New Calix[4]arene-Cored Peripherally Functionalized Dendrimers: Synthesis and Conformational Characteristics

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New calixarene-based dendrimers, containing calix[4]arene as the core and different generations of *Fréchet*-type poly(benzyl ether) dendrons as building blocks, which possess either Br-atoms or COO^{t}Bu groups at their surface were synthesized and presented herein for the first time. The new calix[4]arene-cored dendritic macromolecules were fully characterized and found to prefer strictly the cone conformation.

Introduction. – Since their discovery [1], dendrimers have attracted great attention as a new line of molecular structures opening numerous innovating and promising applications. Excellent reviews and book chapters, over the past decade, describe and analyze the use of dendrimers in chemical applications, as well as, in the interface of chemistry and biology [2]. Dendritic architectures can be formed following the divergent and/or the convergent approach. The class of poly(benzyl ether) dendrimers, which was presented for the first time by *Hawker* and *Fréchet* [3], is a prototype of the convergent synthetic approach and can be used for the formation of dendritic shells. The ability of peripheral modifications allows particular architectures to be optimized in different ways and the final macromolecules to possess lipophilic, hydrophilic or amphiphilic characteristics. The attachment of these dendrons to different cores opened the way for expanding their applications [4]. Moreover, the combination of dendritic molecules and other macromolecular structures as building blocks, such as macrocyclic compounds, is considered as an attractive approach to the study of host–guest chemistry [5]. These observations indicate that mono- or poly-functionalization of dendrimers with active moieties and/or functional groups can occur either to the core, the branching units, the periphery or as a combination of these.

In previous publications, we reported the synthesis and the specific cation-binding properties of poly(benzyl ether) dendritic molecules combined with crown-ether moieties as the core [6]. Depending on the dendrimer generation, positive and negative 'dendritic effects' have been assigned to the complexation behavior of the crown ether-functionalized dendrimers [7].

In view of these results, and as part of our efforts on the design and synthesis of functional dendrimers, we offer an extension of the concept by conjugating one of the most versatile molecular building blocks, the calix[4]arene active core moiety. Calixarenes are well-defined macrocycles, containing a preorganized cavity with a

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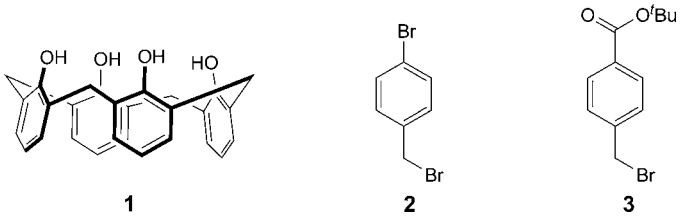
variety of conformations, as a consequence of the flexibility around the Ar–CH_2–Ar groups, useful in host–guest chemistry and with potentially unlimited applications [8]. In calixarene-based dendrimers reported so far, calixarenes have been used as the core in conjugation with dendritic branches or as the branching units in dendritic structures [9]. Furthermore, the use of calixarenes as core, branching unit and surface in the same dendritic structure has been reported [10]. To the best of our knowledge, the previously reported calixarene-cored dendrimers functionalized with poly(benzyl ether) dendritic branches possess *p-tert*-butylcalix[4]arene as core [11].

Results and Discussion. – In our approach, we used the de-alkylated derivative, calix[4]arene **1**, and the dendritic branches were functionalized with Br-atoms or COO^tBu groups at their periphery by using 4-bromobenzyl bromide (**2**) and *tert*-butyl 4-(bromomethyl)benzoate (**3**), respectively, as starting compounds (*Fig. 1*). The peripheral modification with Br-atoms provides the final molecules with increased lipophilicity. On the other hand, COO^tBu groups are potential providers of hydrophilic characteristics, due to their ease transformation to carboxylates when they are treated with acids. In addition, they provide ideal cascade through the synthetic route as they are extremely stable in basic conditions in contrast with other ester groups.

The required calix[4]arene was prepared by transforming *p-tert*-butylcalix[4]arene according to literature procedures [12]. The starting compound *tert*-butyl 4-(bromomethyl)benzoate (**3**) was synthesized by the reaction of 4-(bromomethyl)benzoic acid in the presence of AcO^tBu and $HClO_4$. The preparation of the poly(benzyl ether) branches until the third generation was achieved according to *Fréchet*'s procedures [13], except that the purification steps were modified, using 3,5-dihydroxybenzyl alcohol for the generation growth while the periphery modifications (dendritic substituents) were Br-atoms and COO^tBu (*Scheme 1*).

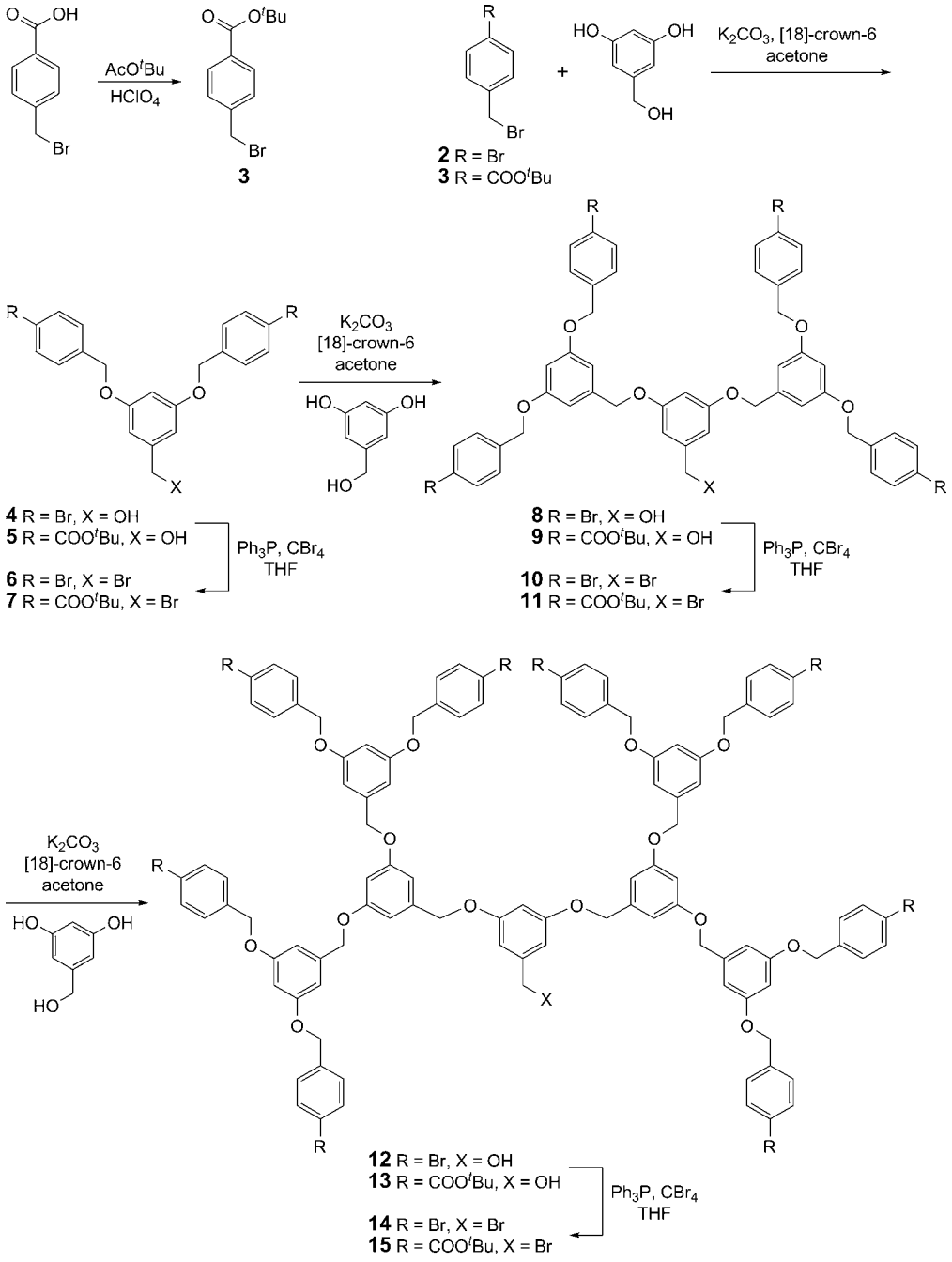
Following the convergent procedure, the calix[4]arene-cored dendrimers have been prepared by conjugating calix[4]arene and dendritic wedges up to the third generation with the aforementioned functionalities at their periphery. For the synthesis of calix[4]arene dendrimers, different reaction conditions (solvent, base, temperature) were tested. Initially, based on phase-transfer reaction conditions bromide branches reacted with calix[4]arene in acetone with K_2CO_3 as base in the presence of 18-crown-6 as catalyst. Under these conditions, calix[4]arene reacted smoothly only with zero generation bromide branches (R–G0–CH_2Br), **2**, and **3**, under *Williamson* etherification conditions to give the desired dendrimers **16** and **17** by tetra-etherification of the four OH groups at the lower rim, while the 1st-, 2nd-, and 3rd-generation dendritic



1 **2** **3**

Fig. 1. *Structures of calix[4]arene* **1** *and the starting compounds* **2** *and* **3** *used for periphery modifications*

Scheme 1. *Syntheses of Peripherally Functionalized* Fréchet*-Type Poly(benzyl ether) Dendrons*

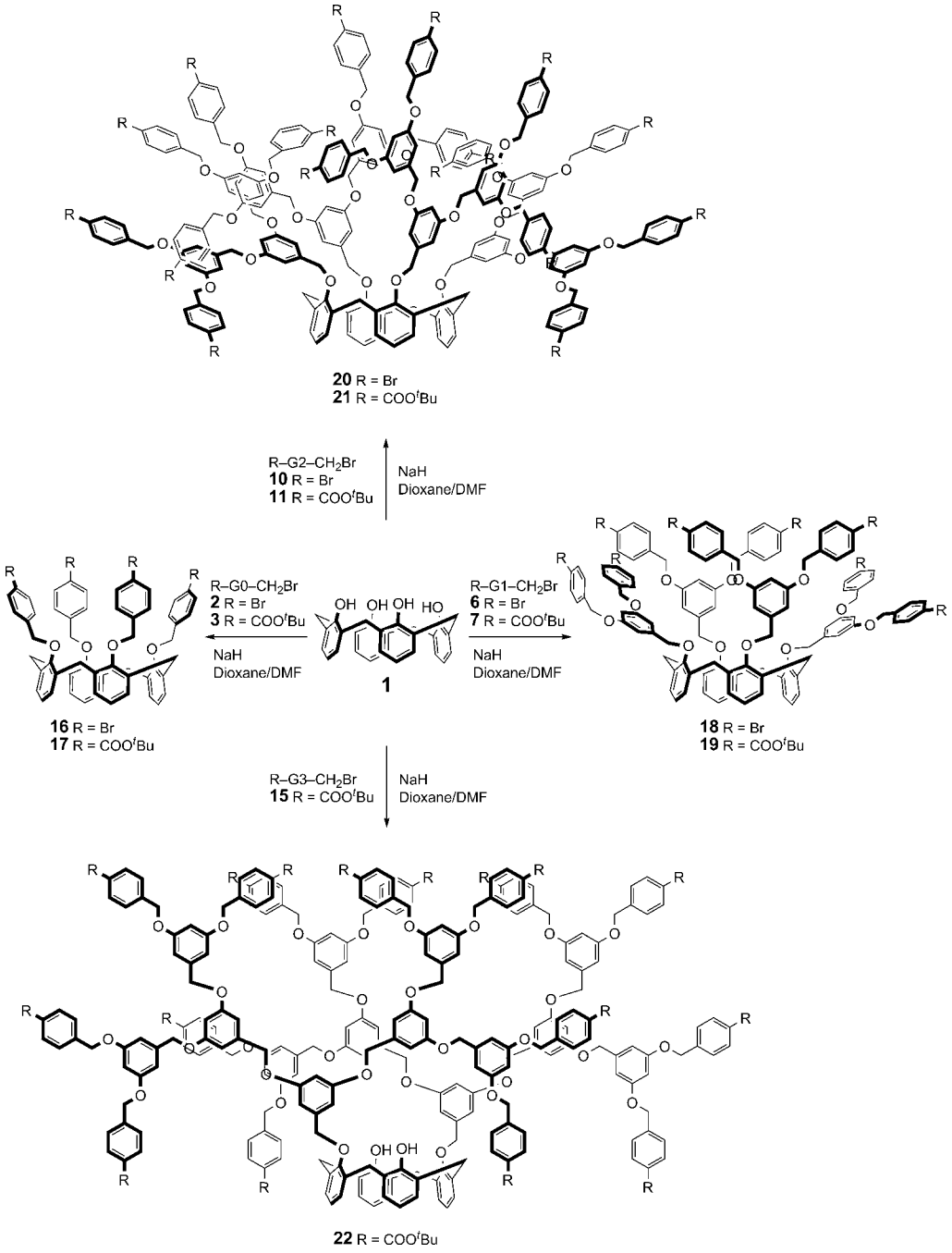


wedges did not afford the tetra-etherificated calix[4]arene dendrimers. When THF or dioxane or mixture of them were used as solvent, with NaH as base, the reaction was unsuccessful, even under most forcing conditions (several days of reflux). Finally, to our surprise when a mixture of dioxane/DMF as solvent and NaH as base were used, progress of the reactions resulted in a remarkable change, *i.e.*, the calix[4]arene with 1st-generation branch bromide afforded the fully conjugated lower rim calix[4]arene-cored dendrimers **18** and **19**. With the optimized reaction conditions in hand, the synthesis of calix[4]arene dendrimers was implemented from the 1st-, to the 2nd- and 3rd-generation bromide branches. The reactions of calix[4]arene with dendrons of zero, first, and second generation afforded the fully tetra-etherificated calix[4]arene dendrimers (*Scheme 2*) in relatively good yields, ranging between 60–70% (for **16** and **17**), 57–62% (for **18** and **19**), and 25–30% (for **20** and **21**). On the other hand, the reactions of calix[4]arene with the third generation dendrons did not give similar results. In more detail, the third generation dendrons, modified at their periphery with COO^{t}Bu groups, afforded only two-fold substitution (compound **22**) in low yield (7%), while the third generation dendrons modified with Br-atoms under the same conditions afforded a mixture of products which were difficult to separate. As these findings are concerned, we believe that periphery modifications, as well as different reaction conditions (base, solvent medium) are very important and play a critical role on the incomplete etherification of the calixarene-core moiety.

Considering the above mentioned, we believe that the conjugation of dendrons to the calixarenic core may proceed through different mechanisms each time, S_N1 and/or S_N2, depending on the reaction conditions. Note that the use of THF or dioxane alone or as a mixture did not afford the desired products. In fact, the higher polarity of DMF as solvent influences the kinetics of the etherification reactions. The progress of all reactions was monitored by thin-layer chromatography, and the crude reaction products were purified by flash chromatography on SiO_2. All final compounds are white solids and soluble in most organic solvents. They were characterized by means of ^{1}H- and ^{13}C-NMR spectroscopy as well as by mass spectroscopy (ESI, MALDI-TOF).

In the ^{1}H-NMR spectra of the final products, characteristic peaks of both calix[4]arene functionalities and dendrons, could be easily identified. The signals in all the ^{1}H-NMR spectra of the calix[4]arene-fuctionalized dendrimers could be grouped into three regions: the first region included signals with chemical shifts between δ(H) 6.30 and 8.00 ppm, which were due to the aromatic H-atoms of the molecules. In this region, two *doublet*s of the *para*-substituted terminal aromatic rings as well as the absorption of the aromatic H-atoms of the calixarenic core were always observed. The second region showed peaks with chemical shifts between δ(H) 4.60 and 5.10 ppm, which were due to the benzylic H-atoms of the branches. The third region included signals with chemical shifts between δ(H) 2.80 and 4.40 ppm. All the signals in this region were due to the benzylic H-atoms of the bridging CH_2 groups of the calixarenic core. The NMR spectra of the final products were quite simple, indicating conclusive evidence of their conformational characteristics: the absorption as two characteristic *doublet* peaks for the equatorial (2.86–3.29 ppm, $^2J = 13.00–14.00$) and axial (4.15–4.30 ppm, $^2J = 13.00–14.00$) H-atoms of Ar–CH_2–Ar-groups indicated that all the final products preferred strictly the cone conformation [14]. Furthermore,

Scheme 2. *Syntheses of Calix[4]arene-Functionalized Dendrimers* via *Convergent Approach*



an additional evidence for the cone conformation of the final lower rim functionalized calix[4]arenes came from the ^{13}C-NMR spectra, where the benzylic C-atoms of the bridging CH_2 groups of the calixarenic core absorbed only at δ(C) *ca.* 31 ppm, and no absorption was observed at δ(C) *ca.* 37 ppm, showing that only a *syn* orientation took place between phenoxy rings while an *anti* orientation was absent [15]. Finally, in the ^{1}H-NMR spectra of the calix[4]arene-fuctionalized dendrimers with COO^{t}Bu groups at their periphery, a single sharp peak was always noted between δ(H) 1.62 and 1.53 ppm due to the H-atoms of the ^{t}Bu groups. *Fig. 2* showed the ^{1}H-NMR spectra of all calix[4]arene-cored dendrimers up to the third generation, modified at their periphery with COO^{t}Bu groups, where all the above mentioned characteristic absorptions were presented, indicating that the calix[4]arene cores adopted, as shown in *Fig. 2*, the well-defined cone conformation.

The molecular weights of all the calix[4]arene-cored dendrimers, **16**–**22**, were confirmed by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) and HR-ESI-MS for two of them, **17** and **19**.

In *Fig. 3*, we show three typical MALDI-TOF mass spectra of zero-, first-, and second-generation calix[4]arene dendrimers with Br-atoms at their surface, **16**, **18**, and **20**, which prove the monodispersity and the high purity of the final products.

In most cases (see *Exper. Part*), the use of [(2*E*)-3-(4-*tert*-butylphenyl)-2-methylprop-2-en-1-ylidene]malononitrile (DCTB) has been shown to be an efficient matrix for the matrix-assisted laser desorption ionization of the calix[4]arene-cored dendritic polyethers, afforded the $[M + Na]^+$ ion.

Conclusions. – In summary, a series of novel dendritic compounds which contain calix[4]arene as the core, surrounded by periphery modified poly(benzyl ether) dendrons of zero, first, second, and third generation have been synthesized and fully

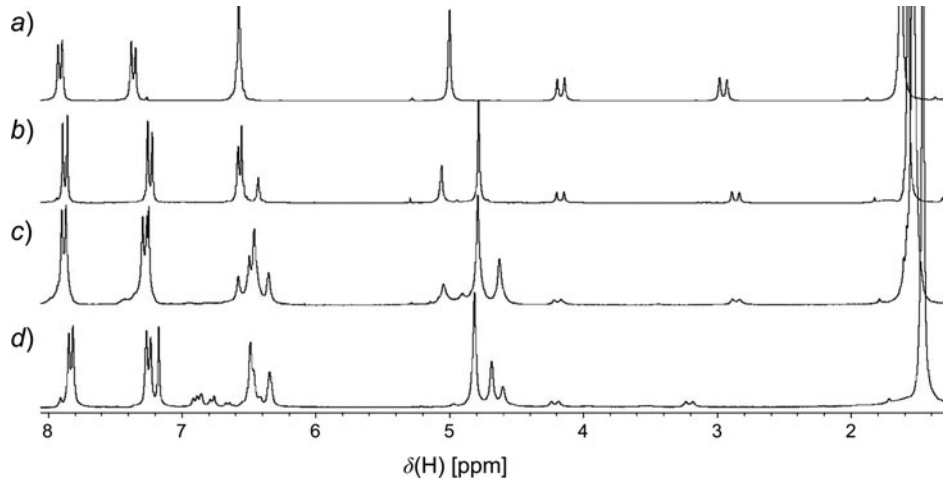


Fig. 2. *^{1}H-NMR Spectra* (250 MHz, $CDCl_3$) *of calix[4]arene-dendrimers, functionalized with COO^{t}Bu groups at their periphery: a*) *zero generation* **17**, *b*) *the first generation* **19**, *c*) *the second generation* **21**, *and d*) *the third generation* **22**

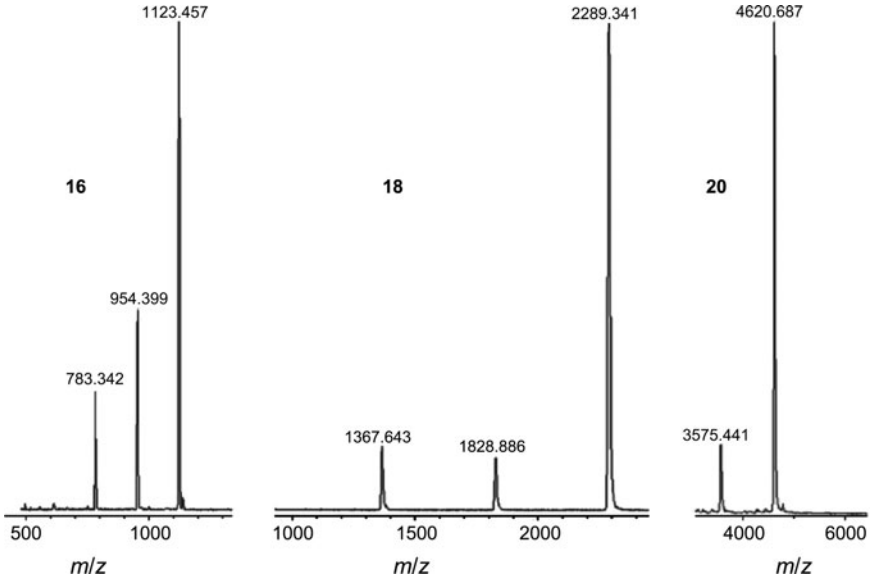


Fig. 3. *MALDI-TOF-MS Spectra of the calix[4]arene dendrimers* **16**, **18**, *and* **20**

characterized. The synthesis of *tert*-butyl ester periphery modified *Fréchet*-type poly(benzyl ether) dendrimers, as well as the conjugation of *Fréchet*-type poly(benzyl ether) dendrons with the de-alkylated derivative of *p-tert*-butylcalix[4]arene are described herein for the first time. Additionally, as evidenced through ^{1}H- and ^{13}C-NMR studies, the calix[4]arene-cored dendrimers prefer strictly the well-defined cone conformation. Taking into account the easy transformation of the COO^{t}Bu peripheral groups to the corresponding carboxylic groups or carboxylate anions, and considering the ability of calixarenes to bind inorganic and organic cations as well as neutral organic molecules selectively, dendrimer compounds with new properties are expected. Experiments involving their host–guest behavior are currently under investigation.

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Experimental Part

1. *General*. All solvents were of anal. grade, and dry solvents were prepared according to procedures described by *Armarego* and *Perrin* and used immediately after preparation [16]. All reagents were purchased from *Sigma–Aldrich*, *Fluka*, and *Merck*. TLC and prep. TLC: silica gel F_{254} (*Fluka*). Flash column chromatography (FC): *9385* silica gel F_{254} (*Merck*). M.p.: *Büchi 510* apparatus; uncorrected. NMR: *Bruker AMX* (250/63 MHz ^{1}H/^{13}C and 400/100 MHz ^{1}H/^{13}C); δ in ppm rel. to Me_4Si as internal

standard, *J* in Hz. MS: *Finnigan MAT-8200*, *Agilent 6210 ESI-TOF*, or *UltrafleXtreme MALDI-TOF/TOF* mass specrometers; in *m*/*z*. Elemental analysis: *Heraeus CHN-Rapid Analyzer*; in %.

2. *Synthesis of* tert-*Butyl 4-(Bromomethyl)benzoate* (**3**). To a stirred soln. of 4-(bromomethyl)benzoic acid (3.0 g, 14 mmol) in AcO^{t}Bu (150 ml) in a flask was added $HClO_4$ (1 ml, 70% aq. soln., 12 mmol), and the flask was tapped quickly with a plastic tap. The mixture was stirred at r.t. until no solid was observed in the flask, and washed with H_2O (3 × 100 ml) and a sat. aq. K_2CO_3 soln. until no bubbling was observed. The org. layer was dried (Na_2SO_4), filtered, and evaporated to afford **3** (2.64 g, 70%) as colorless liquid. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.59 (*s*, Me_3C); 4.49 (*s*, CH_2Br); 7.42 (*d*, ^3J = 8.25, 2 arom. H); 7.96 (*d*, ^3J = 8.25, 2 arom. H). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.49; 32.68; 81.53; 129.15; 130.21; 132.41; 142.58; 165.59.

3. *General Procedure for the Growth of Dendritic Branches with Br-Atoms at Their Periphery.* For the preparation of dendritic branches with Br-atoms at their periphery, the *Fréchet* procedure was followed, starting from 4-bromobenzyl bromide (Br–G0–CH_2Br; **2**). Spectroscopic data for all compounds were in agreement with those in [13].

4. *General Procedure for the Growth of Dendritic Branches with COO^{t}Bu Groups at Their Periphery.* For the preparation of dendritic branches with COO^{t}Bu groups at their periphery, the *Fréchet* procedure was followed, starting from the previously synthesized *tert*-butyl 4-(bromomethyl)benzoate (**3**).

5. *General Procedure for the Synthesis of Dendritic Alcohols with COO^{t}Bu Groups at Their Periphery.* Benzylic bromides (2.1 equiv.) reacted with 3,5-dihydroxybenzylic alcohol (1.0 equiv.) in the presence of K_2CO_3 (2.1 equiv.) and 18-crown-6 (0.2 equiv.) in anh. acetone at refluxing temp. After reaction completion, the solvent was evaporated under reduced pressure, and the residue was taken up in AcOEt and washed with H_2O (3 ×) and a sat. aq. NaCl soln. (2 ×). The org. layer was dried (Na_2SO_4), filtered, and the solvent evaporated under reduced pressure. The benzylic alcohol isolated from the resulting residue by FC as described for each compound.

Di-tert-*butyl 4,4′-{[5-(Hydroxymethyl)benzene-1,3-diyl]bis(oxymethanediyl)}dibenzoate* (**5**). Eluent: hexane/AcOEt (10:1). Yield: 83%. White solid. M.p. 107–108°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.58 (*s*, 2 Me_3C); 3.02 (br. *s*, CH_2OH); 4.58 (*s*, CH_2OH); 5.01 (*s*, 2 Ar′CH_2O); 6.47 (*t*, ^4J = 2.00, 1 arom. H (Ar)); 6.59 (*d*, ^4J = 2.00, 2 arom. H (Ar)); 7.41 (*d*, ^3J = 8.25, 4 arom. H (Ar′)); 7.97 (*d*, ^3J = 8.25, 4 arom. H (Ar′)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.33; 64.97; 69.46; 81.28; 101.38; 105.89; 126.97; 129.82; 131.59; 141.72; 144.08; 159.92; 165.72.

Tetra-tert-*butyl 4,4′,4″,4‴-{[5-(Hydroxymethyl)benzene-1,3-diyl]bis[oxymethanediylbenzene-5,1,3-triylbis(oxymethanediyl)]}tetrabenzoate* (**9**). Eluent: hexane/AcOEt (8:1). Yield: 86%. White solid. M.p. 75°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.60 (*s*, 4 Me_3C); 2.33 (br. *s*, CH_2OH); 4.60 (*s*, CH_2OH); 4.94 (*s*, 2 Ar′CH_2O); 5.06 (*s*, 4 Ar″CH_2O); 6.47 (*t*, ^4J = 2.00, 1 arom. H (Ar)); 6.53 (*t*, ^4J = 2.00, 2 arom. H (Ar′)); 6.57 (*d*, ^4J = 2.00, 2 arom. H (Ar)); 6.65 (*d*, ^4J = 2.00, 4 arom. H (Ar′)); 7.45 (*d*, ^3J = 8.25, 8 arom. H (Ar″)); 7.99 (*d*, ^3J = 8.25, 8 arom. H (Ar″)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.43; 65.47; 69.66; 69.97; 81.35; 101.53; 101.92; 105.90; 106.60; 127.08; 129.92; 131.77; 139.76; 141.63; 144.14; 160.08; 160.12; 165.75.

Octa-tert-*butyl 4,4′,4″,4‴,4⁗,4⁗′,4⁗″,4⁗‴-([5-(Hydroxymethyl)benzene-1,3-diyl]bis{oxymethanediylbenzene-5,1,3-triylbis[oxymethanediylbenzene-5,1,3-triylbis(oxymethanediyl)]})octabenzoate* (**13**). Eluent: hexane/AcOEt (8:1). Yield: 75%. White solid. M.p. 84°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.60 (*s*, 8 Me_3C); 2.19 (*s*, CH_2OH); 4.60 (*s*, CH_2OH); 4.95 (*s*, 12 H, Ar′CH_2O, Ar″CH_2O); 5.05 (*s*, 8 Ar‴CH_2O); 6.53 (*m*, 7 arom. H (Ar′, Ar″)); 6.61 (*d*, ^4J = 1.50, 2 arom. H (Ar)); 6.66 (*m*, 12 arom. H (Ar′, Ar″)); 7.44 (*d*, ^3J = 8.25, 8 arom. H (Ar‴)); 7.99 (*d*, ^3J = 8.25, 8 arom. H (Ar‴)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.32; 65.43; 69.64; 70.08; 81.29; 101.55; 101.81; 101.91; 106.18; 106.67; 127.08; 129.91; 131.78; 139.63; 141.60; 144.10; 160.09; 160.20; 165.68.

6. *General Procedure for the Synthesis of Dendritic Bromides with COO^{t}Bu Groups at Their Periphery.* For the preparation of the benzylic bromides, the corresponding benzylic alcohol (1.0 equiv.) was dissolved in a minimum amount of anh. THF and reacted with CBr_4 (1.25 equiv.) and Ph_3P (1.25 equiv.) at r.t. under inert atmosphere (Ar). After reaction completion, AcOEt was added to the mixture and washed with H_2O (3 ×) and a sat. aq. NaCl soln. (2 ×). The org. layer was dried (Na_2SO_4), filtered, and the solvent evaporated under reduced pressure. The benzylic bromide isolated from the resulting residue by FC as described for each compound.

Di-tert-*butyl 4,4′-{[5-(Bromomethyl)benzene-1,3-diyl]bis(oxymethanediyl)}dibenzoate* (**7**). Eluent: hexane/AcOEt (10:1). Yield: 73%. White solid. M.p. 123–124°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.60 (*s*, 2 Me_3C); 4.38 (*s*, CH_2Br); 5.04 (*s*, 2 Ar′CH_2O); 6.51 (*t*, ^4J = 2.00, 1 arom. H (Ar)); 6.63 (*d*, ^4J = 2.00, 2 arom. H (Ar)); 7.44 (*d*, ^3J = 8.00, 4 arom. H (Ar′)); 8.01 (*d*, ^3J = 8.00, 4 arom. H (Ar′)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.32; 33.58; 69.52; 81.13; 102.31; 108.37; 126.97; 129.82; 131.72; 140.08; 141.34; 159.87; 165.48.

Tetra-tert-*butyl 4,4′,4″,4‴-{[5-(Bromomethyl)benzene-1,3-diyl]bis[oxymethanediylbenzene-5,1,3-triylbis(oxymethanediyl)]}tetrabenzoate* (**11**). Eluent: hexane/AcOEt (10:1). Yield: 80%. White solid. M.p. 76°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.61 (*s*, 4 Me_3C); 4.40 (*s*, CH_2Br); 4.96 (*s*, 2 Ar′CH_2O); 5.09 (*s*, 4 Ar″CH_2O); 6.51 (*t*, ^4J = 2.25, 1 arom. H (Ar)); 6.55 (*t*, ^4J = 2.25, 2 arom. H (Ar′)); 6.61 (*d*, ^4J = 2.25, 2 arom. H (Ar)); 6.66 (*d*, ^4J = 2.25, 4 arom. H (Ar′)); 7.45 (*d*, ^3J = 8.25, 8 arom. H (Ar″)); 8.00 (*d*, ^3J = 8.25, 8 arom. H (Ar″)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.45; 33.99; 69.71; 70.14; 81.31; 102.01; 102.32; 106.66; 108.45; 127.09; 129.95; 131.85; 139.48; 139.96; 141.60; 160.14; 160.15; 165.69.

Octa-tert-*butyl 4,4′,4″,4‴,4⁗,4⁗′,4⁗″,4⁗‴-([5-(Bromomethyl)benzene-1,3-diyl]bis{oxymethanediylbenzene-5,1,3-triylbis[oxymethanediylbenzene-5,1,3-triylbis(oxymethanediyl)]})octabenzoate* (**15**). Eluent: hexane/AcOEt (3:1). Yield: 88%. White solid. M.p. 91–93°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.61 (*s*, 8 Me_3C); 4.39 (*s*, CH_2Br); 4.96 (*s*, 12 H, Ar′CH_2O, Ar″CH_2O); 5.07 (*s*, 8 Ar‴CH_2O); 6,54 (*m*, 7 arom. H (Ar′, Ar″)); 6,63 (*d*, ^4J = 2.00, 2 arom. H (Ar)); 6.68 (*m*, 12 arom. H (Ar′, Ar″)); 7.45 (*d*, ^3J = 8.25, 8 arom. H (Ar‴)); 8.00 (*d*, ^3J = 8.25, 8 arom. H (Ar‴)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.44; 33.94; 69.66; 70.13; 70.21; 81.29; 101.64; 101.93; 102.60; 106.70; 108.73; 127.10; 129.93; 131.82; 139.45; 139.61; 140.21; 141.60; 160.13; 160.25; 165.68.

7. *General Procedure for the Synthesis of the Calix[4]arene Functionalized Dendrimers* **16**–**22**. To a stirred soln. of calix[4]arene (1 equiv.) in anh. dioxane was added under Ar a suspension of NaH (5 equiv.), and the mixture was heated to reflux for *ca.* 30 min (purple color observed). The stirred soln. was cooled to r.t., and the dissolved corresponding dendritic bromide of the zero, first, second, and third generation (4.2 equiv.) in anh. DMF was added dropwise under Ar. The mixture was heated to reflux for 24–48 h, then allowed to cool to r.t., worked up carefully with H_2O, and evaporated under reduced pressure. H_2O was added to the residue, and the resulting aq. suspension was extracted with AcOEt (3×). The combined org. extracts were dried (Na_2SO_4), evaporated, and purified either by crystallization or by FC (SiO_2).

25,26,27,28-Tetrakis[(4-bromobenzyl)oxy]calix[4]arene (**16**). Yield: 60%. Colorless solid. M.p. 190–194° (heptane). ^{1}H-NMR (250 MHz, $CDCl_3$): 3.05 (*d*, ^2J = 13.50, 2 ArCH_2Ar); 4.20 (*d*, ^2J = 13.50, 2 ArCH_2Ar); 4.89 (*s*, 4 ArOCH_2Ar); 6.64 (*m*, 12 arom. H (Ar)); 7.16 (*d*, ^3J = 8.25, 8 arom. H (Ar)); 7.40 (*d*, ^3J = 8.25, 8 arom. H (Ar)). ^{13}C-NMR (63 MHz, $CDCl_3$): 31.57; 75.87; 122.41; 122.84; 128.67; 131.41; 131.54; 135.25; 136.69; 155.29. MALDI-TOF-MS (matrix: DCTB): 1123.457 ($[M+Na]^+$, $C_{56}H_{46}Br_4NaO_4^+$; calc. 1121.0027). Anal. calc. for $C_{56}H_{46}Br_4O_4$ (1102.58): C 61.00, H 4.21; found: C 60.73, H 4.40.

*25,26,27,28-Tetrakis{[4-(*tert-*butoxycarbonyl)benzyl]oxy}calix[4]arene* (**17**). Eluent: hexane/AcOEt (10:1). Yield: 70%. Colorless solid. M.p. 119°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.62 (*s*, 4 Me_3C); 2.95 (*d*, ^2J = 13.50, 2 ArCH_2Ar); 4.17 (*d*, ^2J = 13.50, 2 ArCH_2Ar); 5.00 (*s*, 4 ArOCH_2Ar′); 6.57 (*m*, 12 arom. H (Ar)); 7.36 (*d*, ^3J = 8.00, 8 arom. H (Ar′)); 7.91 (*d*, ^3J = 8.00, 8 arom. H (Ar′)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.47; 31.66; 76.05; 81.28; 122.80; 128.66; 129.51; 131.88; 135.32; 142.17; 155.27; 165.75. HR-ESI-MS (matrix: $CsCO_3$): 1318.4602 ($[M+Cs]^+$, $C_{76}H_{82}CsO_{12}^+$; calc. 1318.4782). MALDI-TOF-MS (matrix: DCTB): 1208.066 ($[M+Na]^+$, $C_{76}H_{82}NaO_{12}^+$; calc. 1209.5704). Anal. calc. for $C_{76}H_{82}O_{12}$ (1187.46): C 76.87, H 6.96; found: C 77.02, H 6.65.

25,26,27,28-Tetrakis({3,5-bis[(4-bromobenzyl)oxy]benzyl}oxy)calix[4]arene (**18**). Eluent: hexane/CH_2Cl_2 (3:1). Yield: 57%. Colorless solid. M.p. 93–94°. ^{1}H-NMR (250 MHz, $CDCl_3$): 2.90 (*d*, ^2J = 13.50, 2 ArCH_2Ar); 4.19 (*d*, ^2J = 13.50, 2 ArCH_2Ar); 4.69 (*s*, 8 ArOCH_2Ar′); 5.06 (*s*, 4 Ar′OCH_2Ar″); 6.41 (*t*, ^4J = 2.00, 4 arom. H (Ar′)); 6.59 (*m*, 20 arom. H (Ar′, Ar″)); 7.06 (*d*, ^3J = 8.25, 16 arom. H (Ar″)); 7.37 (*d*, ^3J = 8.25, 16 arom. H (Ar″)). ^{13}C-NMR (63 MHz, $CDCl_3$): 31.90; 69.37; 76.17; 101.74; 108.66; 122.11; 122.69; 128.58; 129.28; 131.88; 135.45; 135.93; 140.51; 155.35; 159.59. MALDI-TOF-MS (matrix: DCTB): 2289.341 ($[M+Na]^+$, $C_{112}H_{90}Br_8NaO_{12}^+$; calc. 2290.1276). Anal. calc. for $C_{112}H_{90}Br_8O_{12}$ (2267.14): C 59.33, H 4.00; found: C 59.47, H 3.77.

*25,26,27,28-Tetrakis[(3,5-bis{[4-(*tert*-butoxycarbonyl)benzyl]oxy}benzyl)oxy]calix[4]arene* (**19**). Eluent: hexane/AcOEt (10:1). Yield: 62%. Colorless solid. M.p. 99–102°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.57 (*s*, 8 Me_3C); 2.86 (*d*, ^2J = 13.50, 2 $ArCH_2Ar$); 4.17 (*d*, ^2J = 13.50, 2 $ArCH_2Ar$); 4.78 (*s*, 8 $ArOCH_2Ar'$); 5.06 (*s*, 4 $Ar'OCH_2Ar''$); 6.43 (*t*, ^4J = 2.00, 4 arom. H (Ar′)); 6.55–6.58 (*m*, 20 arom. H (Ar′, Ar″)); 7.22 (*d*, ^3J = 8.25, 16 arom. H (Ar″)); 7.87 (*d*, ^3J = 8.25, 16 arom. H (Ar″)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.49; 31.71; 69.39; 76.08; 81.12; 101.81; 108.64; 122.47; 127.08; 128.32; 129.87,131.56; 135.29; 140.32; 141.49; 155.28; 159.51; 165.52. HR-ESI-MS (matrix: $CsCO_3$): 2567.0969 ($[M + Cs]^+$, $C_{152}H_{162}CsO_{28}^+$; calc. 2568.0307). MALDI-TOF-MS (matrix: DCTB): 2459.611 ($[M + Na]^+$, $C_{152}H_{162}CsO_{28}^+$; calc. 2458.1150). Anal. calc. for $C_{152}H_{162}O_{28}$ (2436.90): C 74.92, H 6.70; found: C74.61, H 6.62.

25,26,27,28-Tetrakis{[3,5-bis([3,5-bis[(4-bromobenzyl)oxy]benzyl}oxy)benzyl]oxy}calix[4]arene (**20**). Eluent: hexane/CH_2Cl_2 (4:1). Yield: 25%. Colorless solid. M.p. 77–79°. ^{1}H-NMR (250 MHz, $CDCl_3$): 2.91 (*d*, ^2J = 13.50, 2 $ArCH_2Ar$); 4.21 (*d*, ^2J = 13.50, 2 $ArCH_2Ar$); 4.61 (*s*, 8 $Ar'OCH_2Ar''$); 4.71 (*s*, 16 $Ar''OCH_2Ar'''$); 5.05 (*s*, 4 $ArOCH_2Ar''$); 6.35–6.59 (*m*, 48 arom. H (Ar′, Ar″)); 7.11 (*d*, ^3J = 8.25, 32 arom. H (Ar‴)); 7.39 (*d*, ^3J = 8.25, 32 arom. H (Ar‴)). ^{13}C-NMR (63 MHz, $CDCl_3$): 31.87; 69.37; 69.98; 101.61; 102.02; 106.64; 108.57; 122.17; 122.81; 128.47; 129.34; 131.91; 135.22; 135.87; 139.59; 140.54; 155.69; 159.64; 160.01. MALDI-TOF-MS (matrix: DCTB): 4620.687 ($[M + Na]^+$, $C_{224}H_{178}Br_{16}NaO_{28}^+$; calc. 4619.2471). Anal. calc. for $C_{224}H_{178}Br_{16}O_{28}$ (4596.26): C 58.53, H 3.90; found: C 58.61, H 3.77.

*25,26,27,28-Tetrakis({3,5-bis[(3,5-bis{[(4-*tert*-butoxycarbonyl)benzyl]oxy}benzyl)oxy]benzyl}oxy)-calix[4]arene* (**21**). Eluent: hexane/acetone/AcOEt (12:2:1). Yield: 30%. Colorless solid. M.p. 107–110°. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.55 (*s*, 16 Me_3C); 2.87 (*d*, ^2J = 14.00, 2 $ArCH_2Ar$); 4.21 (*d*, ^2J = 14.00, 2 $ArCH_2Ar$); 4.64 (*s*, 8 $Ar'OCH_2Ar''$); 4.80 (*s*, 16 $Ar''OCH_2Ar'''$); 5.06 (*s*, 4 $ArOCH_2Ar''$); 6.35–6.59 (*m*, 48 arom. H (Ar′, Ar″)); 7.29 (*d*, ^3J = 8.25, 32 arom. H (Ar‴)); 7.89 (*d*, ^3J = 8.25, 32 arom. H (Ar‴)). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.49; 31.81; 69.20; 69.90; 81.05; 101.59; 102.10; 106.37; 108.39; 122.47; 127.14; 128.45; 129.89; 131.64; 135.26; 139.51; 140.45; 141.32; 155.34; 159.66; 159.94; 165.55. HR-ESI-MS (matrix: DHB): 4956.0000 ($[M + Na]^+$, $C_{304}H_{322}NaO_{60}^+$; calc. 4955.2043). Anal. calc. for $C_{304}H_{322}O_{60}$ (4935.77): C 73.98, H 6.58; found C 73.84, H 6.65.

*26,28-Bis{[3,5-bis({3,5-bis[(3,5-bis{[4-(*tert*-butoxycarbonyl)benzyl]oxy}benzyl)oxy]benzyl}oxy)-benzyl]oxy}-25,27-dihydroxycalix[4]arene* (**22**). Eluent: hexane/AcOEt (4:1). Yield: 7%. Colorless solid. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.55 (*s*, 16 Me_3C); 3.30 (*d*, ^2J = 13.00, 2 $ArCH_2Ar$); 4.30 (*d*, ^2J = 13.00, 2 $ArCH_2Ar$); 4.69 (*s*, 4 $Ar'OCH_2Ar''$); 4.77 (*s*, 8 $Ar''OCH_2Ar'''$); 4.90 (*s*, 16 $Ar'''OCH_2Ar''''$); 5.06 (*s*, $ArOCH_2Ar'$); 6.38–7.00 (*m*, 54 arom. H (Ar′, Ar″, Ar‴)); 7.34 (*d*, ^3J = 8.00, 32 arom. H (Ar‴)); 7.92 (*d*, ^3J = 8.00, 32 arom. H (Ar‴)); 7.99 (*s*, 2 ArOH). ^{13}C-NMR (63 MHz, $CDCl_3$): 28.25; 31.69; 69.36; 69.88; 81.19; 101.52; 101.72; 105.63; 106.33; 106.61; 126.84; 128.14; 128.68; 129.68; 131.66; 133.37; 139.40; 139.60; 139.90; 141.35; 152.17; 153.45; 159.95; 160.32; 165.59. MALDI-TOF-MS (matrix: DCTB): 5197.5120 ($[M + Na]^+$, $C_{318}H_{332}NaO_{64}^+$; calc. 5197.2622). Anal. calc. for $C_{318}H_{332}O_{64}$ (5178.00): C 73.76, H 6.46; found C 73.45, H 6.39.

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