Concave Reagents 29 [1]

Dendrimer Fixed Concave Pyridine

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Dedicated to Prof. Dr. F. Vögtle on the Occasion of his 60th Birthday

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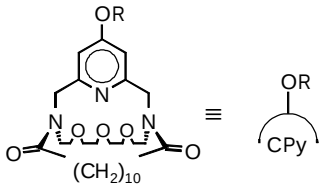
Abstract. A concave pyridine **1c** has been attached to dendrimers of the Fréchet type by an ethylenoxide linker on the convex outside of the catalyst. Two generations of dendrons **[G-1]-OH**, **[G-2]-OH**, **[G-1]-Br** and **[G-2]-Br** and of dendrimers with 4,4'-dihydroxybiphenyl (**3**) and 1,1,1-tris(4-hydroxyphenyl)ethane (**4**) as di- and trivalent cores **[G-1]$_2$–[C2]**, **[G-1]$_3$–[C3]** and **[G-2]$_3$–[C3]** have been synthesized. The resulting molecules possess up to twelve concave catalytic pyridine centers on the outside of the molecules, and can be used as selective catalysts in the base catalyzed addition of alcohols to diphenylketene.

Dendrimers fill the gap between polymers and "normal" organic molecules because they combine the large molecular weight of polymers with monodispersity [2]. Hence the construction of appropriately substituted dendritic molecules should solve some of the problems which are encountered when reagents or catalysts [3] are attached to polymers in order to allow an easier recovery.

A suitable dendrimer catalyst will therefore combine the following properties: (i) Dendrimers are monodispers. Hence the selectivity will be well defined in contrast to polymer bound catalysts where varying selectivities may be observed due to the polydispersity. (ii) A dendrimer can be constructed in such a way that all catalytic groups possess the same environment which will also give a uniform selectivity, in contrast to crosslinked polymers in which the environment of the catalytic centers may vary. (iii) Dendrimers are usually soluble. Thus no problem will occur at the boundary of phases. (iv) In comparison to standard catalysts, dendrimer bound catalysts possess a higher molecular weight which allows separation by nanofiltration. (v) Linear polymers can "sneak" through small holes of a nanofiltration membrane, a process called reptation. This will be avoided if the molecules are branched like dendrimers. (vi) The solubility and the monodispersity allow the standard analytic procedures of organic chemistry like NMR spectroscopy although the molecular weights are rather high.

In this work we describe the exploitation of these advantages of dendrimer bound catalysts for concave reagents [4]. As catalyst we chose the concave pyridine **1a** which has shown remarkable selectivities in the base catalyzed addition of ketenes to alcohols and polyols, *e.g.* monosaccharides [5]. In order to attach a molecule like **1a** to a polymer or a dendrimer, the oxygen atom in 4-position of the pyridine ring must be substituted by a spacer which contains a functionality allowing a further connection.



1

	R
a	Me
b	CH_2CH_2OBn
c	CH_2CH_2OH
d	CH_2CH_2I
e	CH_2CH_2O-mp (mp = Merrifield polymer)
f	CH_2CH_2O-sp (sp = soluble polymer) (polyvinylbenzyl chloride)

The synthesis of concave pyridines like **1a** is well established [5, 6]. In a two step bis-macrocyclization also concave pyridines with a spacer in 4-position of the pyridine ring can be synthesized. Such a synthesis has been demonstrated already for a smaller bimacrocycle (lacking one ethylene oxide unit in the polyether chain of **1b**) [7] and can be copied for the construction of the concave pyridine **1b** [8]. After deprotection of the benzyl protected OH group in **1b** by palladium catalyzed hydrogenolysis [8], the OH group of the product **1c** can be substituted by iodine giving the key intermediate **1d**.

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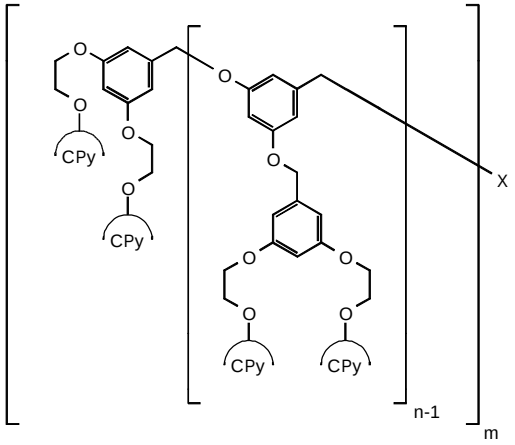
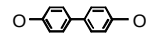
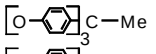
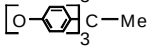
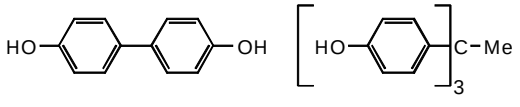
For the dendrimer synthesis we chose a convergent approach in order to allow an easier separation of the products. Therefore we used 3,5-dihydroxybenzyl alcohol (**2**) as branching unit as suggested by Fréchet [9]. This allowed an easy separation of the starting materials and products in the syntheses of the dendrons **[G-n]-OH** and **[G-n]-Br** and the dendrimers **[G-n]$_2$-[C2]** and **[G-n]$_3$-[C3]** because the molecular weight doubles or triples roughly, and even in the case of an incomplete alkylation of the trivalent core molecule **4** the molecular weight ratio of incomplete to complete alkylated products is still ca. 1 : 1.5.



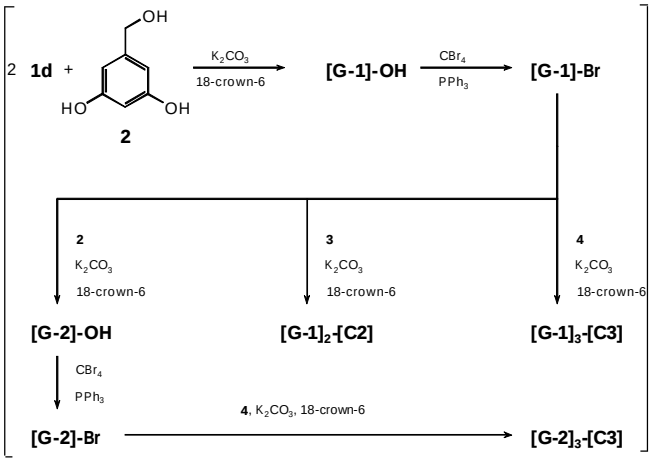
[G-n]$_m$-X	n	m	X
[G-1]-OH	1	1	OH
[G-1]-Br	1	1	Br
[G-2]-OH	2	1	OH
[G-2]-Br	2	1	Br
[G-1]$_2$-[C2]	1	2	
[G-1]$_3$-[C3]	1	3	
[G-2]$_3$-[C3]	2	3	

Scheme 1 First (n = 1) and second (n = 2) generation dendrons **[G-n]-OH** and **[G-n]-Br**, and first (n = 1) and second (n = 2) generation dendrimers with a divalent **[G-n]$_2$-[C2]** and a trivalent core **[G-n]$_3$-[C3]**. CPy is the abbreviation for a concave pyridine with an oxyethoxy spacer on its convex outside.

The synthetic pathways for the preparation of two generations of dendrons (benzyl alcohols **[G-n]-OH** and benzyl bromides **[G-n]-Br**) and for the syntheses of the dendrimers with a divalent or a trivalent core **3** and **4** (**[G-n]$_2$-[C2]** and **[G-n]$_3$-[C3])** are summarized in Scheme 2.



3 **4**



Scheme 2 Convergent synthetic routes for first (n = 1) and second (n = 2) generation dendrons **[G-n]-OH** and **[G-n]-Br**, and first (n = 1) and second (n = 2) generation dendrimers **[G-n]$_m$-[Cm]** starting from a concave pyridine **1d** with a spacer on its convex outside.

The products were purified by column chromatography on silica gel. Size exclusion chromatography was used to prove the absence of impurities in the products, such as the dendritic building blocks (dendrons), or incompletely alkylated dendrimers. The products were analyzed by IR, NMR and elemental analysis. The NMR spectra showed clearly the additional signals for the branching units (for dendrons and dendrimers) and for the cores (dendrimers only), and the composition could be controlled by the integration of appropriate signals. Concave pyridines contain amide bridgeheads which may exist in *E*- or *Z*-conformations. This leads to the formation of *EE*-, *EZ*- (and its *ZE*-enantiomer) and *ZZ*-conformers for each concave pyridine [5, 6]. With the dendritic concave pyridines these conformers are found, too. For all new compounds the following ratios have been determined: *EE* : *EZ*/*ZE* : *ZZ* = 5 : 30 : 65 (±5). The conformer ratios are comparable to those of non-dendritic concave pyridines like **1a** and can be analyzed quantitatively by 1H NMR spectroscopy, in contrast to ^{13}C NMR spectroscopy. Therefore, the ^{13}C data are not completely assigned. But the ^{13}C NMR patterns can be used as fingerprints to identify the compounds. All parts of the spectra resulting from the concave pyridines resemble each other for all dendrimers and dendrons. Assignments in the NMR-spectra have been made on the basis of the assignments for non-dendritic concave pyridines [5, 6, 8].

Several attempts have been undertaken to analyze the dendrimers by MS. Unfortunately with all ionization techniques applied so far (including MALDI-TOF and ESI), no molecular peak could be found. The ether linkages are too weak, and the assignable peaks are only those of the concave pyridine fragments (*e.g.*: CPy–O–CH_2–CH_2^+, *m*/*z* = 532 [100%]) and probably of the tri-

valent core connected to three bridging units (m/z = 660). Although the molecular weights could not be determined by MS, they can be estimated by GPC. Every compound possessed a single peak in the GPC. Crude reactions mixtures show starting materials (**1d** or dendrons) and the new dendron or dendrimer. The high molecular weight also became obvious in first nanofiltration experiments where for a first generation dendrimer **[G-1]$_3$-[C3]** with a molecular weight of 3 863 already a retention of ca. 90% could be observed [10].

Finally, the new concave pyridine derivatives have been used as catalysts in the base catalyzed addition of alcohols to diphenylketene. As expected, the selectivities hardly differed from those measured for standard concave pyridines like **1a**. The results are listed in Table 1.

Table 1 Base catalyzed acylation of an equimolar mixture of ethanol, isopropanol and *tert*-butanol with diphenylketene to give ethyl, isopropyl and *tert*-butyl diphenylacetates. With none of the catalysts, the *tert*-butyl ester could be detected by GC analysis. For experimental details see ref. [5].

catalyst	ethanol	isopropanol	*tert*-butanol
pyridine	4.7	1	0
lutidine	7.1	1	0
1a	12.0	1	0
insoluble polymer **1e**	7.4	1	0
soluble polymer **1f**	9.5	1	0
[G-1]$_2$-[C2]	11.6	1	0
[G-1]$_3$-[C3]	11.4	1	0
[G-2]$_3$-[C3]	11.6	1	0

Thus, with these new dendritic catalysts new reagents exist for a selective acylation of polyols which should be easily recyclable by nanofiltration.

The MALDI-TOF mass spectra were recorded by K. Martin and Dr. H. J. Räder, Max-Planck-Institut für Polymerforschung in Mainz.

Experimental

Melting points were determined on a Büchi hot-stage apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Paragon FT-IR-spectrometer. ^{1}H NMR spectra were recorded on solutions in $CDCl_3$ on Bruker AM 300 (300 MHz) and AM 500 (500 MHz) spectrometers with tetramethylsilane as internal standard. ^{13}C NMR spectra were recorded at 50, 75 and 125 MHz on Bruker AC 200, AM 300 and AM 500 spectrometers with $CDCl_3$ as solvent and the tetramethylsilane carbon signal as internal standard. Mass spectra (EI or CI) were obtained on a Finnigan MAT 44S. Analytical TLC was performed on commercial Merck plates coated with silica gel GF_{254} (0.25 mm thick). Silica gel for column chromatography: Merck Kieselgel (0.063 – 0.2 µm). Size-exclusion chromatography (GPC) was carried out with a Waters 510 HPLC pump connected to a Waters 486 tunable UV-detector; data analysis was performed with Millennium 2000 software; column from MZ laboratories (300 × 8 mm; pore size: 500 Å), tetrahydrofuran as solvent.

29-(2-Iodoethoxy)-17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dione (**1d**)

Iodine (1.5 equiv) was added in small portions to a mixture of the alcohol **1c** [8] (1 equiv), triphenylphosphine (1.5 equiv) and imidazole (3 equiv) in a minimum amount of dry benzene required to dissolve the above reagents, and the reaction mixture was stirred under argon until TLC showed no more starting material (after some hours). The clear, colorless solution was decanted, and the residue was extracted with CH_2Cl_2 (3×). The combined organic layer was evaporated to dryness. The crude product was purified by chromatography. After elution of triphenylphosphine and triphenylphosphine-oxide with ethyl acetate/CH_2Cl_2 (3/1) the product **1d** was isolated with CH_2Cl_2/ethanol (15/1) giving a white crystalline solid after evaporation of the solvents. Scales up to 5 g, yield 89%, *m.p.* 147 °C. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2921, 2852 (C-H), 1646 (C=O), 1600, 1578 (arom.), 1460, 1412 (C-H), 1156 – 1030 (C–O), 672 (C–I). – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 0.94–1.33 (3 m, 12H, (C$\underline{H}_2$)$_6$), 1.39–1.82 (2 m, 4H, C$\underline{H}_2$CH$_2$–CO), 2.12–2.32 (m, 4H, N–C$\underline{H}_2$-polyether), 2.50, 3.05 (2 m$_c$, 0.7H), 3.25–3.95 (m, 24H, C$\underline{H}_2$–CO–N, polyether), 4.27 (m$_c$, 2.7H), 4.66 (d, ^2J = 14 Hz, 0.4H, C$\underline{H}_2$–Py), 4.73 (d, ^2J = 14 Hz, 2.9H, C$\underline{H}_2$–Py), 4.89 (d, ^2J = 14 Hz, 0.3H, C$\underline{H}_2$–Py), 5.20 (d, ^2J = 14 Hz, 0.25H, C$\underline{H}_2$–Py), 5.40 (d, ^2J = 14 Hz, 0.1H, C$\underline{H}_2$–Py), 6.49 (d, J = 2.2 Hz, 0.27H, *EZ*-Py-$\underline{H}$), 6.57 (s, 1.35H, *ZZ*-Py-$\underline{H}$), 6.69 (d, J = 2.2 Hz, 0.27H, *EZ*-Py-$\underline{H}$), 6.94 (s, 0.12H, *EE*-Py-$\underline{H}$). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 24.33, 24.36, 24.82 (C$\underline{H}_2$), 26.93, 27.45–28.47 (C$\underline{H}_2$), 31.99, 33.99, 44.99; 48.00 (C$\underline{H}_2$–I), 50.29, 53.68; 55.50 (C$\underline{H}_2$–OPy), 68.21 (Py–C$\underline{H}_2$), 68.30 (Py–C$\underline{H}_2$), 69.86, 70.69, 70.88, 70.95, 71.00, 71.05, 71.15, 72.63, 76.86, 76.89, 77.11, 77.14, 77.40, 77.46 (Py–C$\underline{H}_2$), 104.61 (*ZZ*-Py–C-3,5), 105.50, 106.06 (*EZ*-Py–C-3,5), 107.47 (*EE*-Py–C-3,5), 158.44 (Py–C-4), 160.28, 160.35 (Py–C-2,6), 165.49, 165.60 (Py–C-2,6), 172.91 (C=O), 174.53, 174.56, 174.58 (Py–C-2,6). – MS (EI, 70 eV): m/z (%) = 659 (100) [M$^+$], 629 (20), 570 (21), 541 (17), 504 (45), 474 (54), 277 (27), 155 (20), 149 (26), 148 (28), 69 (20). – MS (CI, isobutane): m/z (%) = 660 (100) [M$^+$ + 1].

$C_{29}H_{46}IN_3O_6$ (659.62)	Calcd:	C 52.81	H 7.03	N 6.37
	Found:	C 52.67	H 6.99	N 6.37.

Synthesis of Dendritic Benzyl Alcohols (General Procedure)

A mixture of the appropriate dendritic benzyl bromide or **1d** (2.2 equiv), 3,5-dihydroxybenzyl alcohol (**2**) (1.0 equiv), anhydrous potassium carbonate (2.5 equiv) and 18-crown-6 (0.3 equiv) in dry acetone (or dry tetrahydrofuran for **[G-1]-OH**) was heated at reflux and stirred vigorously under argon for five to seven days. The mixture was allowed to cool and evaporated to dryness under reduced pressure. The residue was partitioned between water and CH_2Cl_2, and the aqueous layer extracted with CH_2Cl_2 (5×). The combined organic extract was dried with $MgSO_4$ and evaporated to dryness. The crude product was then purified as described below.

3,5-Bis[2-(17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dion-29-yl)-oxyethoxy]-benzyl alcohol **[G-1]-OH**

was prepared from **1d** in dry tetrahydrofuran and purified by column chromatography eluting with CH_2Cl_2/ethanol (15/1) to give **[G-1]-OH** as a colorless glassy solid. Scales up to 200 mg, yield 76%, *m.p.* 105–110 °C (dec.). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3425 (O-H), 2922, 2854 (C-H), 1642 (C=O), 1596 (arom.), 1458, 1409, 1355 (C-H), 1162 –1030 (C–O). – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 0.93–1.32 (3 m, 26H, C$\underline{H}_2$-polymethylene), 1.40–1.85 (3 m, 11.5H, C$\underline{H}_2$CH$_2$–CO, polyether), 2.12–2.34 (m, 8H, N–C$\underline{H}_2$-polyether), 2.50, 3.02 (2 m$_c$, 1H), 3.26–3.96 (3 m, 32H, C$\underline{H}_2$–CO–N, polyether, C$\underline{H}_2$–OPy, C$\underline{H}_2$–OAr), 4.15, 4.18 (2 t, J = 3.6 Hz, J = 3.6 Hz, 0.6H), 4.28 (m$_c$, 0.6H), 4.61–4.79 (m, 8H, C$\underline{H}_2$–Py, C$\underline{H}_2$-polyether), 4.89, 4.96, 4.99 (s, 2 dd, ^2J = 14 Hz, J = 1.9 Hz, ^2J = 14 Hz, J = 1.9 Hz, 2.6H, C$\underline{H}_2$–Py, Ar–C$\underline{H}_2$OH), 5.18 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.5H, C$\underline{H}_2$–Py), 5.40 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.3H, C$\underline{H}_2$–Py), 6.56 (d, J = 2.2 Hz, 0.7H, *EZ*-Py-$\underline{H}$), 6.61–6.69 (m, 5.5H, *ZZ*-Py-$\underline{H}$, Ar-$\underline{H}$), 6.78 (d, J = 2.2 Hz, 0.7H, *EZ*-Py-$\underline{H}$), 7.04 (s, 0.3H, *EE*-Py-$\underline{H}$). – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 24.33, 24.36, 24.84 (C$\underline{H}_2$), 26.93, 27.45–28.47 (C$\underline{H}_2$), 32.00, 33.89, 44.84, 44.99, 47.98 (C$\underline{H}_2$–OAr), 50.22, 50.59, 53.38, 54.86, 55.53 (C$\underline{H}_2$–OPy, ArC$\underline{H}_2$OH), 68.25, 68.31, 69.98, 70.69, 70.84, 70.95, 71.08, 72.37, 76.43, 77.07, 77.70 (Py–C$\underline{H}_2$), 98.91, 99.44 (Ar–C-4), 104.68 (*ZZ*-Py–C-3,5), 105.50, 105.81 (*EZ*-Py–C-3,5), 106.06 (Ar–C-2,6), 107.47 (*EE*-Py–C-3,5), 145.08, 145.25 (Ar–C-1), 158.44, 158.83 (Py–C-4), 160.23, 160.32 (Py–C-2,6), 160.43, 160.65 (Ar–C-3,5), 164.54, 165.58 (Py–C-2,6), 172.90 (C=O), 174.53, 174.56, 174.58 (Py–C-2,6).

$C_{65}H_{98}N_6O_{15}$	Calcd:	C 64.87	H 8.21	N 6.98
(1203.56)	Found:	C 64.84	H 8.18	N 6.88.

3,5-Bis{3,5-bis[2-(17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dion-29-yl)-oxyethoxy]-benzyloxy}-benzyl alcohol **[G-2]-OH**

was prepared from **[G-1]-Br** and purified by column chromatography eluting with CH_2Cl_2/ethanol (15/1) to give **[G-2]-OH** as a colorless glassy solid. 100 mg scale, yield 82%, *m.p.*: 116–118 °C (dec.). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3421 (O-H), 2922, 2854 (C-H), 1661, 1642 (C=O), 1595, 1582 (arom.), 1459, 1409, 1355, 1304, 1210 (C-H), 1162–1033 (C–O). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 0.88–1.35 (3 m, 53.1H, C$\underline{H}_2$-polymethylene), 1.37–1.87 (2 m, 21.3H, C$\underline{H}_2$CH$_2$–CO, polyether), 2.00–2.32 (m, 15.4H, N–C$\underline{H}_2$-polyether), 2.50, 3.02 (2 m$_c$, 2.1H), 3.27–4.02 (3 m, 66.9H, C$\underline{H}_2$–CO–N, polyether, C$\underline{H}_2$–OPy), 4.15, 4.18 (2 t, J = 3.6 Hz, J = 3.6 Hz, 1.1H), 4.28 (m$_c$, 1.1H), 4.58–4.81 (m, 15.8 H, C$\underline{H}_2$–Py, C$\underline{H}_2$-polyether), 4.88, 4.95, 4.99 (s, 2 dd, ^2J = 14 Hz, J = 1.9 Hz, ^2J = 14 Hz, J = 1.9 Hz, 4.9H, C$\underline{H}_2$–Py, Ar–C$\underline{H}_2$OH), 5.19 (dd, ^2J = 14 Hz, J = 1.9 Hz, 1H, C$\underline{H}_2$–Py), 5.40 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.5H, C$\underline{H}_2$–Py), 6.56 (d, J = 2.2 Hz, 1.4H, *EZ*-Py-$\underline{H}$), 6.56–6.69 (m, 13.3H, *ZZ*-Py-$\underline{H}$, Ar-$\underline{H}$), 6.77 (d, J = 2.2 Hz, 1.4H, *EZ*-Py-$\underline{H}$), 7.03 (s, 0.5H, *EE*-Py-$\underline{H}$). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 24.34, 24.89 (C$\underline{H}_2$), 26.88 26.93, 27.47–28.61 (C$\underline{H}_2$), 31.99, 32.07, 33.97, 44.55, 48.01 (C$\underline{H}_2$–OAr), 50.35, 53.59, 54.88, 55.60 (C$\underline{H}_2$–OPy, ArC$\underline{H}_2$OH), 69.91, 70.58, 70.73, 70.79, 70.88, 70.94, 71.08, 72.62, 76.62, 77.04, 77.47 (Py–C$\underline{H}_2$), 99.01, 99.54 (Ar–C-4), 104.58 (*ZZ*-Py–C-3,5), 105.86, 105.92 (*EZ*-Py–C-3,5), 106.01 (Ar–C-2,6), 107.44 (*EE*-Py–C-3,5), 145.07, 145.25 (Ar–C-1), 158.86 (Py–C-4), 160.46, 160.69 (Py–C-2,6, Ar–C-3,5), 164.43, 165.57 (Py–C-2,6), 172.90 (C=O), 173.28, 174.51, 174.55 (Py–C-2,6).

$C_{137}H_{200}N_{12}O_{31}$	Calcd:	C 65.53	H 8.02	N 6.69
(2511.23)	Found.:	C 65.51	H 8.19	N 6.84.

Synthesis of Dendritic Benzyl Bromides (General Procedure)

Triphenylphosphine (1.3 equiv) was added to a mixture of the appropriate dendritic benzyl alcohol (1.0 equiv) and carbontetrabromide (1.3 equiv) in a minimum amount of dry tetrahydrofuran required to dissolve the above reagents, and the reaction mixture was stirred under argon for 15 min. For the second generation a larger excess of CBr_4 and PPh_3 was required to force the reaction to completion; these were added in amounts of 0.5 equiv in 30 min intervals until TLC and GPC showed no more starting material (up to 4 fold excess). The reaction mixture was then poured into water and extracted with CH_2Cl_2 (5×). The combined organic extract was dried with $MgSO_4$ and evaporated to dryness. The crude product was purified as described below.

3,5-Bis[2-(17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dion-29-yl)-oxyethoxy]-benzyl bromide **[G-1]-Br**

was prepared from **[G-1]-OH** and purified by column chromatography eluting with cyclohexane/ethyl acetate (3/1) to give **[G-1]-Br** as a colorless glassy solid. 150 mg scale, yield 90%, *m.p.* 98–102 °C (dec.). –IR (KBr): $\tilde{\nu}$/cm^{-1} = 2923, 2853 (C-H), 1645 (C=O), 1594 (arom.), 1458, 1410, 1351 (C-H), 1162–1030 (C–O). – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 0.93–1.32 (3 m, 26H, C$\underline{H}_2$-polymethylene), 1.40–1.81 (3 m, 11.5H, C$\underline{H}_2$CH$_2$–CO, polyether), 2.12–2.34 (m, 7.5H, N–C$\underline{H}_2$-polyether), 2.50, 3.02 (2 m$_c$, 1H), 3.26–3.96 (3 m, 31.7H, C$\underline{H}_2$–CO–N, polyether, C$\underline{H}_2$–OPy, C$\underline{H}_2$–OAr), 4.15, 4.18 (2 t, J = 3.6 Hz, J = 3.6 Hz, 0.6H), 4.30 (m$_c$, 0.6 H), 4.60–4.79 (m, 8H, C$\underline{H}_2$–Py, C$\underline{H}_2$-polyether), 4.89, 4.96, 4.99 (s, 2 dd, ^2J = 14 Hz, J = 1.9 Hz, ^2J = 14 Hz, J = 1.9 Hz, 2.6H, C$\underline{H}_2$–Py, Ar–C$\underline{H}_2$Br), 5.18 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.5H, C$\underline{H}_2$–Py), 5.40 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.3H, C$\underline{H}_2$–Py), 6.55 (d, J = 2.2 Hz, 0.7H, *EZ*-Py-$\underline{H}$), 6.59–6.67 (m, 5.5H, *ZZ*-Py-$\underline{H}$, Ar-$\underline{H}$), 6.77 (d, J = 2.2 Hz, 0.7H, *EZ*-Py-$\underline{H}$), 7.03 (s, 0.3H, *EE*-Py-$\underline{H}$). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 24.29, 24.33, 24.89 (C$\underline{H}_2$), 26.91, 27.47–28.62 (C$\underline{H}_2$), 31.96, 32.05, 33.97, 44.45, 48.00 (C$\underline{H}_2$–OAr), 50.36, 53.64, 54.87, 55.60 (C$\underline{H}_2$–OPy), 67.60, 69.87, 70.68, 70.71, 70.87, 70.92, 70.98, 71.03, 71.14 (Ar–C$\underline{H}_2$Br, Py–C$\underline{H}_2$), 76.81, 77.06, 77.32 (Py–C$\underline{H}_2$), 99.01, 99.54 (Ar–C-4), 104.62 (*ZZ*-Py–C-3,5), 105.79, 105.84 (*EZ*-Py–C-3,5), 105.98 (Ar–C-2,6), 107.41 (*EE*-Py–C-3,5), 145.06, 145.23 (Ar–C-1), 158.44 (Py–C-4), 158.84, 160.34 (Py–C-2,6), 160.46, 160.68 (Ar–C-3,5), 164.41, 164.55, 165.59, 165.74 (Py–C-2,6), 172.88, 172.91 (C=O), 174.51, 174.56 (Py–C-2,6).

$C_{65}H_{97}BrN_6O_{14}$	Calcd:	C 61.65	H 7.72	N 6.64
(1266.45)	Found:	C 61.53	H 7.65	N 6.58.

3,5-Bis{3,5-bis[2-(17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dion-29-yl)-oxyethoxy]-benzyloxy}-benzyl bromide **[G-2]-Br**

was prepared from **[G-2]-OH** and purified by column chromatography eluting with CH_2Cl_2/ethanol (15/1) to give **[G-2]-Br** as a colorless glassy solid. 100 mg scale, yield 92%, *m.p.* 117–119 °C (dec.). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2923, 2854 (C-H), 1661, 1642 (C=O), 1595, 1582 (arom.), 1458, 1409, 1355, 1304, 1210 (C-H), 1163–1031 (C–O). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 0.87–1.34 (3 m, 53.4H, C$\underline{H}_2$-polymethylene), 1.37–1.88 (2 m, 21.2H, C$\underline{H}_2$CH$_2$–CO, poly-ether), 1.99–2.32 (m, 15H, N–C$\underline{H}_2$-polyether), 2.51, 3.01 (2 m$_c$, 1.9H), 3.28–4.03 (3 m, 67.5H, C$\underline{H}_2$–CO–N, polyether, C$\underline{H}_2$–OPy), 4.15, 4.19 (2 t, J = 3.6 Hz, J = 3.6 Hz, 1.1H), 4.30 (m$_c$, 1.1H), 4.57–4.82 (m, 15.6H, C$\underline{H}_2$–Py, C$\underline{H}_2$-polyether), 4.88, 4.95, 4.99 (s, 2 dd, ^2J = 14 Hz, J = 1.9 Hz, ^2J = 14 Hz, J = 1.9 Hz, 5.3H, C$\underline{H}_2$–Py, Ar–C$\underline{H}_2$Br), 5.17 (dd, ^2J = 14 Hz, J = 1.9 Hz, 1.1H, C$\underline{H}_2$–Py), 5.40 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.5H, C$\underline{H}_2$–Py), 6.56 (d, J = 2.2 Hz, 1.4H, *EZ*-Py-$\underline{H}$), 6.51–6.69 (m, 13.2H, *ZZ*-Py-$\underline{H}$, Ar-$\underline{H}$), 6.77 (d, J = 2.2 Hz, 1.4H, *EZ*-Py-$\underline{H}$), 7.03 (s, 0.5H, *EE*-Py-$\underline{H}$). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 24.33, 24.88 ($\underline{C}H_2$), 26.87, 26.92, 26.96, 27.46–28.59 ($\underline{C}H_2$), 31.98, 32.07, 33.96, 44.58, 48.01 ($\underline{C}H_2$–OAr), 50.33, 50.60, 53.57, 54.87, 55.58 ($\underline{C}H_2$–OPy), 68.60, 69.91, 70.56, 70.72, 70.87, 70.93, 70.95, 71.04, 71.13, 72.58 (Ar–$\underline{C}H_2$Br, Py–$\underline{C}H_2$), 76.81, 77.07, 77.32 (Py–$\underline{C}H_2$), 99.00, 99.54 (Ar–$\underline{C}$-4), 104.42 (*ZZ*-Py–$\underline{C}$-3,5), 105.87, (*EZ*-Py–$\underline{C}$-3,5), 106.02 (Ar–$\underline{C}$-2,6), 107.44 (*EE*-Py–$\underline{C}$-3,5), 145.07, 145.25 (Ar–$\underline{C}$-1), 158.40 (Py–$\underline{C}$-4), 158.84, 160.45 (Py–$\underline{C}$-2,6), 160.67 (Ar–$\underline{C}$-3,5), 164.42, 164.57, 164.83 (Py–$\underline{C}$-2,6), 172.90, 172.93 (C=O), 174.51, 174.56 (Py–$\underline{C}$-2,6).

$C_{137}H_{199}BrN_{12}O_{30}$	Calcd:	C 63.93	H 7.81	N 6.53
(2574.13)	Found:	C 63.94	H 7.81	N 6.55.

Synthesis of Dendrimers with Divalent Cores (General Procedure)

A mixture of the appropriate dendritic benzyl bromide (2.1 equiv), 4,4'-dihydroxybiphenyl (**3**) (1 equiv), anhydrous potassium carbonate (3 equiv), and 18-crown-6 (0.4 equiv) in dry acetone was heated at reflux and stirred vigorously under argon for one week. The reaction mixture was allowed to cool and evaporated to dryness under reduced pressure. The residue was partitioned between water and CH_2Cl_2, the aqueous layer was extracted with CH_2Cl_2 (5×), and the combined organic layer was dried with $MgSO_4$ and evaporated to dryness. The crude product was purified as described below.

4,4'-Bis{3,5-bis[2-(17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dion-29-yl)-oxyethoxy]-benzyloxy}-biphenyl **[G-1]$_2$-[C2]**

was prepared from **[G-1]-Br** and purified by column chromatography eluting with CH_2Cl_2/ethanol (15/1) to give **[G-1]$_2$-[C2]** as a colorless glassy solid. 100 mg scale, yield 66%, *m.p.* 117–119 °C (dec.). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3421 (O-H), 2923, 2854 (C-H), 1661, 1642 (C=O), 1595 (arom.), 1458, 1409, 1355, 1304 (C-H), 1162–1030 (C–O). – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 0.91–1.33 (3 m, 52H, C$\underline{H}_2$-polymethylene), 1.39–1.77 (3 m, 24H, C$\underline{H}_2$CH$_2$–CO, polyether), 2.12–2.33 (m, 16H, N–C$\underline{H}_2$-polyether), 2.51, 3.05 (2 m$_c$, 2.4H), 3.27–3.98 (m, 62.5H, C$\underline{H}_2$–CO–N, polyether, C$\underline{H}_2$–OPy, C$\underline{H}_2$–OAr), 4.15, 4.18 (2 t, J = 3.6 Hz, J = 3.6 Hz, 1.3H), 4.30 (m$_c$, 1.4H), 4.60–4.79 (m, 15H, C$\underline{H}_2$–Py, C$\underline{H}_2$O-polymethylene), 4.89, 4.95, 4.99 (s, 2 dd, ^2J = 14 Hz, J = 1.9 Hz, ^2J = 14 Hz, J = 1.9 Hz, 4.1H, C$\underline{H}_2$–Py, Ar–C$\underline{H}_2$O-core), 5.17 (dd, ^2J = 14 Hz, J = 1.9 Hz, 1.1H, C$\underline{H}_2$–Py), 5.39 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.6H, C$\underline{H}_2$–Py), 6.56 (d, J = 2.2 Hz, 1.4H, *EZ*-Py-$\underline{H}$), 6.59–6.68 (m, 11H, *ZZ*-Py-$\underline{H}$, Ar-$\underline{H}$, core-$\underline{H}$), 6.78 (d, J = 2.2 Hz, 1.4H, *EZ*-Py-$\underline{H}$), 6.88 (d, J = 8 Hz, 3.9H, core-$\underline{H}$), 7.06 (s, 0.5H, *EE*-Py-$\underline{H}$), 7.38 (d, J = 8 Hz, 4.1H, core-$\underline{H}$). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 24.28, 24.33, 24.89 ($\underline{C}H_2$), 26.83, 27.44–28.60 ($\underline{C}H_2$), 31.96, 32.08, 33.96, 44.52, 48.05 ($\underline{C}H_2$–OAr), 50.38, 53.65, 54.88, 55.59 ($\underline{C}H_2$–OPy), 69.85, 70.72, 70.88, 70.92, 70.93, 70.95, 71.03, 71.06, 71.12, 72.64 (Ar–$\underline{C}H_2$O-core, Py–$\underline{C}H_2$), 76.79, 77.05, 77.30 (Py–$\underline{C}H_2$), 99.04, 99.60 (Ar–$\underline{C}$-4), 104.60 (*ZZ*-Py–$\underline{C}$-3,5), 105.86, 105.88 (*EZ*-Py–$\underline{C}$-3,5), 106.02 (Ar–$\underline{C}$-2,6), 107.42 (*EE*-Py–$\underline{C}$-3,5), 109.56, 110.39 (core-$\underline{C}$-3), 115.64 (core-$\underline{C}$-2), 132.83 (core-$\underline{C}$-1), 145.03, 145.22 (Ar–$\underline{C}$-1), 155.80 (core-$\underline{C}$-4), 158.79 (Py–$\underline{C}$-4), 160.39 (Py–$\underline{C}$-2,6), 160.64 (Ar–$\underline{C}$-3,5), 164.43, 165.59, 165.79 (Py–$\underline{C}$-2,6), 173.03 (C=O), 174.61, 174.68 (Py–$\underline{C}$-2,6).

$C_{142}H_{202}N_{12}O_{30}$	Calcd:	C 66.65	H 7.96	N 6.57
(2555.46)	Found:	C 66.41	H 7.94	N 6.45.

Synthesis of Dendrimers with Trivalent Cores (General Procedure)

A mixture of the appropriate dendritic benzyl bromide (3.2 equiv), 1,1,1-tris(4'-hydroxyphenyl)ethane (**4**) (1 equiv), anhydrous potassium carbonate (4.5 equiv), and 18-crown-6 (0.5 equiv) in dry acetone was heated at reflux and stirred vigorously under argon for one week. The reaction mixture was allowed to cool and evaporated to dryness under reduced pressure. The residue was partitioned between water and CH_2Cl_2, the aqueous layer was extracted with CH_2Cl_2 (5×), and the combined organic layer was dried with $MgSO_4$ and evaporated to dryness. The crude product was purified as described below.

1,1,1-Tris<4-{3,5-bis[2-(17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dion-29-yl)-oxyethoxy]-benzyloxy}-phenyl>-ethane **[G-1]$_3$-[C3]**

was prepared from **[G-1]-Br** and purified by column chromatography eluting with CH_2Cl_2/ethanol (15/1) to give **[G-1]$_3$-[C3]** as a colorless glassy solid. 150 mg scale, yield 81%, *m.p.* 118–120 °C (dec.). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2923, 2854 (C-H), 1661, 1643 (C=O), 1594 (arom.), 1458, 1409, 1354, 1304 (C-H), 1161–1032 (C–O). – ^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 0.91–1.33 (3 m, 78H, C$\underline{H}_2$-polyme-thylene), 1.39–1.75 (3 m, 35H, C$\underline{H}_2$CH$_2$–CO, polyether), 2.12–2.33 (m, 24H, N–C$\underline{H}_2$-polyether), 2.51, 3.05 (2 m$_c$, 2.9H), 3.26–3.96 (3 m, 98H, C$\underline{H}_2$–CO–N, polyether, C$\underline{H}_2$–OPy, C$\underline{H}_2$–OAr, Ar$_3$CC$\underline{H}_3$), 4.15, 4.18 (2 t, J = 3.6 Hz, J = 3.6 Hz, 1.6H), 4.30 (m$_c$, 1.4H), 4.60–4.79 (m, 22.4H, C$\underline{H}_2$-Py, Ar–C$\underline{H}_2$O-core), 4.89, 4.95, 4.99 (s, 2 dd, ^2J = 14 Hz, J = 1.9 Hz, ^2J = 14 Hz, J = 1.9 Hz, 5.8H, C$\underline{H}_2$–Py, Ar–C$\underline{H}_2$O-core), 5.17 (dd, ^2J = 14 Hz, J = 1.9 Hz, 1.6H, C$\underline{H}_2$–Py), 5.39 (dd, ^2J = 14 Hz, J = 1.9 Hz, 0.5H, C$\underline{H}_2$–Py), 6.54 (d, J = 2.2 Hz, 2.1H, *EZ*-Py-$\underline{H}$), 6.58–6.67 (m, 16.9H, *ZZ*-Py-$\underline{H}$, Ar-$\underline{H}$, core-$\underline{H}$), 6.69 (d, J = 8 Hz, 5.8H, core-$\underline{H}$), 6.76 (d, J =

2.2 Hz, 2H, *EZ*-Py-H), 6.90 (d, *J* = 8 Hz, 5.9H, core-H), 7.02 (s, 0.6H, *EE*-Py-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 24.15, 24.21, 24.24 (CH_2), 26.71, 27.37–28.49 (CH_2, Ar_3C-CH_3), 31.84, 31.95, 33.84, 44.34, 47.89, 47.91 (CH_2–OAr), 50.27, 55.48 (CH_2–OPy), 69.75, 70.59, 70.75, 70.81, 70.85, 70.90, 70.97, 70.99, 71.01 (Ar–CH_2O-core, Py–CH_2), 72.54 (Ar_3C-CH_3), 76.69, 76.95, 77.20 (Py–CH_2), 98.91, 99.46 (Ar–C-4), 104.51 (*ZZ*-Py–C-3,5), 105.64, 105.73 (*EZ*-Py–C-3,5), 105.89 (Ar–C-2,6), 107.27 (*EE*-Py–C-3,5), 109.46, 110.24, 114.46 (core-C-2), 129.51 (core-C-3), 141.03 (core-C-1), 144.92, 145.11 (Ar–C-1), 154.52 (core-C-4), 158.68 (Py–C-4), 160.20, 160.22 (Py–C-2,6), 160.53 (Ar–C-3,5), 164.31, 164.45 (Py–C-2,6), 172.83, 173.22 (C=O), 174.44, 174.49, 174.52 (Py–C-2,6).

$C_{215}H_{306}N_{18}O_{45}$	Calcd:	C 66.85	H 7.98	N 6.52
(3863.00)	Found:	C 66.71	H 7.80	N 6.43.

1,1,1-Tris⊂4-<3,5-bis{3,5-bis[2-(17,20,23-trioxa-1,14,33-triazatricyclo-[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dion-29-yl)-oxyethoxy]-benzyloxy}-benzyloxy>-phenyl⊃-ethane **[G-2]$_3$-[C3]**

was prepared from **[G-2]-Br** and purified by column chromatography eluting with CH_2Cl_2/ethanol (15/1) to give **[G-2]$_3$-[C3]** as a colorless glassy solid. 100 mg scale, yield 45%, *m.p.* 120–122 °C (dec.). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2922, 2854 (C-H), 1661, 1642 (C=O), 1595, 1581 (arom.), 1459, 1409, 1355, 1304, 1210 (C-H), 1162–1033 (C–O). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 0.88–1.37 (3 m, 160.5H, CH_2-polymethylene), 1.38–1.86 (2 m, 63.3H, CH_2CH_2–CO, polyether), 2.03–2.33 (m, 45H, N–CH_2-polyether), 2.48, 3.01 (2 m_c, 6.7H), 3.19–4.01 (3 m, 201.8H, CH_2–CO–N, polyether, CH_2–OPy, CH_2-OAr, Ar_3CCH_3), 4.14, 4.17 (2 t, *J* = 3.6 Hz, *J* = 3.6 Hz, 3.1H), 4.28 (m_c, 3.0H), 4.55–4.82 (m, 47.8H, CH_2–Py, Ar–CH_2O-core), 4.87, 4.93, 4.97 (s, 2 dd, ^2J = 14 Hz, *J* = 1.9 Hz, ^2J = 14 Hz, *J* = 1.9 Hz, 14.5H, CH_2–Py, Ar–CH_2O-core), 5.16 (dd, ^2J = 14 Hz, *J* = 1.9 Hz, 3.3H, CH_2–Py), 5.38 (dd, ^2J = 14 Hz, *J* = 1.9 Hz, 1H, CH_2–Py), 6.55 (d, *J* = 2.2 Hz, 3.5H, *EZ*-Py-H), 6.58–6.68 (m, 43H, *ZZ*-Py-H, Ar-H, core-H), 6.70 (d, *J* = 8 Hz, 5.7H, core-H), 6.77 (d, *J* = 2.2 Hz, 3.4H, *EZ*-Py-H), 6.89 (d, *J* = 8 Hz, 5.9H, core-H), 7.02 (s, 1.2H, *EE*-Py-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 24.19, 24.25, 24.81 (CH_2), 26.95, 27.47–28.54 (CH_2, Ar_3C-CH_3), 31.86, 32.03, 33.94, 44.49, 48.00, 48.11 (CH_2–OAr), 50.30, 55.58 (CH_2–OPy), 70.00, 70.63, 70.74, 70.88, 70.92, 70.96, 70.99, 71.07, 71.13 (Ar–CH_2O-core, Py–CH_2), 72.47 (Ar_3C-CH_3), 76.81, 77.07, 77.32 (Py–CH_2), 98.98, 99.52 (Ar–C-4), 104.92 (*ZZ*-Py–C-3,5), 105.79, 105.91 (*EZ*-Py–C-3,5), 106.10 (Ar–C-2,6), 107.48 (*EE*-Py–C-3,5), 109.84, 110.35, 114.60 (core-C-2), 129.64 (core-C-3), 145.10, 145.28 (core-C-1, Ar–C-1), 154.63 (core-C-4), 158.85 (Py–C-4), 160.44 (Py–C-2,6), 160.69 (Ar–C-3,5), 164.44, 164.59 (Py–C-2,6), 172.97, 173.29 (C=O), 174.54, 174.49, 174.60 (Py–C-2,6).

$C_{431}H_{612}N_{36}O_{93}$	Calcd:	C 66.49	H 7.92	N 6.48
(7786.02)	Found:	C 66.60	H 8.07	N 6.46.

References

[1] Concave Reagents 28: ref. [5a]
[2] G. R. Newkome, C. N. Moorefield, F. Vögtle, Dendritic Molecules: Concepts, Syntheses, Perspectives, VCH, Weinheim – New York – Basel – Cambridge – Tokyo 1996
[3] In this paper, only catalysts will be discussed but the arguments are valid for bound reagents as well.
[4] a) U. Lüning, Top. Curr. Chem. **1995**, *175*, 57; b) U. Lüning, J. Mater. Chem. **1997**, *7*, 175; c) U. Lüning, Molecular Recognition and Inclusion (A. W. Coleman, Ed.) **1998**, 203
[5] a) S. Petersen, U. Lüning, Eur. J. Org. Chem., in press; b) U. Lüning, S. Petersen, W. Schyja, W. Hacker, T. Marquardt, K. Wagner, M. Bolte, Eur. J. Org. Chem. **1998**, 1077; c) W. Schyja, S. Petersen, U. Lüning, Liebigs Ann. **1996**, 2099; d) Refs. cited in [5a–c]
[6] a) U. Lüning, R. Baumstark, M. Müller, Liebigs Ann. Chem. **1991**, 987; b) U. Lüning, R. Baumstark, K. Peters, H. G. v. Schnering, Liebigs Ann. Chem. **1990**, 129; c) U. Lüning, Liebigs Ann. Chem. **1987**, 949
[7] U. Lüning, M. Gerst, J. Prakt. Chem. **1992**, *334*, 656
[8] W. Hacker, Dissertation, Universität Freiburg 1996
[9] a) J. M. J. Fréchet, C. Hawker, J. Am. Chem. Soc. **1990**, *112*, 7638; b) J. M. J. Fréchet, C. Hawker, Chem. Commun. **1990**, 1010
[10] T. Marquardt, U. Lüning, Chem. Commun. **1997**, 1681

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