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

by **Dieter Seebach***, **Jean-Marc Lapierre**[1]), **Guy Greiveldinger**[2]), and **Konstantinos Skobridis**[3])

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum, Universitätstrasse 16, CH–8092 Zürich

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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_2, or 6 and 12 NO_2 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_2- and NO_2-substituted compounds avidly clathrate smaller molecules; they are sorbents exchanging host molecules through the gas phase.

Introduction. – Starburst dendrimers[4]) 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.

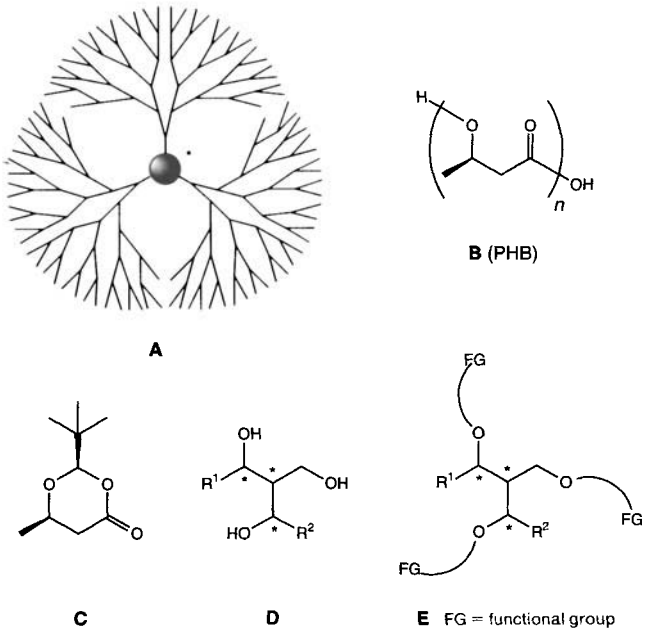
Previously, we have developed [3] an efficient method for the synthesis of chiral triols of type **D** from the dioxanone **C** (which is easily accessible from the biopolymer PHB (**B**) [4]). The triols **D** can be used as central core units themselves, or they can be further

[1]) Postdoctoral research at ETH-Zürich (1991–93), financed by a fellowship from the *Natural Sciences and Engineering Research Council of Canada*. Present address: *Syntex Corp.*, Institute of Bio-organic Chemistry, 3401 Hillview Avenue, Building R6-E3, Palo Alto, CA 94304, USA.

[2]) Part of the Diplomarbeit of *G. G.*, ETH-Zürich, 1993.

[3]) Postdoctoral research at ETH-Zürich 1992/93, financed by the *Deutsche Forschungsgemeinschaft (DFG)*, Bonn. Present address: *Ciba AG*, R-1060.1.28, CH–4002 Basel.

[4]) 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[5][6]). 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.

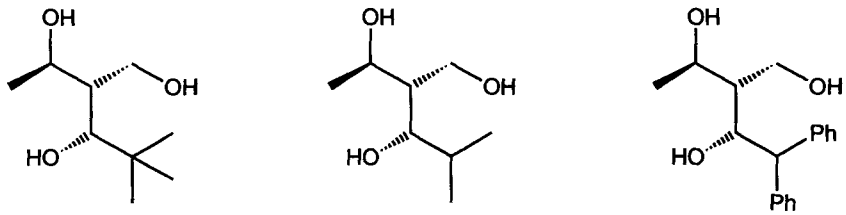
Syntheses of the Dendrimers 13–27. – The center pieces in our dendrimer synthesis are the triols **1**–**3**, prepared as described previously [2] [3]. The choice of **1** as the center piece for nearly all of our work so far was based on the following reasons: *i*) ease of preparation[7]), *ii*) ease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

[5]) 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.

[6]) 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].

[7]) For a one-pot procedure for the preparation of **1** from the dioxanone **C** in 76% yield, see *Exper. Part.*

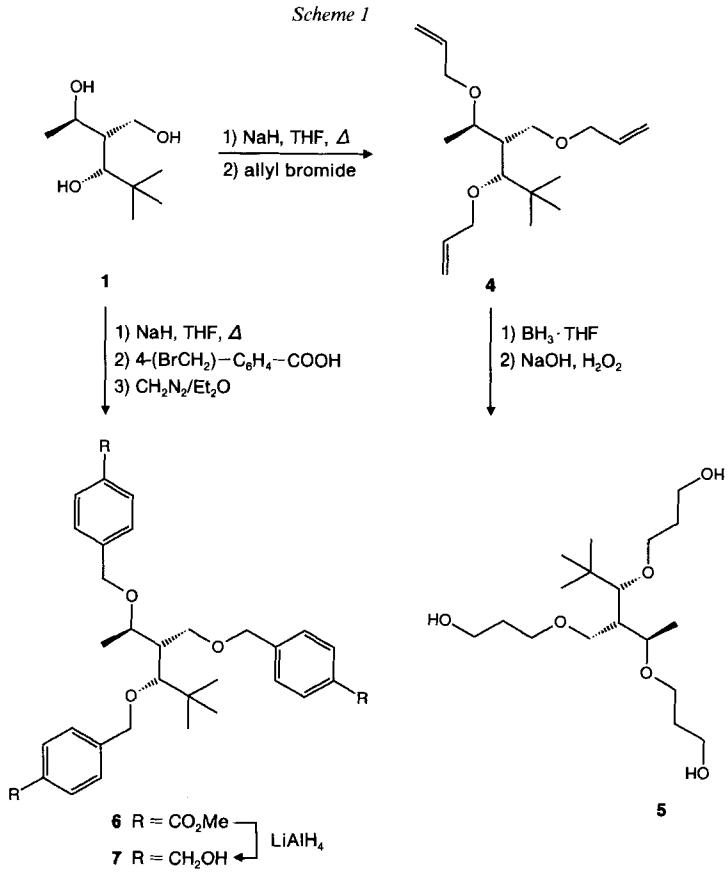
[8]) Weighing and manipulating a solid rather than a viscous oil proved to be especially advantageous, when high accuracy and strict anhydrous conditions were required for the step combining three large branches (mol. wt. up to 808 Da in the present work) to the triol **1** (mol. wt. 174 Da).



^{1}H-NMR spectra[9]). 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

Scheme 1

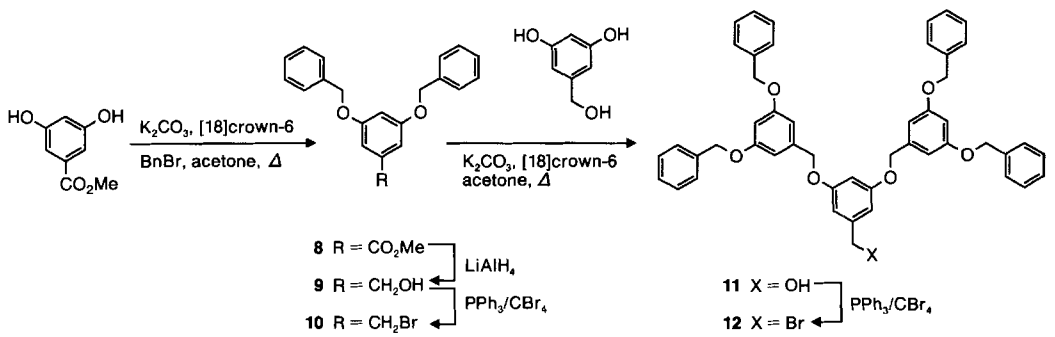


[9]) The ^{1}H-NMR signal of the *t*-Bu group is in the high-field window of most ^{1}H-NMR spectra, it is always a *singlet*; its 9 protons can be used for integration comparison; by-products and products of incomplete conversions can be readily detected.

center pieces with an increased distance between the three functional groups involved in the coupling step[10])[11]). 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

Scheme 2



Exper. Part). Thus, commercial methyl 3,5-dihydroxybenzoate was *O*-benzylated (→**8**), reduced (→**9**), and converted to the benzyl bromide **10**, which, in turn, was used to benzylate the phenolic OH groups of 3,5-dihydroxybenzyl alcohol (→**11**). Treatment of **11** with CBr_4/PPh_3 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** (→**16**–**18**) and **7** (→**19**–**21**) were thus obtained in

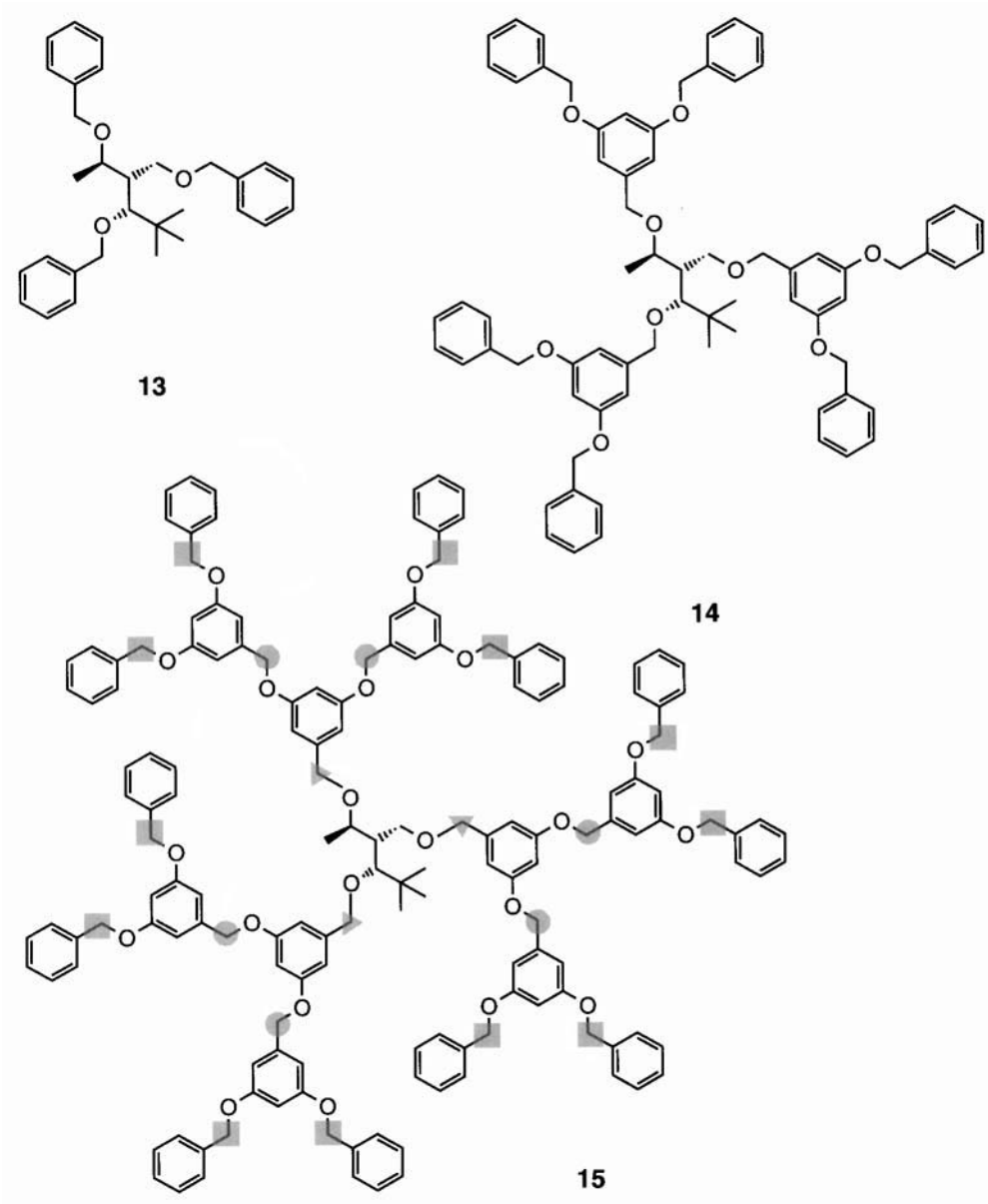
Table 1. *Yields, Optical Activities, Molecular Weights, and Molecular Rotations of Chiral Dendrimers of Generation 1* (**13**, **16**, and **19**), *2* (**14**, **17**, and **20**), *and 3* (**15**, **18**, and **21**). These dendrimers were obtained by benzylation of the triols **1**, **5**, and **7**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

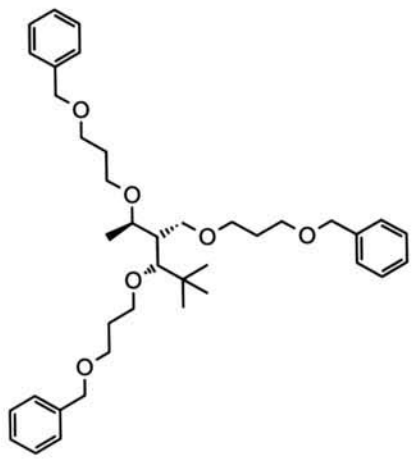
Triol	Benzylbromide	Product	Yield [%]	$[\alpha]_D^{rt.}$ (*c* in $CHCl_3$)	Mol. wt. [Da]	$[\Phi]_D^{rt.}$
1	BnBr	**13**	82	+10.7 (2.7)	447	+48
1	**10**	**14**	93	+4.3 (4.0)	1083	+46
1	**12**	**15**	85	+3.7 (2.5)	2357	+87
5	BnBr	**16**	80	−0.8 (1.1)	620	−5
5	**10**	**17**	33	−1.5 (1.0)	1258	−14
5	**12**	**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

[10]) 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.

[11]) 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 (^{1}H- and ^{13}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.





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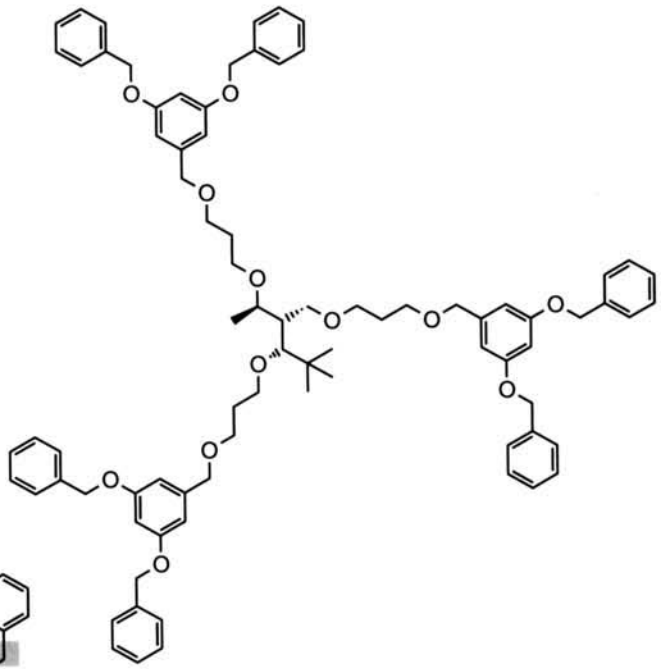

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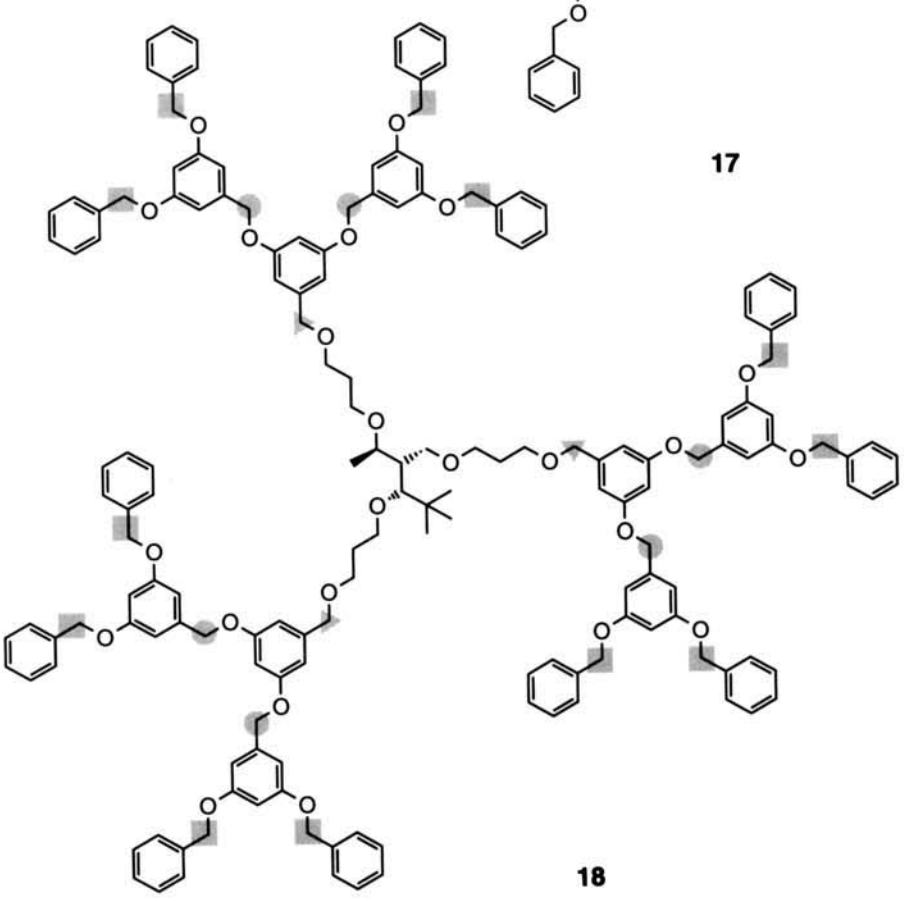

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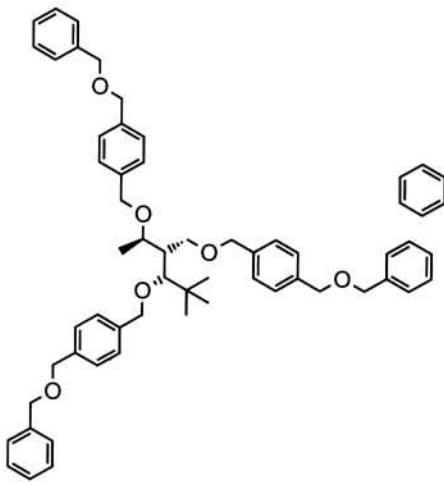

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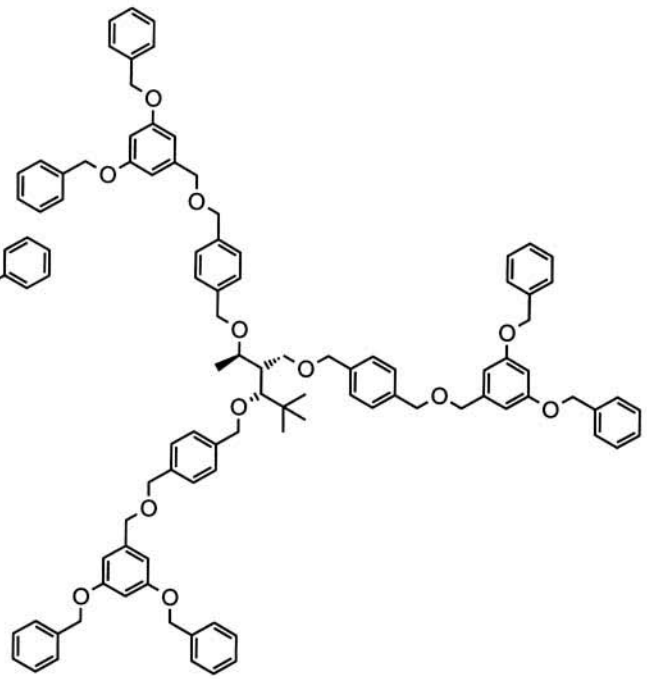

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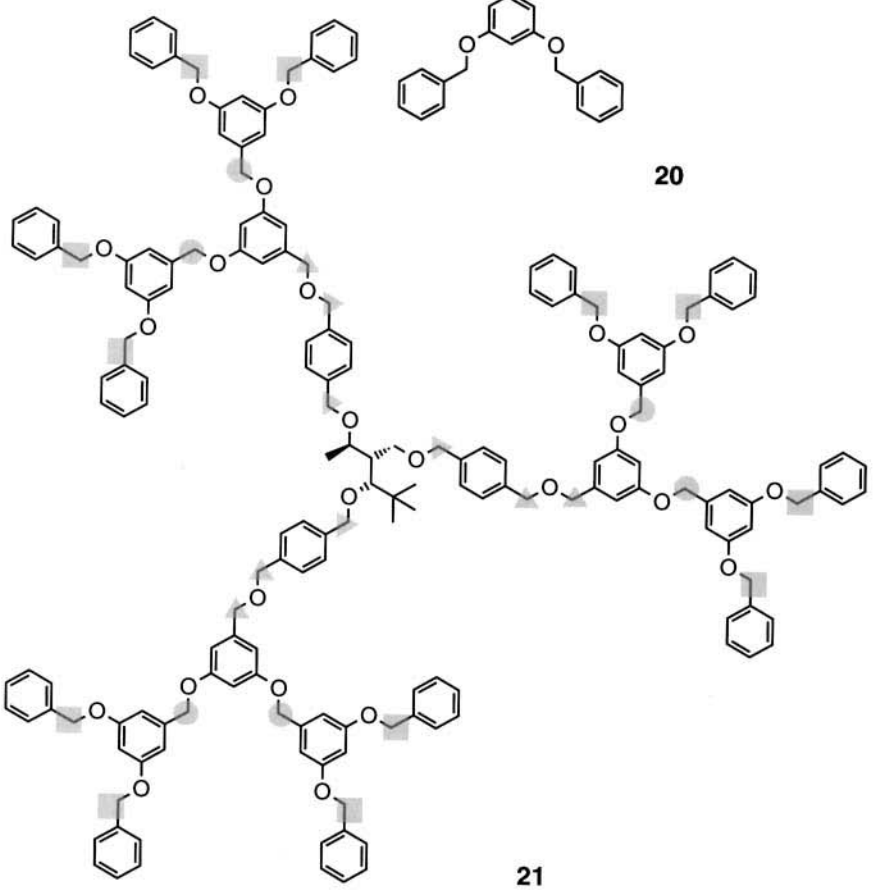

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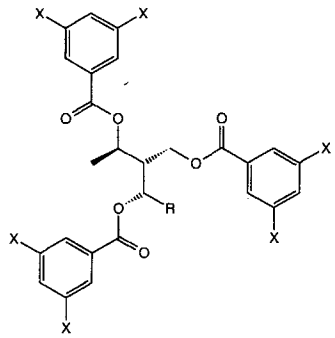
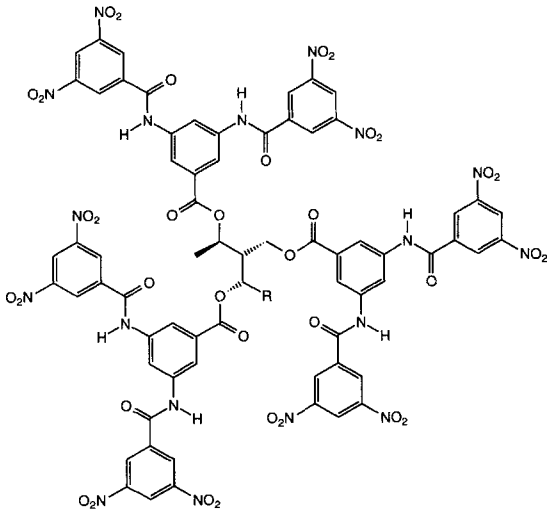


22 R = i-Pr, X = NO_2
23 R = Ph_2CH, X = NO_2
24 R = i-Pr, X = NH_2
25 R = Ph_2CH, X = NH_2



26 R = i-Pr
27 R = Ph_2CH

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[12]) 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_2 groups of triester **23** to NH_2 groups gave the hexaamino derivative **25** with a diphenylmethyl group on the center piece. Acylation of the 6 NH_2 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.)[13]). 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

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[12]) 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].

[13]) Interestingly, the sign of optical rotation reverses on going from the tris(allylic ether) **4** ($[\alpha]_D^{r.t.} = +10.8$) 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_2 groups in the ^1H- and ^{13}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_2 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_2 groups influences the degree of anisochrony of the corresponding H-atoms. This is evident from the 300-MHz ^1H-NMR spectra of the 3rd-generation dendrimers **18**, **21**, and **15** shown in the *Figure*

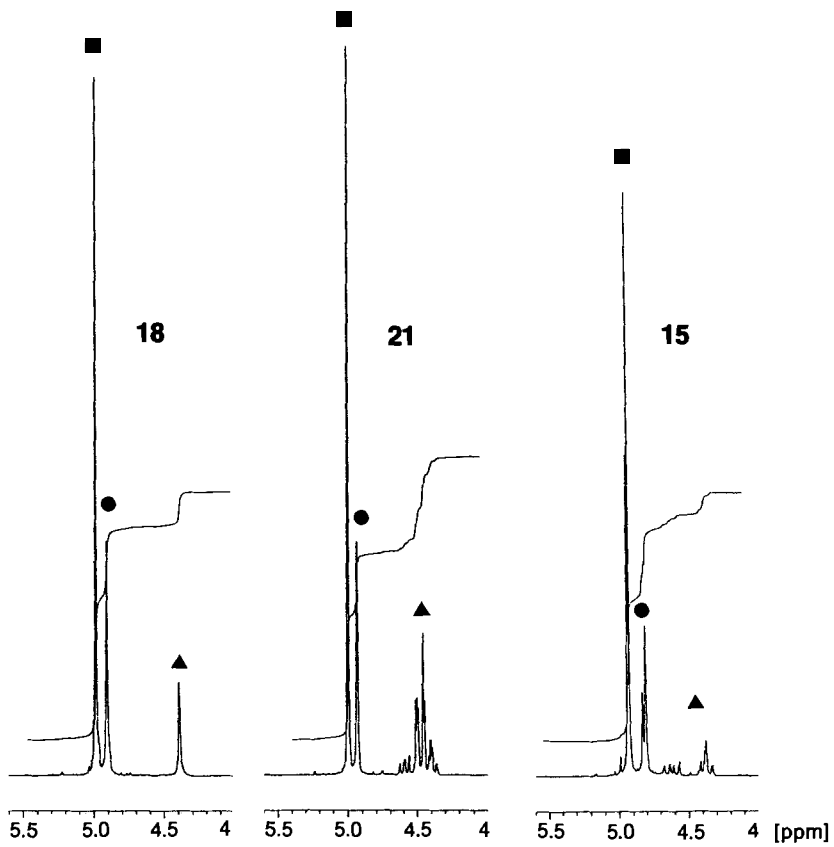

Figure. *Benzylic region of the 300-MHz ^1H-NMR spectra of the 3rd-generation dendrimers* **18**, **21**, *and* **15**. The labelling of signals or groups of signals refers to the sets of CH_2 groups in the corresponding formulae (see text). On going from the 12 outermost (■) to the 6 intermediate (●), and then the 3 (**18**, **15**) or 9 (**21**) innermost (▲) CH_2 groups, the ^1H-NMR signals move upfield and their multiplicity increases.

(benzylic region). There are essentially 3 *singlet*s for the 3 sets of 12, 6, and 3 CH_2 groups in **18**, the dendrimer with a floppy aliphatic spacer group. In the ^{1}H-NMR spectrum of **21**, the dendrimer with aromatic spacers, the outer 12 and the intermediate 6 CH_2 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 *singlet*s for any of the sets of analogous benzylic H-atoms. In the ^{13}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]	$[\Phi]^{r.t.}$
22	i-Pr	NO_2	−16.7 (3.0, acetone)	744	−124
26	i-Pr	NO_2	+9.0 (1.0, dioxane)	1729	+155
23	Ph_2CH	NO_2	−95.3 (2.3, acetone)	868	−827
27	Ph_2CH	NO_2	−15.2 (2.4, dioxane)	1853	−282
24	i-Pr	NH_2	0 (1.7, acetone)	564	0
25	Ph_2CH	NH_2	−69.5 (1.1, acetone)	688	−446

on going from the 1st to the 2nd generation, both with the i-Pr-substituted ($[\Phi]_D^{r.t.}$ from −124 to +155) and the Ph_2CH-substituted ($[\Phi]_D^{r.t.}$ 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_2-substituted dendrimers in a quality suitable for X-ray analysis[14]) to learn details of its structure.

The NO_2- and NH_2-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** · $C_4H_8O_2$] and [**25** · $C_4H_8O_2$], respectively. The dodecanitrodendrimers **26** and **27**, when recrystallized from a mixture of MeOH/AcOEt, also gave inclusion compounds, [2 **26** · AcOEt · 8 H_2O] and [**27** · 2 AcOEt · 2 H_2O], 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_2 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.

We are grateful for postdoctoral fellowships granted to *J.-M. Lapierre* by the *Natural Sciences and Engineering Research Council of Canada* and to *K. Skobridis* by the *Deutsche Forschungsgemeinschaft (DFG)*.

[14]) 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^{-1}. NMR: *Bruker-AMX400*, *Varian-XL-300*, *Bruker-WM-300*, or *Varian-Gemini-200* spectrometer; in $CDCl_3$, unless mentioned otherwise; chemical shifts δ in ppm downfield from internal $SiMe_4$, 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 $(i\text{-Pr})_2NH$ (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°. 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°; 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°. The reaction mixture was maintained at −78° 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_2O (100 ml), and sat. aq. NaCl soln. (20 ml). The org. phase was dried ($MgSO_4$) and evaporated under vacuum and h.v. The residue in Et_2O (80 ml) was added without further purification to a suspension of $LiAlH_4$ (8.83 g, 232.5 mmol, 5 equiv.) in Et_2O (330 ml) at 0°. The mixture was stirred under reflux for 4 h. After cooling to 0° H_2O (8.83 ml), 15% NaOH soln. (8.83 ml), and H_2O (26.5 ml) were added consecutively, and the resulting mixture was stirred vigorously, until a white precipitate was formed. Addition of $MgSO_4$, filtration, and evaporation yielded a colorless liquid. FC (Et_2O), 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′-[(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_2O (100 ml), extracted with Et_2O (3 × 150 ml). The combined org. extract was dried ($MgSO_4$) and evaporated and the crude product distilled ('Kugelrohr' apparatus, 100°/0.1 Torr): 2.99 g (89%) of pure **4**. $[\alpha]_D^{r.t.} = +10.8$ ($c = 1.69$, $CHCl_3$). IR ($CHCl_3$): 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*. ^{1}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(3′)); 3.08 (*d*, $J = 1.93$, H–C(4′)); 3.41 (*dd*, *AB*, $J = 10.16$, 8.83, 1 H, CH_2–C(3′)); 3.60 (*qd*, $J = 6.44$, 3.73, H–C(2′)); 3.66 (*dd*, *AB*, $J = 10.16$, 3.66, 1 H, CH_2–C(3′)); 3.87–4.15 (*m*, 3 CH_2=CHCH_2); 5.05–5.29 (*m*, 3 CH_2=CHCH_2); 5.81–5.97 (*m*, 3 CH_2=C*H*CH_2). ^{13}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, $[M + 1]^+$), 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 $C_{18}H_{32}O_3$: 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_3·THF (5.1 ml, 5.1 mmol). The mixture was kept at r.t. for 1 h (TLC monitoring (hexanes/Et_2O 10:1)), then H_2O (6.2 ml) added, followed by 15% NaOH soln. (8.1 ml) in one portion and 30% H_2O_2 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_2O (200 ml) and H_2O (100 ml), the aq. phase saturated with NaCl and extracted with Et_2O (2 × 100 ml), and the combined org. extract dried ($MgSO_4$) and evaporated. FC (Et_2O/MeOH 19:1) gave 0.931 (33%) of pure **5**. $[\alpha]_D^{r.t.} = -14.2$ ($c = 1.13$, $CHCl_3$). IR ($CHCl_3$): 3437*m*, 3007*m*, 2956*s*, 2870*m*, 1478*m*, 1425*m*, 1365*m*, 1262*m*, 1070*s*, 1009*m*. ^{1}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 $CH_2CH_2CH_2OH$); 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 $CH_2CH_2CH_2OH$, CH_2–C(3″)); 3.67–3.81 (*m*, 3 $CH_2CH_2CH_2OH$); 3.83–3.92 (*m*, H–C(2″)). ^{13}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, $[M + 1]^+$), 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 $C_{18}H_{38}O_6$: C 61.68, H 10.93; found: C 61.56, H 11.22.

Dimethyl 4,4′-{{(2″R,3″S,4″R)-3″-{[4-(Methoxycarbonyl)phenyl]methoxymethyl}-5″,5″-dimethylhexane-2″,4″-diyl}bis(oxymethylene)}bis(benzoate) (**6**). To NaH (1.77 g, 74 mmol, 13 equiv.) in THF (35 ml) was added **1** (1.0 g, 5.7 mmol) in THF (25 ml) and the mixture stirred under reflux for 30 min. After addition of 4-(bromo-

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_2O (20 ml) and 10% HCl soln. (*ca.* 20 ml; until pH 1–2). Then Et_2O (100 ml) was added, the aq. phase extracted with Et_2O (2×), the combined org. extract dried ($MgSO_4$) and evaporated, and the residue dissolved in Et_2O (100 ml) and treated with diazomethane/Et_2O until the yellow color persisted. The mixture was stirred for 1 h and then carefully evaporated. FC (hexane/Et_2O 1:1) gave 1.98 g (56%) of pure **6**. $[\alpha]_D^{r.t.} = +18.9$ (*c* = 2.13, $CHCl_3$). IR ($CHCl_3$): 3539*w*, 3008*w*, 2955*m*, 2869*w*, 1718*s*, 1614*m*, 1577*w*, 1437*m*, 1416*w*, 1364*w*, 1283*s*, 1176*m*, 1105*s*, 1020*m*, 968*w*. ^{1}H-NMR (300 MHz): 0.96 (*s*, *t*-Bu); 1.30 (*d*, *J* = 6.40, 3 H–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, 8.27, 1 H, CH_2–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_2–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). ^{13}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^+), 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 $C_{36}H_{44}O_9$: C 69.66, H 7.14; found: C 69.84, H 7.15.

4,4′-{{(2″R,3″S,4″R)-3″-{[4-(Hydroxymethyl)phenyl]methoxymethyl}-5″,5″-dimethylhexane-2″,4″-diyl}bis(oxymethylene)}bis(benzenemethanol) (**7**). To a suspension of $LiAlH_4$ (0.70 g, 18 mmol) in Et_2O (15 ml) was added **6** (1.98 g, 3.19 mmol) in Et_2O (20 ml). The mixture was stirred under reflux for 5 h, then cooled to 0°, and quenched by the successive addition of H_2O (0.7 ml), 15% NaOH soln. (0.7 ml), and H_2O (2.1 ml) under vigorously stirring. The solid formed was removed and the filtrate dried ($MgSO_4$) and evaporated: colorless oil. FC (Et_2O/MeOH 19:1) gave 1.37 g (83%) of pure **7**. $[\alpha]_D^{r.t.} = +19.2$ (*c* = 1.43, $CHCl_3$). IR ($CHCl_3$): 3602*w*, 3392*w* (br.), 3053*w*, 3007*m*, 2956*m*, 2873*m*, 1514*w*, 1467*w*, 1421*w*, 1380*m*, 1364*m*, 1262*w*, 1098*s*, 1017*m*. ^{1}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″)); 3.54 (*dd*, *AB*, *J* = 10.00, 8.42, 1 H, CH_2–C(3″)); 3.70 (*qd*, *J* = 6.45, 3.84, H–C(2″)); 3.73 (*dd*, *AB*, *J* = 10.03, 3.59, 1 H, CH_2–C(3″)); 4.35–4.60 (*m*, 6 H); 4.63 (*s*, 6 H); 7.13–7.35 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz): 16.70; 26.35; 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 $C_{33}H_{44}O_6$: 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_c] = center piece **5**, with aliphatic spacer (c = chain); [C_a] = 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_2O (20 ml) and the mixture extracted with Et_2O (3 × 50 ml). The combined org. extracts were dried ($MgSO_4$) and evaporated. FC (hexane/Et_2O 19:1) followed by a short-path distillation gave 1.23 g (82%) of pure **13**. Colorless liquid. B.p. 250°/0.1 Torr. $[\alpha]_D^{r.t.} = +10.7$ (*c* = 2.66, $CHCl_3$). IR (neat): 3090*w*, 3065*m*, 2960*s*, 2870*s*, 1605*w*, 1495*m*, 1455*s*, 1360*m*, 1305*w*, 1245*w*, 1205*w*, 1100*s*, 1030*m*. ^{1}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_2–C(3′)); 3.72 (*qd*, *J* = 6.51, 3.80, H–C(2′)); 3.79 (*dd*, *AB*, *J* = 10.13, 3.58, 1 H, CH_2–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). ^{13}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, $[M + 1]^+$), 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 $C_{30}H_{38}O_3$: 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_2O 4:1) gave 2.86 (93%) of pure **14**. $[\alpha]_D^{r.t.} = +4.3$ ($c = 4.01$, $CHCl_3$). IR ($CHCl_3$): 3065*w*, 3010*m*, 2960*m*, 2870*m*, 1595*s*, 1500*m*, 1455*s*, 1375*s*, 1340*m*, 1290*m*, 1155*s*, 1100*m*, 1055*s*. ^{1}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_2–C(3′)); 3.71 (*qd*, $J = 6.46, 3.91$, H–C(2′)); 3.80 (*dd*, *AB*, $J = 10.01$, 3.61, 1 H, CH_2–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). ^{13}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 $C_{72}H_{74}O_9$: 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}methyl}-5′,5′-dimethylhexane-2′,4′-diyl Diether*; **15**). As described for **13**, with **1** (100 mg, 0.57 mmol) NaH (122 mg, 5.1 mmol, 9 equiv.), and [G-3]-Br **12** (1.60 g, 1.99 mmol, 3.5 equiv.). FC (CCl_4/CH_2Cl_2 1:2) gave 1.14 g (85%) of **15** as a fluffy white solid. Careful removal of the volatiles under h.v. gave material with a wrong elemental analysis (probably a host-quest complex of **15** with CCl_4), but by heating it at 120° in a 'Kugelrohr' apparatus for 48 h, a glassy solid with correct elemental analysis was obtained. $[\alpha]_D^{r.t.} = +3.7$ ($c = 2.54$, $CHCl_3$). IR ($CHCl_3$): 3065*w*, 3010*w*, 2875*w*, 1595*s*, 1500*w*, 1455*s*, 1375*s*, 1345*m*, 1295*m*, 1155*s*, 1055*s*. ^{1}H-NMR (300 MHz): 0.95 (*s*, *t*-Bu); 1.31 (*d*, $J = 6.34$, Me); 2.28 (*m*, 1 H); 3.17 (*d*, $J = 1.80$, H–C(4′)); 3.65 (*m*, 1 H, CH_2–C(3′)); 3.74 (*m*, H–C(2′)); 3.82 (*dd*, *AB*, $J = 10.12$, 3.58, 1 H, CH_2–C(3′)); 4.30–4.45 (*m*, 4 benzyl. H); 4.55 (*m*, 2 benzyl. H); 4.70 (*m*, 12 benzyl. H); 4.95 (*m*, 24 benzyl. H); 6.45–6.65 (*m*, 24 arom. H); 7.2–7.4 (*m*, 63 arom. H). ^{13}C-NMR (75 MHz): 16.96, 26.41; 37.39; 45.20; 68.40; 69.85; 70.05; 70.90; 73.03; 73.78; 76.86; 77.23; 86.73; 100.87; 101.25; 101.59; 105.74; 106.14; 106.43; 106.56; 127.57; 127.80; 127.96; 128.12; 128.55; 136.84; 139.33; 139.43; 141.54; 142.14; 159.76; 159.90; 160.14. FAB-MS: 2357 (6, $[M + 1]^+$), 2356 (9, M^+), 1451 (5), 1361 (5), 1149 (11), 1058 (11), 1028 (14), 968 (10), 937 (25), 847 (27), 815 (32), 725 (100), 709 (10). Anal. calc. for $C_{156}H_{146}O_{21}$: C 79.50, H 6.24; found: C 79.51, H 6.12.

[G-1]$_3$-[C$_c$] (= *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_2O 3:1) gave 142 mg (80%) of pure **16**. $[\alpha]_D^{r.t.} = -0.8$ ($c = 1.12$, $CHCl_3$). UV ($c = 1 \cdot 10^{-3}$, MeCN): 216 (ε 2868). IR ($CHCl_3$): 3005*w*, 2955*m*, 2867*m*, 1496*w*, 1454*m*, 1364*m*, 1262*m*, 1096*s*, 1027*m*. ^{1}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 $OCH_2CH_2CH_2O$); 2.05–2.09 (*m*, H–C(3′)); 2.95 (*d*, $J = 1.95$, H–C(4′)); 3.25–3.65 (*m*, 3 $OCH_2CH_2CH_2O$, CH_2–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). ^{13}C-NMR (75 MHz): 16.28; 26.25; 30.23; 30.59; 30.78; 37.20; 44.57; 65.78; 67.65; 67.81; 68.56; 68.82; 72.97; 76.59; 85.75; 127.48; 127.61; 128.34; 138.64. MS: 620 (< 1, M^+), 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 $C_{39}H_{56}O_6$: 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_2O 2:1) gave 120 mg (33%) of pure **17**. $[\alpha]_D^{r.t.} = -1.5$ ($c = 1.04$, $CHCl_3$). UV ($c = 1 \cdot 10^{-3}$, MeCN): 241 (ε 4141). IR ($CHCl_3$): 2950*w*, 1596*m*, 1453*m*, 1375*m*, 1293*w*, 1262*w*, 1157*m*, 1097*m*, 1061*w*, 1028*w*. ^{1}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 $OCH_2CH_2CH_2O$); 2.04–2.10 (*m*, H–C(3′)); 2.95 (*d*, $J = 1.79$, H–C(4′)); 3.29–3.69 (*m*, 3 $OCH_2CH_2CH_2O$, CH_2–C(3′), 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). ^{13}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^+), 907 (< 1), 695 (< 1), 605 (3), 513 (1), 447 (< 1), 393 (2), 304 (13), 303 (49), 181 (12), 91 (100). Anal. calc. for $C_{81}H_{92}O_{12}$: 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]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_2Cl_2/CCl_4 2:1) gave 890 mg (75%) of **18**. A second FC (CH_2Cl_2/CCl_4 2:1) gave a anal. pure sample. $[\alpha]_D^{r.t.} = -0.2$ ($c = 1.60$, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2926*w*, 2870*m*, 1596*s*, 1498*w*, 1453*m*, 1374*m*, 1343*m*, 1295*m*, 1158*s*, 1057*m*, 1028*m*, 835*m*. ^{1}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 $OCH_2CH_2CH_2O$); 2.04–2.11 (*m*, H–C(3')); 2.94 (br. *s*, H–C(4')); 3.29–3.68 (*m*, 3 $OCH_2CH_2CH_2O$, CH_2–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). ^{13}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 $C_{165}H_{164}O_{24}$: 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_2O 3:1) gave 130 mg (58%) of pure **19**. $[\alpha]_D^{r.t.}$ = +12.2 (*c* = 1.35, $CHCl_3$). IR ($CHCl_3$): 3008*m*, 2860*m*, 1496*w*, 1454*m*, 1362*m*, 1261*m*, 1094*s*, 1020*m*. ^{1}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_2–C(3')); 3.71–3.80 (*m*, 1 H, CH_2–C(3'), H–C(2')); 4.38–4.64 (*m*, 18 benzyl. H); 7.19–7.36 (*m*, 27 arom. H). ^{13}C-NMR (75 MHz): 16.67; 26.35; 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 $C_{54}H_{62}O_6$: 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'-{{4-{[3,5-Bis(benzyloxy)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_2O 1:1) gave 136 mg (50%) of pure **20**. A second FC (hexanes/Et_2O 1:1) gave an anal. pure sample. $[\alpha]_D^{r.t.}$ = +7.0 (*c* = 1.45, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2933*w*, 2867*m*, 1596*s*, 1498*w*, 1453*m*, 1376*m*, 1293*m*, 1158*s*, 1094*m*, 1061*m*, 1020*m*, 834*w*. ^{1}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_2–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_2–C(3')); 4.38–4.77 (*m*, 18 benzyl. H); 5.00 (*s*, *AA'*, 6 benzyl. H); 5.01 (*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). ^{13}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 $C_{96}H_{98}O_{12}$: C 79.86, H 6.84; found: C 79.57, H 6.90.

[G-3]$_3$-[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]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_2Cl_2/pentane/Et_2O 19.5:10:0.5) gave 275 mg (55%) of pure **21**. $[\alpha]_D^{r.t.}$ = +3.8 (*c* = 1.67, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2930*w*, 2869*w*, 1596*s*, 1498*w*, 1453*m*, 1374*m*, 1295*m*, 1262*m*, 1158*s*, 1057*m*, 1028*m*, 835*w*. ^{1}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_2–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_2–C(3')); 4.35–4.62 (*m*, 18 benzyl. H); 4.93 (*s*, 12 benzyl. H); 4.99 (*s*, 24 benzyl. H); 6.51–6.66 (*m*, 27 arom. H); 7.18–7.64 (*m*, 72 arom. H). ^{13}C-NMR (75 MHz): 16.60; 26.38; 37.45; 44.50; 68.41; 69.96; 70.11; 70.57; 71.96; 72.86; 76.18; 86.00; 101.37; 101.62; 106.43; 106.65; 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 (< 1, $[M + 1]^+$), 1778 (< 1), 1227 (< 1), 1132 (< 1), 847 (1), 755 (1), 725 (1), 303 (65), 123 (65), 91 (100). Anal. calc. for $C_{180}H_{170}O_{24}$: 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_2 (aq.) (0.12 g) in dioxane (40 ml) was vigorously stirred under a static H_2 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°. $[\alpha]_D^{r.t.}$ = –69.5 (*c* = 1.1, acetone). IR (KBr): 3400*m*, 3320*s*, 3190*w*, 2920*w*, 2810*w*, 1695*s*, 1590*s*, 1460*m*, 1440*m*, 1360*s*, 1230*s*, 1200*s*, 1180*m*, 1105*s*, 980*w*, 850*m*, 830*w*, 750*m*, 690*w*. ^{1}H-NMR (400 MHz, (D_6)acetone): 1.37 (*d*, *J* = 6.40, 3 H–C(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* = 2.07, 1 arom. H); 6.22 (*t*, *J* = 2.06, 1 arom. H); 6.38 (*dd*, *J* = 10.60, 2.03, H–C(4')); 6.48 (*d*, *J* = 2.04, 1 arom. H); 6.65 (*d*, *J* = 2.05, 1 arom. H); 6.66 (*d*, *J* = 2.12, 1 arom. H); 7.03–7.51 (*m*, 10 arom. H). ^{13}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$_2$)$_{12}$]$_3$-[C] (= *(2′R,3′S,4′R)-3′-{[3,5-Bis(3,5-dinitrobenzoylamino)benzoyloxy]methyl}-5′-methylhexane-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; →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 ($MgSO_4$), 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_2O (2.3 g, 83%). M.p. > 250° (dec.). $[\alpha]_D^{r.t.} = 0$ ($c = 1.05$, dioxane). IR (KBr): 3385*w*, 3100*m*, 2970*w*, 1690*s*, 1610*m*, 1540*s*, 1445*m*, 1345*s*, 1285*m*, 1225*m*, 1160*w*, 1110*w*, 1080*w*, 920*w*, 765*w*, 730*m*. ^{1}H-NMR (300 MHz, (D_5)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(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_2O); 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 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). ^{13}C-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^+), 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 $C_{71}H_{48}N_{18}O_{36}$ · AcOEt · 8 H_2O: 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] (= *(2′R,3′S,4′R)-3′-{[3,5-Bis(3,5-dinitrobenzoylamino)benzoyloxy]methyl}-5′,5′-diphenylpentane-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.). $[\alpha]_D^{r.t.} = -15.2$ ($c = 1.20$, dioxane). IR (KBr): 3300*w*, 3060*m*, 1710*m*, 1680*m*, 1530*s*, 1440*m*, 1330*s*, 1210*s*, 905*m*, 715*m*, 705*m*. ^{1}H-NMR (400 MHz, (D_6)acetone): 1.62 (*d*, $J = 6.38$, 3 H–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*, $J = 7.33$, 1 arom. 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). ^{13}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^+), 772 (7), 523 (27), 522 (100), 506 (41), 490 (10), 477 (10), 459 (17), 413 (21). Anal. calc. for $C_{81}H_{52}N_{18}O_{36} \cdot 2$ H_2O: C 51.00, H 2.96, N 13.22; found: C 50.92, H 2.89, N 13.60.

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