol, 9 equiv.) in THF (20 ml) was added 1 (591 mg, 3.35 mmol) in THF (10 ml), and the mixture was stirred under reflux for 30 min. Then benzyl bromide (3.6 ml, 30.2 mmol, 9 equiv.) was added at once, and the mixture was kept at reflux for 18 h. The reaction was quenched with H<sub>2</sub>O (20 ml) and the mixture extracted with Et<sub>2</sub>O (3 × 50 ml). The combined org. extracts were dried (MgSO<sub>4</sub>) and evaporated. FC (hexane/ Et<sub>2</sub>O 19:1) followed by a short-path distillation gave 1.23 g (82%) of pure 13. Colorless liquid. B.p. 250°/0.1 Torr. [ $\alpha$ ] $_{5}^{1-}$  = +10.7 (c = 2.66, CHCl<sub>3</sub>). IR (neat): 3090w, 3065m, 2960s, 2870s, 1605w, 1495m, 1455s, 1360m, 1305w, 1245w, 1205w, 1100s, 1030m. <sup>1</sup>H-NMR (300 MHz): 0.94 (s, t-Bu); 1.28 (d, J = 6.44, Me); 2.30 (m, 1 H)) 3.20 (d, J = 2.12, H–C(4')); 3.58 (dd, AB, J = 10.11, 8.60, 1 H, CH<sub>2</sub>–C(3')); 3.72 (dd, J = 6.51, 3.80, H–C(2')); 3.79 (dd, AB, J = 10.13, 3.58, 1 H, CH<sub>2</sub>–C(3')); 4.35–4.50 (m, 4 benzyl. H); 4.58 (d, J = 13.19, 1 benzyl. H); 4.62 (d, J = 11.89, 1 benzyl. H); 7.15–7.40 (m, 15 arom. H). <sup>13</sup>C-NMR (75 MHz): 16.64; 26.35; 37.45; 44.87; 68.30; 70.82; 73.09; 73.86; 76.30; 86.30; 126.94; 127.32; 127.61; 127.77; 128.10; 128.25; 128.42; 138.97; 139.10; 139.66. MS: 447 (< 1, [M + 1]<sup>+</sup>), 389 (5), 355 (1), 281 (2), 259 (1), 247 (2), 203 (2), 181 (15), 161 (3), 147 (12), 135 (3), 107 (4), 91 (100), 57 (3). Anal. calc. for C<sub>30</sub>H<sub>38</sub>O<sub>3</sub>: C 80.68, H 8.58; found: C 80.69, H 8.52.  $[G-2]_3-[C]$  (= Bis[3,5-bis(benzyloxy)benzyl] (2' R,3' S,4' R)-3'-{[3,5-Bis(benzyloxy)benzyloxy]methyl}-5',5'-dimethylhexane-2',4'-diyl Diether; 14). As described for 13, with 1 (500 mg, 2.84 mmol), NaH (613 mg, 25.5 mmol, 9 equiv.), and [G-2]-Br 10 (3.81 g, 9.93 mmol, 3.5 equiv.). FC (hexanes/Et<sub>2</sub>O 4:1) gave 2.86 (93%) of pure 14. [ $\alpha$ ]<sub>D</sub><sup>1-1</sup> = +4.3 (c = 4.01, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3065w, 3010m, 2960m, 2870m, 1595s, 1500m, 1455s, 1375s, 1340m, 1290m, 1155s, 1100m, 1055s. <sup>1</sup>H-NMR (300 MHz): 0.95 (s, t-Bu); 1.29 (d, J = 6.36, Me); 2.29 (m, 1 H); 3.18 (d, J = 1.75, H-C(4')); 3.61 (m, 1 H, CH<sub>2</sub>-C(3')); 3.71 (gd, J = 6.46, 3.91, H-C(2')); 3.80 (dd, AB, J = 10.01, 3.61, 1 H, CH<sub>2</sub>-C(3')); 4.30-4.50 (m, 4 benzyl. H); 4.55-4.65 (m, 2 benzyl. H); 4.80-5.00 (m, 12 benzyl. H); 6.40-6.65 (m, 10 arom. H); 7.25-7.45 (m, 29 arom. H). <sup>13</sup>C-NMR (75 MHz): 16.80; 26.39; 37.39; 45.06; 68.39; 69.97; 70.86; 72.99; 73.80; 76.60; 77.04; 86.56; 100.80; 101.20; 105.85; 106.15; 106.59; 127.52; 127.90; 128.52; 136.93; 137.00; 141.49; 141.55; 142.08; 159.85; 159.98. MS: 1083 (< 1,  $M^+$ ), 606 (1), 515 (< 1), 423 (< 1), 393 (< 1), 318 (13), 227 (2), 181 (12), 91 (100). Anal. calc. for C<sub>72</sub>H<sub>74</sub>O<sub>9</sub>: C 79.82, H 6.88; found: C 79.71, H 6.74.

 $[G-3]_{3}-[C]$  (= Bis {3,5-bis[3,5-bis(benzyloxy)benzyloxy]benzyl} (2' R,3' S,4' R)-3'- {{3,5-Bis[3,5-bis(benzyloxy)benzyloxy]benzyloxy}benzyloxy<br/>benzyloxy}benzyloxy}benzyloxy benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy}benzyloxy<br/>benzyloxy}benzyloxy}benzyloxy}benzyloxy<br/>benzyloxy}benzyloxy}benzyloxy<br/>benzyloxy}benzyloxy}benzyloxy benzyloxy be

[*G*-1]<sub>3</sub>-[*C<sub>c</sub>*] (= *Bis*[3-(*benzyloxy*)*propyl*] (2' R,3' S,4' R)-3'- {[3-(*Benzyloxy*)*propyloxy*]*methyl*}-5',5'-dimethylhexane-2',4'-diyl Diether; **16**). As described for **13**, with **5** (100 mg, 0.29 mmol), NaH (61.7 mg, 2.6 mmol, 9 equiv.), and benzyl bromide (0.31 ml, 2.6 mmol, 9 equiv.), reaction time 24 h. FC (hexanes/Et<sub>2</sub>O 3:1) gave 142 mg (80%) of pure **16**. [2]<sub>D</sub><sup>-1</sup> = -0.8 (*c* = 1.12, CHCl<sub>3</sub>). UV (*c* = 1 ·10<sup>-3</sup>, MeCN): 216 (*e* 2868). IR (CHCl<sub>3</sub>): 3005*w*, 2955*m*, 2867*m*, 1496*w*, 1454*m*, 1364*m*, 1262*m*, 1096*s*, 1027*m*. <sup>1</sup>H-NMR (300 MHz): 0.87 (*s*, *t*-Bu); 1.15 (*d*, *J* = 6.41, 3 H-C(1')); 1.75-1.90 (*m*, 3 OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O); 2.05-2.09 (*m*, H-C(3')); 2.95 (*d*, *J* = 1.95, H-C(4')); 3.25-3.65 (*m*, 3 OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O, CH<sub>2</sub>-C(3'), H-C(2')); 4.481 (*s*, 2 benzyl. H); 4.483 (*s*, 2 benzyl. H); 4.489 (*s*, 2 benzyl. H); 7.21-7.39 (*m*, 15 arom. H). <sup>13</sup>C-NMR (75 MHz): 16.28; 26.25; 30.23; 30.59; 30.78; 37.20; 44.57; 65.78; 67.81; (8.56; 68.82; 72.97; 76.59; 85.75; 127.48; 127.61; 128.34; 138.64. MS: 620 (< 1, M<sup>+</sup>), 563 (< 1), 538 (< 1), 505 (< 1), 473 (< 1), 455 (1), 397 (2), 343 (3), 289 (< 1), 261 (< 1), 235 (9), 205 (27), 165 (4), 149 (13), 107 (7), 91 (100), 57 (5), 28 (10). Anal. calc. for C<sub>39</sub>H<sub>36</sub>O<sub>6</sub>: C 75.45, H 9.09; found: C 75.26, H 9.36.

 $[G-2]_{3}-[C_c]$  (= Bis {3-[3,5-bis(benzyloxy)benzyloxy]propyl} (2' R,3' S,4' R)-3'-{{3-[3,5-Bis(benzyloxy)benzyloxy]propyloxy}methyl}-5',5'-dimethylhexane-2',4'-diyl Diether; 17). As described for 13, with 5 (100 mg, 0.29 mmol), NaH (61.7 mg, 2.6 mmol, 9 equiv.), and [G-2]-Br 10 (390 mg, 1.1 mmol, 3.5 equiv.), reaction time 40 h. FC (hexanes/Et<sub>2</sub>O 2:1) gave 120 mg (33%) of pure 17. [a]\_{5}^{L} = -1.5 (c = 1.04, CHCl<sub>3</sub>). UV (c = 1 \cdot 10^{-3}, MeCN): 241 (c 4141). IR (CHCl<sub>3</sub>): 2950w, 1596m, 1453m, 1375m, 1293w, 1262w, 1157m, 1097m, 1061w, 1028w. <sup>1</sup>H-NMR (300 MHz): 0.88 (s, t-Bu); 1.16 (d, J = 6.38, 3 H-C(1')); 1.72-1.89 (m, 3 OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O); 2.04-2.10 (m, H-C(3')); 2.95 (d, J = 1.79, H-C(4')); 3.29-3.69 (m, 3 OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OC, H-C(2'); 4.40 (m, 6 benzyl. H); 5.00 (s, 12 benzyl. H); 6.52 (t, J = 2.23, 3 arom. H); 6.58 (d, J = 2.18, 3 arom. H); 6.62 (d, J = 2.31, 3 arom. H); 7.28-7.41 (m, 30 arom. H). <sup>13</sup>C-NMR (75 MHz): 16.35; 26,28; 30.20; 30.57; 30.76; 37.23; 44.56; 65.83; 67.77; 68.56; 68.82; 70.05; 72.84; 73.13; 77.21; 85.76; 101.22; 106.50; 127.54; 127.93; 128.54; 136.96; 141.17; 160.04. FAB-MS: 1257 (<1, M<sup>+</sup>), 907 (<1), 695 (<1), 605 (3), 513 (1), 447 (<1), 393 (2), 304 (13), 303 (49), 181 (12), 91 (100). Anal. calc. for C<sub>81</sub>H<sub>92</sub>O<sub>12</sub>: C 77.36, H 7.37; found: C 77.47, H 7.32.

 $[G-3]_3$ - $[C_c]$  (= Bis {3-{3,5-bis[3,5-bis[benzyloxy]benzyloxy]benzyloxy]propyl} (2' R,3' S,4' R)-3'-{{3-{3,5-Bis[3,5-bis(benzyloxy]benzyloxy]propyloxy}methyl}-5',5'-dimethylhexane-2',4'-diyl Diether; **18**). As described for **13**, with **5** (100 mg, 0.29 mmol), NaH (61.7 mg, 2.6 mmol, 9 equiv.), and [G-3]-Br **12** (890 mg, 1.1 mmol, 3.5 equiv.), reaction time 60 h. FC (CH<sub>2</sub>Cl<sub>2</sub>/CCl<sub>4</sub> 2:1) gave 890 mg (75%) of **18**. A second FC (CH<sub>2</sub>Cl<sub>2</sub>/CCl<sub>4</sub> 2:1) gave a anal. pure sample.  $[\alpha]_{D^4}^{T^4} = -0.2$  (c = 1.60, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3008w, 2926w, 2870m, 1596s, 1498w, 1453m, 1374m, 1343m, 1295m, 1158s, 1057m, 1028m, 835m. <sup>1</sup>H-NMR (300 MHz): 0.87 (s, t-Bu); 1.16 (d, J = 6.37,

3 H–C(1')); 1.74–1.86 (*m*, 3 OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O); 2.04–2.11 (*m*, H–C(3')); 2.94 (br. *s*, H–C(4')); 3.29–3.68 (*m*, 3 OCH<sub>2</sub>CH<sub>2</sub>O, CH<sub>2</sub>–C(3'), H–C(2')); 4.39 (*s*, 6 benzyl. H); 4.90 (*s*, 12 benzyl. H); 4.98 (*s*, 24 benzyl. H); 6.47 (*m*, 3 arom. H); 6.53–6.55 (*m*, 12 arom. H); 6.64 (*m*, 12 arom. H); 7.25–7.40 (*m*, 60 arom. H). <sup>13</sup>C-NMR (75 MHz): 16.38; 26.29; 29.95; 30.15; 30.20; 37.22; 44.50; 65.00; 65.81; 67.85; 68.60; 68.81; 69.93; 70.11; 72.85; 77.21; 85.78; 101.17; 101.60; 106.44; 127.54; 127.97; 128.58; 136.83; 141.20; 159.95; 160.17. FAB-MS: 2531 ( < 1,  $M^+$ ), 2472 ( < 1), 1149 (19), 725 (5), 513 (15), 423 (30), 303 (75), 181 (65), 123 (87), 91 (100). Anal. calc. for C<sub>165</sub>H<sub>164</sub>O<sub>24</sub>: C 78.30, H 6.53; found: C 78.13, H 6.81.

 $[G-1]_{3}$ - $[C_a]$  (= Bis {4-[(benzyloxy)methyl]benzyl} (2' R,3' S,4' R)-3'-{{4- $[(Benzyloxy)methyl]benzyloxy}methyl}-5',5'-dimethylhexane-2',4'-diyl Diether; 19). As described for 13, with 7 (150 mg, 0.28 mmol), NaH (61.7 mg, 2.6 mmol, 9 equiv.), and benzyl bromide (0.30 ml, 2.52 mmol, 9 equiv.), reaction time 30 h. FC (hexanes/Et<sub>2</sub>O 3:1) gave 130 mg (58%) of pure 19. <math>[\alpha]_{5^{1-}}^{L_3} = +12.2$  (c = 1.35, CHCl<sub>3</sub>). 1R (CHCl<sub>3</sub>): 3008m, 286m, 1496w, 1454m, 1362m, 1261m, 1094s, 1020m. <sup>1</sup>H-NMR (300 MHz): 0.94 (s, t-Bu); 1.28 (d, J = 6.43, 3 H–C(1')); 2.25–2.35 (m, H–C(3')); 3.20 (d, J = 1.90, H–C(4')); 3.53–3.59 (m, 1 H, CH<sub>2</sub>–C(3')); 3.71–3.80 (m, 1 H, CH<sub>2</sub>–C(3'), H–C(2')); 4.38–4.64 (m, 18 benzyl: H); 7.19–7.36 (m, 27 arom. H). <sup>13</sup>C-NMR (75 MHz): 166.726.35; 37.42; 44.83; 68.32; 70.60; 71.93; 72.87; 73.67; 76.30; 86.28; 127.02; 127.63; 127.76; 128.40; 136.99; 137.35; 137.41; 138.39; 138.51; 139.06. MS: 807 (16,  $M^+$ ), 749 (36), 701 (6), 643 (23), 595 (47), 487 (8), 431 (7), 397 (11), 367 (41), 339 (20), 313 (51), 261 (46), 211 (43), 157 (5), 119 (10), 105 (75), 91 (100), 77 (9). Anal. calc. for C<sub>54</sub>H<sub>62</sub>O<sub>6</sub>: C 80.36, H 7.74; found: C 80.61, H 7.82.

 $[G-2]_3-[C_a]$  (= Bis {4-{ $[3,5-bis(benzyloxy)benzyloxy]methyl}benzyl}$  (2' R,3' S,4' R)-3'-{{ $\{-\{3,5-bis(benzyloxy)benzyloxy]methyl}benzyl}$ , (2' R,3' S,4' R)-3'-{{ $\{-\{3,5-bis(benzyloxy)benzyloxy]methyl}benzyloxy}methyl}benzyloxy}methyl}-5',5'-dimethylhexane-2',4'-diyl Diether;$ **20**). As described for**13**, with 7 (100 mg, 0.19 mmol), NaH (41 mg, 1.71 mmol, 9 equiv.), and [G-2]-Br**10**(257 mg, 0.67 mmol, 3.5 equiv.). FC (hexanes/Et<sub>2</sub>O 1:1) gave 136 mg (50%) of pure**20** $. A second FC (hexanes/Et<sub>2</sub>O 1:1) gave an anal. pure sample. [<math>\alpha$ ]<sub>1</sub><sup>TL</sup> = +7.0 (c = 1.45, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3008w, 2933w, 2867m, 1596s, 1498w, 1453m, 1376m, 1293m, 1158s, 1094m, 1061m, 1020m, 834w. <sup>1</sup>H-NMR (300 MHz): 0.94 (s, t-Bu); 1.29 (d, J = 6.38, 3 H–C(1')); 2.29–2.35 (m, H–C(3')); 3.21 (d, J = 1.73, H–C(4')); 3.57 (t, AB, J = 9.36, 9.36, 1 H, CH<sub>2</sub>–C(3')); 3.74 (qd, J = 6.42, 3.80, H–C(2')); 3.79 (dd, AB, J = 10.11, 3.44, 1 H, CH<sub>2</sub>–C(3')); 4.38–4.77 (m, 18 benzyl. H); 5.00 (s, AA', 6 benzyl. H); 6.12 (m, 3 arom. H); 6.54 (m, 6 arom. H); 7.19–7.42 (m, 42 arom. H). <sup>13</sup>C-NMR (75 MHz): 16.35; 26.09; 37.16; 44.51; 68.11; 69.79; 70.31; 71.63; 72.60; 73.39; 76.73; 85.91; 101.12; 106.34; 126.73; 127.25; 127.36; 127.49; 128.29; 136.64; 136.96; 137.04; 138.12; 138.24; 138.77; 140.57; 159.80. FAB-MS: 1465 (< 1,  $[M + 23]^+$ ), 1443 (< 1,  $M^+$ ), 1242 (< 1), 1123 (< 1), 845 (< 1), 495 (< 1), 304 (35), 91 (100). Anal. calc. for C<sub>96</sub>H<sub>98</sub>O<sub>12</sub>: C 79.86, H 6.84; found: C 79.57, H 6.90.

 $[G-3]_{5}$ - $[C_a]$  (= Bis {4-{3,5-bis[3,5-bis(benzyloxy)benzyloxy]benzyloxy}methyl}benzyl} (2' R,3' S,4' R)-3'-{{4-{{3,5-Bis[3,5-bis(benzyloxy}benzyloxy}methyl}benzyloxy}methyl}-5',5'-dimethylhexane-2',4'-diyl Diether; **21**). As described for **13**, with 7 (100 mg, 0.19 mmol), NaH (41 mg, 1.71 mmol, 9 equiv.), and [G-3]-Br **12** (542 mg, 0.67 mmol, 3.5 equiv.). The mixture was kept under reflux for 5 days. FC (CH<sub>2</sub>Cl<sub>2</sub>/pentane/Et<sub>2</sub>O 19.5:10:0.5) gave 275 mg (55%) of pure **21**.  $[\alpha]_{D}^{ct} = +3.8$  (c = 1.67, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3008w, 2930w, 2869w, 1596s, 1498w, 1453m, 1374m, 1295m, 1262m, 1158s, 1057m, 1028m, 835w. <sup>1</sup>H-NMR (300 MHz): 0.92 (s, t-Bu); 1.26 (d, J = 6.31, 3 H-C(1')); 2.27-2.35 (m, H-C(3')); 3.19 (d, J = 1.70, H-C(4')); 3.54 (t, AB, J = 9.24, 9.24, 1 H, CH<sub>2</sub>-C(3')); 3.72 (qd, J = 6.48, 3.83, H-C(2')); 3.77 (dd, AB, J = 10.07, 3.24, 1 H, CH<sub>2</sub>-C(3')); 4.35-4.62 (m, 14.99 (s, 12 benzyl. H); 4.93 (s, 12 benzyl. H); 4.93 (s, 12 benzyl. H); 4.95 ( $s, 14.50, 68.41; 69.96; 70.11; 70.57; 71.96; 72.86; 76.18; 86.00; 101.37; 101.62; 106.43; 106.065; 127.02; 127.56; 127.80; 127.99; 128.58; 136.82; 137.25; 137.32; 138.42; 138.55; 139.09; 139.36; 140.88; 160.00; 160.19. FAB-MS: 2717 (<math>< 1, [M + 1]^+$ ), 1778 (< 1), 1122 (< 1), 847 (1), 755 (1), 725 (1), 303 (65), 123 (65), 91 (100). Anal. calc. for C<sub>180</sub>H<sub>170</sub>O<sub>24</sub>: C 79.55, H 6.31; found: C 79.45, H 6.75.

 $[G-1(NH_2)_6]_{3^-}[C]$  (= (2' R.3' S.4' R)-3'-[(3,5-Diaminobenzoyloxy)methyl]-5',5'-diphenylpentane-2',4'-diyl Bis(3,5-diaminobenzoate); **25**). A mixture of **23** (1.2 g, 1.4 mmol) and PtO<sub>2</sub> (aq.) (0.12 g) in dioxane (40 ml) was vigorously stirred under a static H<sub>2</sub> atmosphere at r.t. for 16 h. Filtration and evaporation gave, after drying at 50°/h.v. for 1 h, **25** · 2 dioxane (quant.). M.p. 94–103°. [ $\alpha$ ]<sub>D</sub><sup>1-1</sup> = -69.5 (c = 1.1, acetone). IR (KBr): 3400m, 3320s, 3190w, 2920w, 2810w, 1695s, 1590s, 1460m, 1440m, 1360s, 1230s, 1200s, 1180m, 1105s, 980w, 850m, 830w, 750m, 690w. <sup>1</sup>H-NMR (400 MHz, (D<sub>6</sub>)acetone): 1.37 (d, J = 6.40, 3 + CC(1')); 2.42 (m, H-C(3')); 3.58 (dioxane); 4.44–4.54 (m, 13 H); 4.73 (d, J = 10.60, H-C(5')); 4.82 (dd, J = 11.87, 4.83, 1 H,  $CH_2-C(3')$ ); 5.28 (quint., J = 6.46, H-C(2')); 6.14 (t, J = 2.06, 1 arom. H); 6.20 (t, J = 2.05, 1 arom. H); 6.66 (d, J = 2.12, 1 arom. H); 7.03–7.51 (m, 10 arom. H). <sup>13</sup>C-NMR (100 MHz): 17.88; 46.11; 55.81; 61.91; 67.57 (dioxane); 70.70; 73.61; 105.44; 105.94; 106.03; 127.27; 127.68; 128.97; 129.53; 129.64; 129.71; 132.24; 132.49; 132.64; 148.08;

142.43; 149.87; 150.02; 150.12; 166.82; 166.85; 167.57. MS: 689 (19,  $[M + 1]^+$ ), 688 (21,  $M^+$ ), 391 (4), 306 (9), 288 (8), 284 (4), 268 (7), 266 (8), 167 (20), 165 (18), 155 (23), 154 (68), 153 (22), 152 (32), 150 (10), 149 (20), 137 (47), 136 (72), 135 (100), 90 (39), 76 (47), 65 (21), 55 (33). Anal. calc. for  $C_{39}H_{40}N_6O_6 \cdot 2$  dioxane: C 65.26, H 6.53, N 9.72; found: C 64.81, H 6.59, N 9.64.

 $[G-2(NO_2)_{12}]_{7}$   $[C] (= (2'R,3'S,4'R)-3'-{[3,5-Bis(3,5-dinitrobenzovlamino)benzovloxy]methyl}-5'-methyl$ hexane-2',4'-diyl Bis[3,5-bis(3,5-dinitrobenzoylamino)benzoate]; 26). To an ice-cold soln. of 24 · 2 dioxane (0.91 g, 1.5 mmol) in THF (50 ml) and pyridine (5 ml) was added dropwise a soln. of 3,5-dinitrobenzoyl chloride (3.45 g, 15 mmol) in THF (30 ml;  $\rightarrow$  yellow precipitate). The mixture was stirred vigorously at 0° for 2 h and at r.t. for 18 h, then poured into ice, acidified with 10% HCl soln., and extracted with AcOEt. The combined org. extracts were washed with dil. HCl soln., dried (MgSO<sub>4</sub>), and evaporated. FC (AcOEt) followed by a recrystallization from MeOH/AcOEt gave, after drying at r.t. under h.v. for 12 h, 2 26 AcOEt 8 H<sub>2</sub>O (2.3 g, 83%). M.p. > 250° (dec.).  $[\alpha_{1D}^{r.t.} = 0 (c = 1.05, \text{dioxane}). \text{ IR (KBr): } 3385w, 3100m, 2970w, 1690s, 1610m, 1540s, 1445m, 1345s, 1285m, 1225m, 1225m, 1205m, 1205m$ 1160w, 1110w, 1080w, 920w, 765w, 730m. <sup>1</sup>H-NMR (300 MHz, (D<sub>5</sub>)pyridine): 0.88 (d, J = 6.56, Me-C(5')); 0.99 (d, J = 6.65, Me-C(5')); 1.10 (AcOEt); 1.51 (d, J = 6.41, 3 H-C(1')); 1.96 (AcOEt); 2.20 (m, H-C(5')); 2.59 (m, H-C(5')); 2.5H-C(3'); 4.08 (AcOEt); 4.65 (dd, AB, J = 11.42, 4.99, 1 H,  $CH_2-C(3')$ ); 4.79 (dd, AB, J = 12.01, 5.01, 1 H,  $CH_2-C(3')$ ; 5.07 (H<sub>2</sub>O); 5.44 (dd, J = 7.79, 2.66, H-C(4')); 5.70 (quint., J = 6.01, H-C(2')); 8.47 (d, J = 1.91, 2.66, H-C(4')); 5.70 (quint., J = 6.01, H-C(2')); 8.47 (d, J = 1.91, 2.66, H-C(4')); 5.70 (quint., J = 6.01, H-C(2')); 8.47 (d, J = 1.91, 2.66, H-C(4')); 5.70 (quint., J = 6.01, H-C(2')); 8.47 (d, J = 1.91, 2.66, H-C(4')); 5.70 (quint., J = 6.01, H-C(2')); 8.47 (d, J = 1.91, 2.66, H-C(4')); 5.70 (quint., J = 6.01, H-C(2')); 8.47 (d, J = 1.91, 2.60, H-C(2'arom. H); 8.55 (d, J = 1.90, 2 arom. H); 8.73 (d, J = 1.86, 2 arom. H); 9.06–9.42 (m, 21 arom. H); 12.21 (br. s, 2 NHCO); 12.24 (br. s, 2 NHCO); 12.31 (br. s, 2 NHCO). 13C-NMR (75 MHz): 14.24 (AcOEt); 18.28; 18.77; 19.43; 21.05 (AcOEt); 31.42; 44.75; 60.27 (AcOEt); 62.10; 72.35; 78.81; 118.28; 118.36; 118.67; 118.85; 121.48; 122.55; 122.78; 124.16; 128.60; 128.67; 131.75; 132.04; 132.20; 134.82; 134.90; 136.18; 138.53; 140.16; 140.25; 148.68; 148.97; 149.15; 150.58; 162.85; 162.94; 163.14; 165.12; 165.43; 165.93; 170.25 (AcOEt). MS: 1729 (7, M<sup>+</sup>), 1188 (3), 663 (12), 623 (15), 619 (20), 522 (31), 515 (27), 400 (24), 399 (85), 391 (100), 371 (58), 355 (24). Anal. calc. for 2 C<sub>71</sub>H<sub>48</sub>N<sub>18</sub>O<sub>36</sub> · AcOEt · 8 H<sub>2</sub>O: C 47.49, H 3.27, N 13.66; found: C 47.99, H 3.31, N 13.68.

 $[G-2(NO_2)_{12}]-[C] \quad (= (2'R,3'S,4'R)-3'-\{/3,5-Bis(3,5-dinitrobenzoylamino)benzoyloxy]methyl\}-5',5'-di$ phenylpentane-2',4'-diyl Bis/3,5-bis(3,5-dinitrobenzoylamino)benzoate ]; 27). As described for 26, with 25 · 2 dioxane (0.95 g, 1.1 mmol), pyridine (3 ml), and 3,5-dinitrobenzoyl chloride (2.53 g, 11 mmol) in THF. FC (AcOEt) and recrystallization from MeCN gave an inclusion compound. Drying at 200°/h.v. for 3 h (dec. of the clathrate) gave 1.87 g (92%) of pure 27. M.p. > 230° (dec.).  $[\alpha]_{T^{L}}^{r.t} = -15.2$  (c = 1.20, dioxane). IR (KBr): 3300w, 3060m, 1710m, 1680m, 1530s, 1440m, 1330s, 1210s, 905m, 715m, 705m. <sup>1</sup>H-NMR (400 MHz, (D<sub>6</sub>)acetone): 1.62 (d, J = 6.38, 3H-C(1'); 2.76 (m, H-C(3')); 4.88 (d, J = 11.15, H-C(5')); 5.04 (m,  $CH_2-C(3')$ ); 5.59 (quint., J = 6.16, H-C(2')); 6.55 (dd, J = 11.03, 1.48, H-C(4')); 7.03 (t, J = 7.38, 1 arom. H); 7.17 (t, J = 7.88, 2 arom. H); 7.28 (t, J = 7.33, 1arom. H); 7.40 (t, J = 7.77, 2 arom. H); 7.57 (d, J = 7.23, 2 arom. H); 7.70 (d, J = 7.29, 2 arom. H); 7.95 (d, J = 1.99, 2 arom. H); 7.98 (d, J = 2.01, 2 arom. H); 8.21 (d, J = 1.98, 2 arom. H); 8.51 (d, J = 1.97, 1 arom. H); 8.56 (d, J = 1.98, 1 arom. H); 8.64 (t, J = 1.91, 1 arom. H); 8.99–9.16 (m, 18 arom. H); 10.15 (br. s, 2 NHCO); 10.22 (br. s, 2 NHCO); 10.36 (br. s, NHCO). <sup>13</sup>C-NMR (100 MHz): 19.55; 45.66; 55.91; 61.94; 73.53; 76.57; 116.68; 117.07; 117.96; 118.23; 118.34; 121.95; 122.08; 127.53; 128.10; 128.61; 128.90; 129.17; 129.42; 129.56; 130.05; 131.69; 132.11; 132.16; 138.47; 139.62; 139.81; 139.93; 141.98; 142.04; 149.45; 149.57; 161.98; 162.04; 162.34; 165.20; 165.40; 166.20. MS: 1853 (14, M<sup>+</sup>), 772 (7), 523 (27), 522 (100), 506 (41), 490 (10), 477 (10), 459 (17), 413 (21). Anal. calc. for C<sub>81</sub>H<sub>52</sub>N<sub>18</sub>O<sub>36</sub> · 2 H<sub>2</sub>O: C 51.00, H 2.96, N 13.22; found: C 50.92, H 2.89, N 13.60.

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