Enantiomerically Pure Dendrimers Based on a *trans*-3,4-Dihydroxypyrrolidine

Stefano Cicchi[a], Andrea Goti[b], Carlo Rosini*[c], and Alberto Brandi*[a]

Dipartimento di Chimica Organica "Ugo Schiff"[a],
Centro dei Composti Eterociclici C. N. R., Università degli Studi di Firenze[b],
Via G. Capponi 9, I-50121 Firenze, Italy
Fax: (internat.) +39-55/2476964
E-mail: brandi@chimorg.unifi.it

Dipartimento di Chimica, Università degli Studi della Basilicata[c],
Via N. Sauro 85, I-85100 Potenza, Italy
Fax: (internat.) + 39-971/474223
E-mail: rc204sci@unibas.it

Received June 30, 1998

Keywords: Cascade molecules / Dendrimers / Chirality / Amides

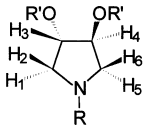
The synthesis of the first and second generation of enantiopure dendrimers based on a chiral *trans*-3,4-dihydroxypyrrolidine is reported. Benzenepolycarboxylic acids were used as central nucleus to afford linear and radial growth, and terephthalic acid was used as spacer between the pyrrolidine nuclei. The analysis of the chiroptical properties ($[\alpha]_D$, circular dichroism) of these new dendrimers suggests that those with radial growth present a self organisation of chiral units.

Since the publication of the first work[1] on cascade molecules the research in this area has flourished, addressing various aspects of the subject, like the synthesis of new dendrimeric molecules,[2] their physical properties,[3] and their applications.[4]

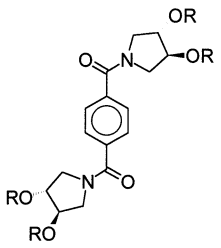
Despite of the large body of structures assembled, a limited, even if rapidly increasing, number of enantiomerically pure dendrimers was synthesised.[5] Meijer divided the group of chiral dendrimers, already synthesised or not, into seven classes[5], differing in the part of the molecule bearing the chiral information. These classes reflect the complexity and the variety of the structures and the peculiar properties that can be provided by these materials. The research efforts are directed both towards the synthesis of new chiral molecules for applications in the field of molecular recognition[2a] as well as towards a deeper comprehension of the concept of chirality in molecules characterised by a high degree of symmetry.[5] The chiral dendrimeric molecules already synthesised may have a chiral core[6], or the stereogenic centres may reside on the branches[7] or on the groups laying on the surface.[8] We turned our attention on chiral dendrimers with stereogenic centres on the branches and noted that often the chirality resides on spacers between the branching units.[7c][7d] Chiral branching units are often represented by amino acids[7e] or, in one example reported by Seebach, by a chiral triol.[7a]

In this work we report on the synthesis of a new family of enantiopure dendrimers **4**–**9** (Schemes 1 and 2) based on a chiral pyrrolidine nucleus **1** derived from (3*S*,4*S*)-*N*-benzyl-3,4-dihydroxypyrrolidine (**2**).[9] Compound **1** revealed an ideal AB_2 monomer since it is easily obtained

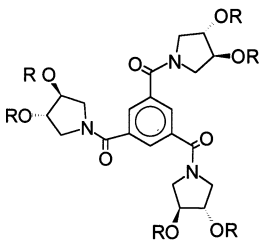
Scheme 1



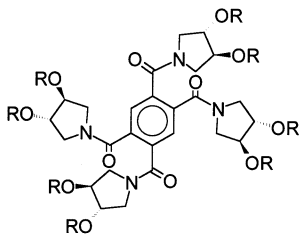
1 R = R' = H
2 R = CH_2Ph, R' = H
3 R = H, R' = Si*t*-BuMe_2



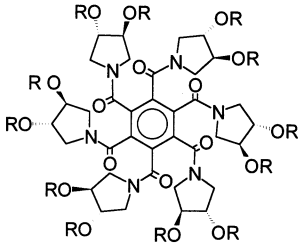
4 R = TBDMS (100%)



6 R = TBDMS (87%)



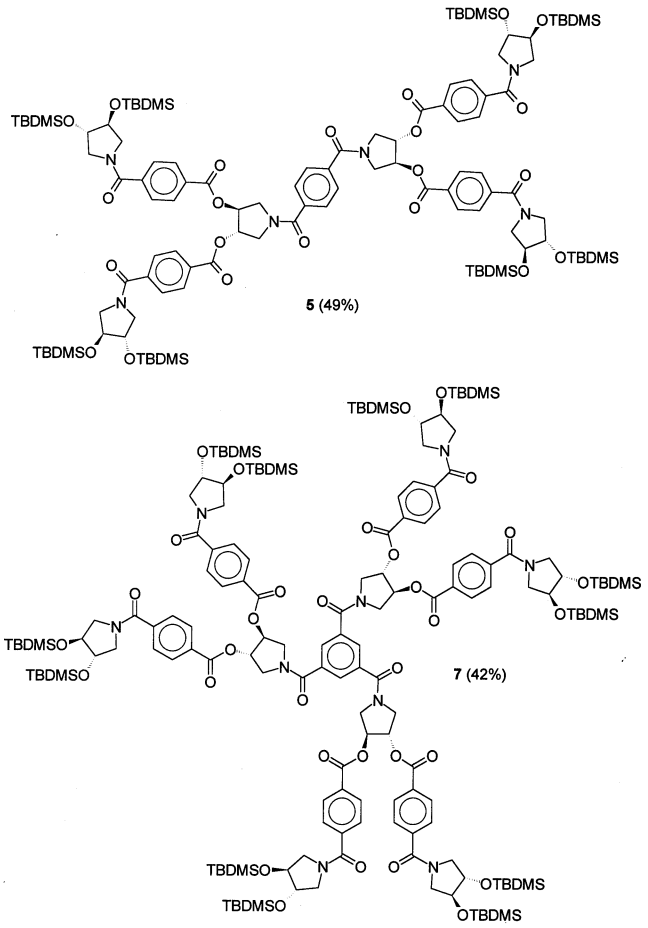
8 R = TBDMS (70%)



9 R = TBDMS (44%)

  1434–193X/98/1111–2591 $ 17.50+.50/0

Scheme 2



from tartaric acid in both enantiomeric forms in crops of 20−30 g and the three functional groups present on the ring can be selectively protected and subjected to reaction. This allows an easy branching of the intermediate dendrons and their coupling with the central nucleus in a convergent synthetic approach. The two stereogenic centres on the pyrrolidine ring allow a tridimensional growth of the branch in a stereodefined manner due to the dihedral angle between the two hydroxylic functions.

Benzene polycarboxylic acids have been selected as dendrimer nuclei to afford a linear and radial growth of the molecules and, at the same time, to confer a central rigidity to these molecules. The high concentration of polar groups (amide and ester groups) in the final molecules should provide strong enthalpic contribution to guest binding due to hydrogen bonding.

The first generation molecules **4**, **6**, **8**, and **9** were produced by the reaction of pyrrolidine **3**[10] with the correspondent acyl chloride in Schotten-Baumann conditions (Scheme 1). The successful synthesis of the hexasubstituted derivative **9** in acceptable yield shows how this reaction is moderately influenced by the steric hindrance, allowing the reaction of all the six functional groups on the benzene ring.

^{1}H- and ^{13}C-NMR spectroscopic analysis revealed the high symmetry of the structures and a common spectral pattern for the first generation molecules. Due to the hindered rotation around the amide bonds all the atoms on the five-membered ring are nonequivalent and give resonances that are only slightly differentiated going from **4** to **9** (see Tables 1 and 2). The highest deviation is observed for N-CH_2 protons in compound **9**, but this must be clearly related to the peculiar assembly of the pyrrolidine units around the highly substituted phenyl ring. The IR C=O stretching frequencies increase from **4** to **9** (see Table 2) attesting to a lowering of the "amide character" of the C=O group or the release from a coplanarity of the system, caused by the increasing steric hindrance around the phenyl ring in these compounds. The ^{13}C NMR quaternary signals of the central core move upfield with the same sequence, confirming the decreasing of the conjugation of the system. The C=O groups also show a similar trend that, however, appears at the moment to be contradictory.

The synthesis of the second generation molecules was accomplished by a convergent approach[11] using terephtalic acid as a spacer between the pyrrolidine nuclei. The first and second generation dendrons **10** and **12** were synthesised according to scheme 3.

The synthesis of compound **10** was accomplished in a one-step process by treating pyrrolidine **3** with an excess of terephthaloyl chloride in pyridine as a solvent, followed by addition of benzyl alcohol. Debenzylation of **10** and coupling with pyrrolidine **1** mediated by dicyclohexylcarbodiimmide afforded the second generation dendron **12** in 38% overall yield. The debenzylation of **12** gives **13** ready to be coupled with a nucleus to afford the second generation dendrimer. This convergent approach can be reiterated to afford higher generation dendrons. Coupling of **13** with the appropriate acyl chloride in the simple Schotten-Baumann condition proved to be successful and afforded, in 49% and 42% yield, respectively, the second generation dendrimers **5** and **7** (see Scheme 2).

Nuclear magnetic resonance analysis is of key importance for the structural assignment as **5** and **7**, particularly to assess the symmetric feature of the molecules which should be guaranteed by the convergent approach to the synthesis. In particular, two broad singlets at δ = 5.6, assigned to the HCOR protons of the pyrrolidine rings of the inner layer, were diagnostic for **7** (Scheme 2). These protons are probably nonequivalent because of hindered rotation around the amide bond. A sharp signal emerging from aromatic resonances of the outer terephthalic group (δ = 8.06) was assigned to the three equivalent hydrogen atoms of the central aromatic ring. For the outer pyrrolidine rings ^{1}H and ^{13}C spectra presented a pattern of signals similar to the first generation molecules with six distinct resonances for the six hydrogen atoms of the ring. In all cases a careful integration of signals related to the groups of nonequivalent hydrogen atoms confirmed the theoretical ratio expected for these molecules.

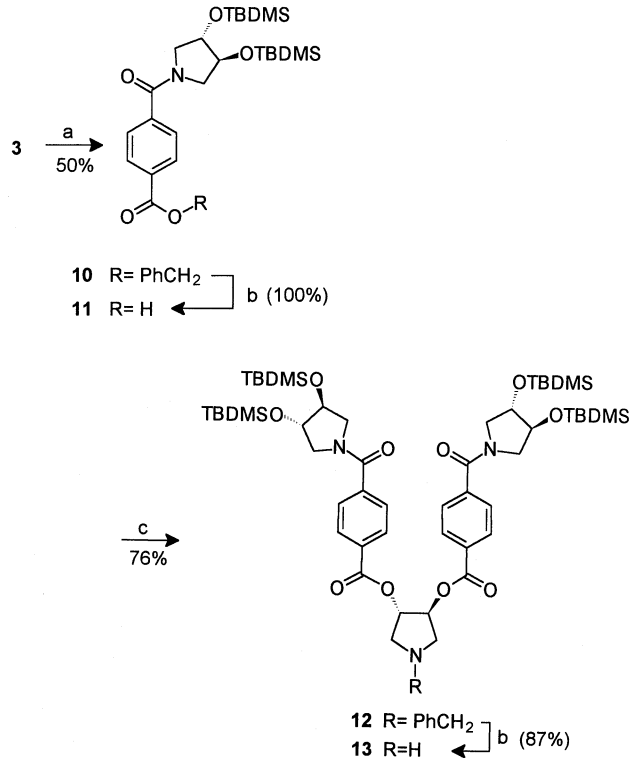
Table 1. ^{1}H-NMR data of compounds **4**, **6**, **8**, and **9**

	Aromatic H	H^1 H^6	H^2 H^5	H^3 H^4	Me_3C-Si	Me−Si
4	7.52 (s, 4 H)	3.52 (d, J = 12.8 Hz, 2 H) 3.17 (d, J = 11.0 Hz, 2 H)	3.87 (dd, J = 12.6, 4.2 Hz, 2 H) 3.64 (dd, J = 11.0, 3.7 Hz, 2 H)	4.08 (bs, 2 H) 3.95 (bs, 2 H)	0.90 (s, 18 H) 0.82 (s, 18 H)	0.12 (s, 6 H) 0.10 (s, 6 H) 0.04 (s, 6 H) −0.02 (s, 6 H)
6	7.74 (s, 3 H)	3.52 (d, J = 12.8 Hz, 3 H) 3.19 (d, J = 11.0 Hz, 3 H)	3.89 (dd, J = 13.0, 3.8 Hz, 3 H) 3.73 (dd, J = 10.6, 3.2 Hz, 3 H)	4.09 (bs, 3 H) 3.96 (bs, 3 H)	0.90 (s, 27 H) 0.83 (s, 27 H)	0.12 (s, 9 H) 0.11 (s, 9 H) 0.04 (s, 9 H) −0.02 (s, 9 H)
8	7.35 (s, 2 H)	3.40 (dd, J = 12.4, 3.0 Hz,4 H) 3.08 (dd, J = 10.7, 3.0 Hz, 4 H)	3.81 (dd, J = 12.4, 5.0 Hz, 4 H) 3.73 (dd, J = 10.8, 4.5 Hz, 4 H)	4.07 (q, J = 4.0 Hz, 4 H) 3.99 (q, J = 3.9 Hz, 4 H)	0.90 (s, 36 H) 0.83 (s, 36 H)	0.12 (s, 24 H) 0.11 (s, 12 H) 0.04 (s, 12 H)
9	–	3.12 (m, 12 H)	3.72 (dd, J = 12.0, 6.1 Hz, 6 H) 3.65 (dd, J = 11.5 , 6.0 Hz, 6 H)	4.07 (q, J = 6.1 Hz, 6 H) 3.95 (q, J = 6.0 Hz, 6 H)	0.83 (s, 54 H) 0.90 (s, 54 H)	0.12 (s, 36 H) 0.11 (s, 18 H) 0.04 (s, 18 H)

Table 2. IR (selected) and ^{13}C-NMR data of compounds **4**, **6**, **8**, and **9**

	IR (C=O)	^{13}C (*ipso C*)	^{13}C (C−H)	^{13}C (C=O)	^{13}C (N−CH_2)	^{13}C (O−CH)	^{13}C (Me_3C−Si)	^{13}C (Me_3C−Si)	^{13}C (Me−Si)
4	1616	138.2 (2)	127.1 (4)	169.7 (2)	55.2 (2) 52.5 (2)	76.3 (2) 75.2 (2)	25.7 (6) 25.5 (6)	17.9 (2) 17.8 (2)	−4.8 (4) −5.0 (4)
6	1623	137.3 (3)	127.6 (3)	168.7 (3)	55.4 (3) 52.9 (3)	76.4 (3) 75.2 (3)	25.8 (9) 25.6 (9)	17.8 (6)	−4.7 (12)
8	1634	136.4 (4)	125.5 (2)	167.5 (4)	53.7 (4) 51.6 (4)	76.3 (4) 75.3 (4)	25.7 (12) 25.6 (12)	17.8 (4) 17.7 (4)	−4.8 (8) −4.9 (8)
9	1651	132.8 (6)	–	165.3 (6)	51.4 (6) 50.3 (6)	75.8 (6) 75.2 (6)	25.8 (36)	18.0 (6) 17.7 (6)	−4.5 (6) −4.7 (12) −5.0 (6)

Scheme 3



a) i: **3**, terephthaloyl chloride, pyridine; ii: benzyl alcohol. − b) H_2/$Pd(OH)_2$. − c) **2**, DCC, DMAP

Φ/*N* (molar rotatory power divided by number of chiral units) is a parameter often used to derive structural information for dendrimeric compounds.[7b][12] In the present case the chiral units are the pyrrolidine rings present in the compound. The numerical values of this parameter are collected in Table 3.

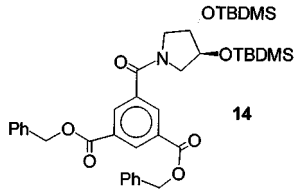
Table 3. Chiroptical properties of compounds **4**−**10** and **14**

Entry	Compound	$[\alpha]_D^{20}$	Φ	Φ/chiral unit
1	**10**	−22.7	−129.2	−129.2
2	**4**	−30.5	−241.9	−120.9
3	**5**	−32.4	−706.3	−117.7
4	**14**	−32.5	−228.4	−228.4
5	**6**	−49.7	−600.0	−200.0
6	**7**	−40.4	−1307.3	−145.3
7	**8**	11.9	179.5	44.9
8	**9**	39.7	882.6	147.1

Entries 1−3 refer to linear-growth compounds and entries 4−6 refer to radial-growth compounds. It is noteworthy that the linear compounds show a very similar value of Φ/*N* (ca. -122) (Table 3, entries 1−3), indicating that there is almost complete additivity of contributions to the molar rotatory power. This is generally assumed as an indication of the absence of chiral conformations for the dendrimeric compounds: the subunits must be completely independent of each other without any self-organization.[12a] On

the contrary, for the radial-growth dendrimers **7** and **6** and for the model compound **14** (Scheme 4), such an additivity is not observed.

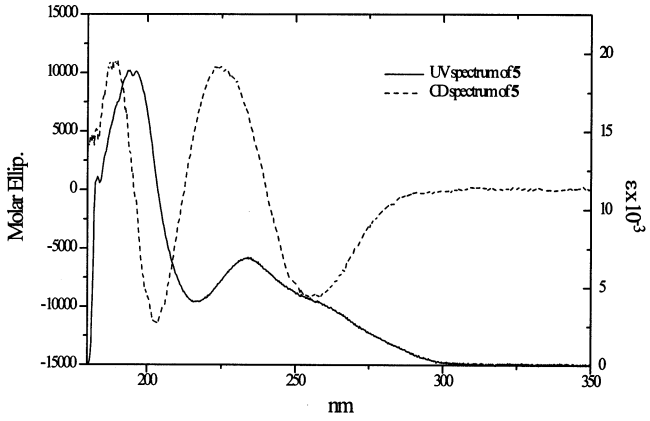
Scheme 4



In fact the molar rotatory power of **14**, i. e. a simple 1,3,5-trisubstituted benzene derivative having only a chiral pyrrolidine residue, is −228, whereas for **6** and **7** it is −200 and −145, respectively. The rotation of **7** clearly does not fit with the sum of the contributions of the single units. For tetra- and hexasubstituted compounds **8** and **9** (entries 6 and 7, Table 3) there is not a constant contribution which can be attributed to a single chiral unit, because the Φ/N parameter changes in absolute value and even in sign.

In order to verify the significance of the additivity phenomena discussed above a deeper study of the chiroptical properties of these compounds was carried out by measuring and comparing their CD spectra. The CD spectra of compounds **4**, **5**, **6**, **7**, and **12** were recorded in the 350−185 nm spectral range, in acetonitrile as solvent.

Figure 1. UV and circular dichroism spectra of compound **5**



The electronic absorption and CD spectra of compound **5** are reported in Figure 1 and chosen as representative. The UV spectrum shows two main regions of absorption: a first one between 350 and 220 nm, characterised by a maximum centred at about 230 nm with a shoulder at ca. 260 nm and a second one (220−185 nm) which presents a strong absorption at 190 nm. The CD spectrum shows a sequence of Cotton effects having -, +, -, + signs going from 350 to 185 nm. The intensities of the peaks are related to the number of the aromatic groups present. It is reasonable that both the electronic absorption and the CD spectrum of **5** are dominated by electronically allowed π-π* transitions localised on the aromatic moieties and, in particular, that the CD Cotton effects are related to the exciton coupling of the above transitions.[13] However, instead of trying to analyse the spectra of all the compounds in order to formulate simple correlations with the structure, we used the spectra of the model compounds to predict the spectra of the dendrimers **5** and **7**, in order to verify the additivity relationships of the molar rotatory power. Taking into account what has been discussed before (i.e. the CD spectra are dominated by exciton-coupled allowed π-π* transitions) compound **5** can be considered as consisting of two units of compound **12** plus one unit of compound **4** and compound **7** can be considered, approximately, to derive from three units of compound **12** plus one unit of **6**. The relationships in Eqs. 1 and 2 can be derived, which relate the CD spectrum of **5** or **7** to the CD spectra of their constituents.

$$CD(\mathbf{5}) = 2 \times CD(\mathbf{12}) + CD(\mathbf{4}) \quad (1)$$

$$CD(\mathbf{7}) = 3 \times CD(\mathbf{12}) + CD(\mathbf{6}) \quad (2)$$

It is interesting to note, at this point, that we use simple algebraic combinations of spectra without the need of the knowledge of the origin of the various Cotton effects observed.

Figure 2. Experimental and calculated circular dichroism (CD) spectra of compound **5**

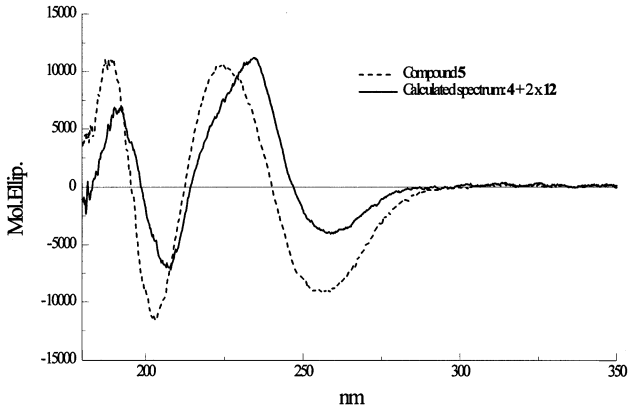
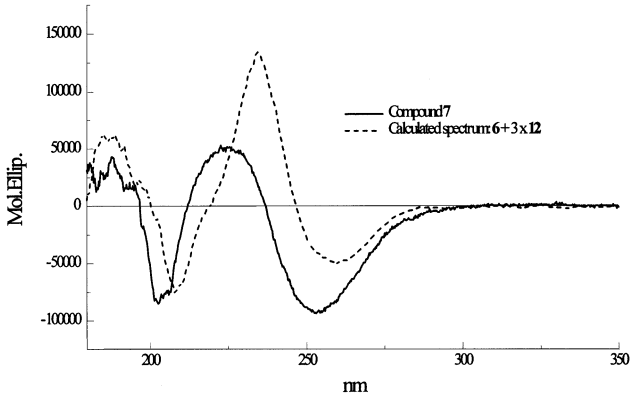


Figure 3. Experimental and calculated circular dichroism (CD) spectra of compound **7**



A comparison of the experimental spectrum of compound **5** and that calculated according to Eq. 1 (Figure 2) shows that there is a particularly good agreement between the two spectra in terms of position, sign and intensity of

the measured Cotton effects. This results fits with the observation of the additivity of the optical rotation and strongly suggests that in **5** each chiral unit provides its own contribution to the chiroptical properties and this contribution is independent of the contribution provided by the other units. The single constituents must then be independent of one another. When the same calculation, applying Eq. 2, is repeated for **7** the agreement between the calculated and the experimental spectrum is much worse (Figure 3), particularly in the 210−230 nm range. In summary, the CD analysis seems to confirm the observation from optical rotation that the chiroptical properties are additive in the case of the linear dendrimer **5** and not in the case of the radial dendrimer **7**. Therefore, following McGrath[14] in the first case "... the conformational equilibria for the model compound(s) and the monomeric units of the dendrimer are similar", whilst in the case of the radial dendrimer **7**, each chiral subunit could be not independent of the other, but, reasonably, there is some extent of self-organisation of the monomeric units in a chiral conformation, so that the CD spectrum cannot be expressed as the sum of individual contributions.

An X-ray crystallographic analysis to prove the presence of a stable chiral conformation for our radial dendrimers would be necessary, but compound **6** failed to give an ordered single crystal. As a second option, a molecular mechanics calculation (MACROMODEL, force field MM2, Montecarlo method) study of **6** suggested that in the lowest energy conformation all the pyrrolidine rings are on the same side of the aromatic ring as the carboxyamide group, thus forming a left-handed helix. Such a conformation is 7 kcal mol^{-1} more stable than a conformation with one of the three carbonyl groups on the opposide side of the aromatic ring. In the most stable conformation three carbonyl groups form a dihedral angle of 56° with the plane of the central ring.[15] The molecule then assumes a bell-shaped conformation with a helical arrangement that would produce another element of symmetry and might be responsible of the observed lack of additivity.

A helical arrangement of amide residues has been very recently reported for an optically active C_3 derivative of trimesic acid.[16] Such chiral arrangement was induced by lateral asymmetrically substituted groups and has found application in supramolecular chemistry.

A bell-shaped conformation of dendrimer **6** is highly relevant for applications in molecular recognition, as it would resemble an enzyme cavity with many possible donor-acceptor interactions. The synthesis of other derivatives which will contribute to the understanding of the preferred conformations of the radial-growth dendrimers is under way in our laboratory.

The authors thank *M. U. R. S. T. (Ministero dell'Università e della Ricerca Scientifica e Tecnologica-Italy)* for financial support. Dr. *Maria Caporali* and Dr. *Elisa Chierroni* are also gratefully acknowledged for their contribution during the thesis work.

Experimental Section

General: All operations were carried out under inert gas and with anhydrous solvents where required. − R_f values refer to TLC on 0.25-mm silica gel plates (Merck F_{254}) with the same eluent used for the chromatographic separation of the compound. −Melting points (mp) are uncorrected. − ^{1}H- and ^{13}C-NMR spectra (in $CDCl_3$ solution) were recorded at 200 MHz and 50 MHz, respectively, with a Varian Gemini; the chemical shifts for ^{1}H- and ^{13}C-NMR spectra are given in ppm from TMS. − IR spectra were recorded with a Perkin-Elmer 881 spectrophotometer. − Optical rotation measurements were carried out with a Jasco DIP-370 polarimeter. − Circular dichroism spectra (CH_3CN solution) were recorded with a Jasco J-600 polarimeter. − Pyrrolidine **3** was synthesised according to ref.[10]

Benzyl (3′S,4′S)-4-[3′,4′-Bis[(tert-butyldimethylsily)oxy]pyrrolidinocarbonyl]benzoate (**10**): In a 1-l round-bottomed flask 9.75 g (48 mmol) of terephthaloyl chloride and 122 mg (1 mmol) of DMAP were dissolved in 400 ml of dry CH_2Cl_2. The solution was cooled in an ice bath and 4 g (12 mmol) of pyrrolidine **3**, dissolved in 20 ml of dry pyridine, was added through a dropping funnel. The resulting solution was stirred for 1 h at 0°C and then 8.7 ml (84 mmol) of benzyl alcohol was added. The solution was left overnight at room temperature then washed with 1 N HCl and brine. The organic phase was dried with Na_2SO_4 and concentrated. The residue was purified by passage through a short pad of silica gel to give 3.4 g of **10** (50%) as a colourless oil. − R_f (CH_2Cl_2/diethyl ether, 20:1) = 0.59. − $[\alpha]_D^{20} = -22.7$ (c = 1.055, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2958 cm^{-1} (C−H), 1726 (O−C=O), 1620 (N−C=O), 1097 (C−O). − ^{1}H NMR ($CDCl_3$): δ = −0.06 (s, 3 H, *Me*Si), 0.01 (s, 3 H, *Me*Si), 0.08 (s, 3 H, *Me*Si), 0.09 (s, 3 H, *Me*Si), 0.80 (s, 9 H, *tBu*Si), 0.88 (s, 9 H, *tBu*Si), 3.13 (d, J = 11 Hz, 1 H, C*H*N), 3.52 (d, J = 12.8 Hz, 1 H, C*H*N), 3.64 (dd, J = 11, 3.3 Hz, 1 H, C*H*N), 3.87 (dd, J = 12.8, 4.1 Hz, 1 H, C*H*N), 3.95 (s, 1 H, C*H*OSi), 4. 07 (s, 1 H, C*H*OSi), 5.32 (s, 2 H, CH_2Ph), 7.35 (m, 5 H, aromatic H), 7.52 (d, J = 8.5 Hz, 2 H, aromatic H), 8.08 (d, J = 8 Hz, 2 H, aromatic H), − ^{13}C NMR ($CDCl_3$): δ = −5.2 (q, 2 C, *Me*Si), −5.0 (q, 2 C, *Me*Si), 17.5 (s, 1 C, *C*Si), 17.6 (s, 1 C, *C*Si), 25.3 (q, 3 C, *tBu*Si), 25.5 (q, 3 C, *tBu*Si), 52.3 (t, 1 C, *C*H_2N), 54.9 (t, 1 C, *C*H_2N), 66.6 (t, 1 C, *C*H_2Ph), 74.9 (d, 1 C, *C*OSi), 76.0 (d, 1 C, *C*OSi), 126.8 (d, 2 C, aromatic C), 127.9 (d, 1 C, aromatic C), 128.0 (d, 2 C, aromatic C), 128.3 (d, 2 C, aromatic C), 129.5 (d, 2 C, aromatic C), 130.9 [s, 1 C, =*C*(C=O)N], 135.5 (s, 1 C, =*C*CH_2O), 140.9 [s, 1 C,=*C*(C=O)O], 165.3 (s, 1 C, O*C*=O), 169.1 (s, 1 C, N*C*=O). − MS (70 eV); *m/z*: 469, 239, 147, 91, 73, 57. − $C_{31}H_{47}NO_5Si_2$ (569.7): calcd. C 65.34, H 8.31, N 2.46; found C 65.52, H 8.25, N 2.48.

(3′S,4′S)-4-[3′,4′-Bis[(tert-butyldimethylsily)oxy]pyrrolidinocarbonyl]benzoic Acid (**11**): A solution of 1.27 g (2.23 mmol) of **10** in 15 ml of MeOH was added to 600 mg of 20% $Pd(OH)_2$/C and stirred under hydrogen overnight. The suspension was filtered through a Celite pad and the resulting solution concentrated to afford 1.07 g of the free acid **11** (100%) which was used for next reaction without further purification. − IR ($CHCl_3$): $\tilde{\nu}$ = 3046 cm^{-1} (C−H), 2933 (C−H), 1736 (O−C=O), 1627 (N−C=O), 1102 (C−O). − ^{1}H NMR ($CDCl_3$): δ = −0.03 (s, 3 H, *Me*Si), 0.04 (s, 3 H, *Me*Si), 0.10 (s, 3 H, *Me*Si), 0.12 (s, 3 H, *Me*Si), 0.83 (s, 9 H, *tBu*Si), 0.90 (s, 9 H, *tBu*Si), 3.16 (d, J = 10.6 Hz, 1 H, C*H*N), 3.56 (d, J = 10.6 Hz, 1 H, C*H*N), 3.67 (dd, J = 10.8, 3.6 Hz, 1 H, C*H*N), 3.92 (dd, J = 12.8, 4.4 Hz, 1 H, C*H*N), 3.97 (s, 1 H, C*H*OSi), 4.10 (s, 1 H, C*H*OSi), 7.58 (d, J = 8.4 Hz, 2 H, aromatic H), 8.15 (d, J = 8.4 Hz, 2 H, aromatic H), 10.20 (br. s, 1 H, O*H*). − ^{13}C NMR ($CDCl_3$): δ = −5.0 (q, 2 C, *Me*Si), −4.8 (q, 2

C, *Me*Si), 17.8 (s, 1 C, *C*-Si), 17.9 (s, 1 C, *C*Si), 25.6 (q, 3 C, *tBu*Si), 25.7 (q, 3 C, *tBu*Si), 52.7 (t, 1 C, *C*H_2N), 55.3 (t, 1 C, *C*H_2N), 75.1 (d, 1 C, *C*HO), 76.3 (d, 1 C, *C*HO), 127.1 (d, 2 C, aromatic C), 130.2 (d, 2 C, aromatic C), 130.9 [s, 1 C, =*C*(C=O)N], 141.4 [s, 1 C, =*C*(C=O)O], 169.6 (s, 1 C, N*C*=O), 170.4 (s, 1 C, O*C*=O). − MS (70 eV); *m/z*: 479, 422, 149, 73.

Diester **12**: A solution of 504 mg (1.05 mmol) of **11** in 10 ml of dry CH_2Cl_2 was added with 101 mg (0.52 mmol) of pyrrolidine **2** and 10 mg of DMAP. To the resulting solution, cooled at 0°C, was added 217 mg (1.052 mmol) of DCC and left stirring at room temperature for 24 h. The final suspension was filtered through a Celite pad and the oil obtained by evaporation of the solvent was purified by passage through a short pad of silica gel to afford 450 mg of **12** (76%) as a pale yellow oil. − R_f (CH_2Cl_2/diethyl ether, 10:1) = 0.42. − $[\alpha]_D^{20}$ = 16.2 (*c* = 0.96, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2956 cm^{-1} (CH), 1718 (O−C=O), 1621 (N−C=O), 1103 (C−O). − ^{1}H NMR ($CDCl_3$): δ = −0.03 (s, 6 H, *Me*Si × 2), 0.04 (s, 6 H, *Me*Si × 2), 0.10 (s, 6 H, *Me*Si × 2), 0.12 (s, 6 H, *Me*Si × 2), 0.83 (s, 18 H, *tBu*Si × 2), 0.90 (s, 18 H, *tBu*Si × 2), 2.79 (dd, *J* = 11.8, 4.1 Hz, 2 H, C*H*N × 2), 3.12 (d, *J* = 10.6 Hz, 2 H, C*H*N × 2), 3.29 (dd, *J* = 10.1, 6.4 Hz, 2 H, C*H*N × 2), 3.49 (d, *J* = 2.9 Hz, 2 H, C*H*N × 2), 3.64 (dd, *J* = 11.0, 3.3 Hz, 2 H, C*H*N × 2), 3.72 (s, 2 H, PhCH_2N), 3.89 (dd, *J* = 12.6, 4.0 Hz, 2 H, C*H*N × 2), 3.96 (br. s, 2 H, C*H*OSi × 2), 4.09 (br. s, 2 H, C*H*OSi × 2), 5.56 (m, 2 H, C*H*OC=O × 2), 7.33 (m, 5 H, aromatic H), 7.56 (d, *J* = 8.2 Hz, 4 H, aromatic H), 8.10 (d, *J* = 8.2 Hz, 4 H, aromatic H). − ^{13}C NMR ($CDCl_3$): δ = −4.8 (q, 4 C, *Me*Si × 4), −4.6 (q, 4 C, *Me*Si × 4), 17.7 (s, 2 C, *C*Si × 2), 17.9 (s, 2 C, *C*Si × 2), 25.5 (q, 6 C, *tBu*Si), 25.6 (q, 6 C, *tBu*Si), 52.5 (t, 2 C, *C*H_2N × 2), 55.1 (t, 2 C, *C*H_2N × 2), 58.0 (t, 2 C, *C*H_2N × 2), 59.6 (t, 1 C, Ph*C*H_2N), 75.0 (d, 2 C, *C*HOSi × 2), 76.2 (d, 2 C, *C*HOSi × 2), 78.4 (d, 2 C, *C*HOC=O × 2), 127.0 (d, 4 C, aromatic C), 127.3 (d, 1 C, aromatic C), 128.3 (d, 2 C, aromatic C), 128.7 (d, 2 C, aromatic C), 129.8 (d, 4 C, aromatic C), 130.6 [s, 2 C, =*C*(C=O)N × 2], 137.5 (s, 1 C, =*C*CH_2), 141.4 [s, 2 C, =*C*(C=O)O × 2], 165.2 (s, 2 C, O*C*=O × 2), 169.2 (s, 2 C, N*C*=O × 2). − $C_{59}H_{93}O_{10}N_3Si_4$ (1116.4): calcd. C 63.44, H 8.41, N 3.76; found C 63.38, H 8.42, N 3.42.

Amine **13**: To a solution of 440 mg (0.395 mmol) of **12** in 6 ml of MeOH was added 220 mg of $Pd(OH)_2$/C and the mixture was stirred under hydrogen overnight. The suspension was then filtered through a Celite pad and the solution concentrated to afford crude 350 mg of **13** (87%) as a colourless oil which was used without further purification. − ^{1}H NMR ($CDCl_3$): δ = −0.05 (s, 6 H, *Me*Si × 2), 0.02 (s, 6 H, *Me*Si × 2), 0.09 (s, 6 H, *Me*Si × 2), 0.10 (s, 6 H, *Me*Si × 2), 0.81 (s, 18 H, *tBu*Si × 2), 0.89 (s, 18 H, *tBu*Si × 2), 3.10 (d, *J* = 10.6 Hz, 2 H, C*H*N × 2), 3.51 (d, *J* = 13.2 Hz, 2 H, C*H*N × 2), 3.75−3.60 (m, 4 H, C*H*N × 4), 3.90−3.80 (m, 4 H, C*H*N × 4), 3.95 (br. s, 2 H, C*H*OSi × 2), 4.07 (br. s, 2 H, C*H*OSi × 2), 5.68 (br. s, 2 H, C*H*OC=O × 2), 7.56 (d, *J* = 8.2 Hz, 4 H, aromatic H), 8.14 (d, *J* = 8.2 Hz, 4 H, aromatic H). − ^{13}C NMR ($CDCl_3$): δ = −4.9 (q, 8 C, *Me*Si × 8), 17.7 (s, 2 C, *C*Si × 2), 17.8 (s, 2 C, *C*Si × 2), 25.5 (q, 6 C, *tBu*Si × 2), 25.6 (q, 6 C, *tBu*Si × 2), 49.2 (t, 2 C, *C*H_2N × 2), 52.5 (t, 2 C, *C*H_2N × 2), 55.1 (t, 2 C, *C*H_2N × 2), 75.1 (d, 2 C, *C*HOSi × 2), 75.3 (d, 2 C, *C*HOSi × 2), 76.2 (d, 2 C, *C*HOC=O × 2), 127.2 (d, 4 C, aromatic C), 129.3 [s, 2 C, =*C*(C=O)N × 2], 130.2 (d, 4 C, aromatic C), 141.9 [s, 2 C, =*C*(C=O)O × 2], 164.3 (s, 2 C, O*C*=O × 2), 169.0 (s, 2 C, N*C*=O × 2).

First and Second Generation Dendrimers **4−9**. − *General Procedure:* In a 250-ml round-bottomed flask 5 mmol of pyrrolidine (**3** for first generation dendrimers and model compound **14**, **13** for second generation) were dissolved in 40 ml of toluene together with 40 ml of NaOH (2 N). The suspension was kept at 0°C in an ice bath and a solution of the acyl chloride (1 equiv.) in 15 ml of toluene was added dropwise over 15 min. The organic layer was separated and the aqueous phase was extracted twice with diethyl ether (20 ml each). The organic phase was then washed with HCl (2 N) and brine. After drying with Na_2SO_4, the organic phase was concentrated to give the crude product and purified by passage through a short pad of silica gel.

4: Yield 100%. − R_f (petroleum ether/ethyl acetate, 5:2) = 0.55. − IR ($CHCl_3$): $\tilde{\nu}$ = 2932 cm^{-1} (CH), 1616 (C=O), 1102 (C−O). − $[\alpha]_D^{20}$ = −30.5 (*c* = 1.065, $CHCl_3$). − Mp 102−104°C. − MS (70 eV); *m/z*: 462, 377, 330, 147, 73. − $C_{40}H_{76}N_2O_6Si_4$ (793.0): calcd. C 60.55, H 9.67, N 3.53, found C 60.22, H 9.60, N 3.88.

6: Yield 87%. − R_f (petroleum ether/ethyl acetate, 5:2) = 0.53. − IR ($CHCl_3$): $\tilde{\nu}$ = 2957 cm^{-1} (CH), 1623 (C=O), 1102 (C−O). − $[\alpha]_D^{20}$= −49.7 (*c* = 0.925, $CHCl_3$). − Mp 179−181°C. − $C_{57}H_{111}O_9N_3Si_6$ (1207.2): calcd. C 59.46, H 9.74, N 3.65 found C 59.18, H, 9.74, N, 3.36.

8: Yield 70%. − R_f (petroleum ether/ethyl acetate, 6:1) = 0.46. − IR ($CHCl_3$): $\tilde{\nu}$ = 2931 cm^{-1} (CH), 1634 (C=O), 1105 (C−O). − $[\alpha]_D^{20}$ = 11.9 (*c* = 1.10, $CHCl_3$). − Mp 190−191°C. − $C_{74}H_{146}N_4O_{12}Si_8$ (1508.68): calcd. C 58.94, H 9.76, N 3.77, found C 59.29, H 10.03, N 3.50.

9: Yield 44%. − R_f (petroleum ether/ethyl acetate, 10:1) = 0.65. − IR ($CHCl_3$): $\tilde{\nu}$ = 2957 cm^{-1} (CH), 1651 (C=O), 1113 (C−O). − $[\alpha]_D^{20}$ = 39.7 (*c* = 0.900, $CHCl_3$). − Mp 154−155°C. − $C_{108}H_{216}N_6O_{18}Si_{12}$ (2223.9): calcd. C 58.3, H 9.79, N 3.78 found C 58.57, H 9.76, N 3.91.

5: Yield 49%. − R_f (ethyl acetate/petroleum ether, 1:1) = 0.38. − $[\alpha]_D^{20}$ = −32.4 (*c* = 1.005, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2956 cm^{-1} (CH), 1726 (O−C=O), 1622 (N−C=O), 1098 (C−O). − ^{1}H NMR ($CDCl_3$): δ = −0.04 (s, 12 H, *Me*Si × 4), 0.03 (s, 12 H, *Me*Si × 4), 0.09 (s, 12 H, *Me*Si × 4), 0.11 (s, 12 H, *Me*Si × 4), 0.82 (s, 36 H, *tBu*Si × 4), 0.89 (s, 36 H, *tBu*Si × 4), 3.12 (d, *J* = 10.2 Hz, 4 H, C*H*N × 4), 3.53 (d, *J* = 12.8 Hz, 4 H, C*H*N × 4), 3.64 (d, *J* = 10.6 Hz, 4 H, C*H*N × 4), 3.85 (m, 8 H, C*H*N × 8), 3.95 (br. s, 4 H, C*H*OSi × 4), 4.08 (br. s, 4 H, C*H*OSi × 4), 4.17 (m, 2 H, C*H*N × 2), 4.32 (m, 2 H, C*H*N × 2), 5.57 (br. s, 2 H, C*H*OC=O × 2), 5.68 (br. s, 2 H, C*H*OC=O × 2), 7.59 (m, 8 H, aromatic H), 7.63 (s, 4 H, aromatic H), 8.06 (dd, *J* = 15.3, 8.1 Hz, 8 H, aromatic H). − ^{13}C NMR ($CDCl_3$): δ = −5.0 (q, 8 C, *Me*Si × 8), −4.8 (q, 8 C, *Me*Si × 8), 17.7 (s, 4 C, *C*Si × 4), 17.9 (s, 4 C, *C*Si × 4), 25.5 (q, 12 C, *tBu*Si × 4), 25.7 (q, 12 C, *tBu*Si × 4), 48.9 (t, 2 C, *C*H_2N × 2), 50.5 (t, 2 C, *C*H_2N × 2), 52.7 (t, 4 C, *C*H_2N × 4), 55.2 (t, 4 C, *C*H_2N × 4), 74.9 (d, 2 C, *C*HOC=O × 2), 75.1 (d, 4 C, *C*HOSi × 4), 75.6 (d, 2 C, *C*HOC=O × 2), 76.2 (d, 4 C, *C*HOSi × 2), 127.2 (d, 8 C, aromatic C), 127.6 (d, 4 C, aromatic C), 129.3 [s, 2 C, =*C*(C=O)N × 2], 129.9 [d, 8 C, aromatic C), 137.6 (s, 4 C, =*C*(C=O)N × 4], 142.0 [s, 4 C, =*C*(C=O)O × 4], 164.5 (s, 6 C, N*C*=O × 2 + O*C*=O × 4), 169.0 (s, 4 C, N*C*=O × 4). − $C_{112}H_{176}N_6O_{22}Si_8$ (2183.3): calcd. C 61.61, H 8.13, N 3.85 found C 61.37, H, 8.25, N 3.48.

7: Yield 42%. − R_f (ethyl acetate/petroleum ether, 1:1) = 0.38. − $[\alpha]_D^{20}$= −40.4 (*c* = 0.505, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2954 cm^{-1} (CH), 1726 (O−C=O), 1622 (N−C=O), 1098 (C−O). ^{1}H NMR ($CDCl_3$): δ = −0.05 (s, 18 H, *Me*Si × 6), 0.03 (s, 18 H, *Me*Si × 6), 0.09 (s, 18 H, *Me*Si × 6), 0.10 (s, 18 H, *Me*Si × 6), 0.81 (s, 54 H, *tBu*Si × 6), 0.89 (s, 54 H, *tBu*Si × 6), 3.12 (d, *J* = 9.9 Hz, 6 H, C*H*N × 6), 3.52 (d, *J* = 12.8 Hz, 6 H, C*H*N × 6), 3.65 (d, *J* = 10.7 Hz, 6 H, C*H*N × 6), 3.87 (m, 12 H, C*H*N × 12),

3.96 (br. s, 6 H, C*H*OSi × 6), 4.09 (br. s, 6 H, C*H*OSi × 6), 4.29 (m, 6 H, C*H*N × 6), 5.58 (br. s, 3 H, *C*HOC=O × 3), 5.70 (br. s, 3 H, *C*HOC=O × 3), 7.58 (m, 12 H, aromatic C), 8.06(s, 3 H, aromatic C) 8.08 (m, 12 H, aromatic C). – ^{13}C NMR ($CDCl_3$): δ = −4.9 (q, 12 C, *Me*Si × 12), −4.8 (q, 12 C, *Me*Si × 12), 17.8 (s, 6 C, *C*Si × 6), 17.9 (s, 6 C, *C*Si × 6), 25.6 (q, 18 C, *tBu*Si × 6), 25.7 (q, 18 C, *tBu*Si × 6), 49.0 (t, 3 C, *C*H_2N × 3), 50.7 (t, 3 C, *C*H_2N × 3), 52.6 (t, 6 C, *C*H_2N × 6), 55.2 (t, 6 C, *C*H_2N × 26), 74.1 (d, 3 C, *C*HOC=O × 3), 75.2 (d, 6 C, *C*HOSi × 6), 75.7 (d, 3 C, *C*HOC=O × 3), 76.3 (d, 6 C, *C*HOSi × 6), 127.3 (d, 12 C, aromatic C), 129.4 (d, 3 C, aromatic C), 129.4 [s, 3 C, =*C*(C=O)N × 3], 130.0 (d, 12 C, aromatic C), 135.9 [s, 6 C, =*C*(C=O)N × 6], 142.7 [s, 6 C, =*C*(C=O)O × 6], 164.6 (s, 6 C, O*C*=O × 6), 167.4 (s, 3 C, N*C*=O × 3), 169.0 (s, 6 C, N*C*=O × 6). – $C_{165}H_{261}N_9O_{33}Si_{12}$ (3235.9): calcd. C 61.23, H 8.15, N 3.90 found C 61.03, H 8.04, N 3.56.

14: Yield 50%. – R_f (ethyl acetate/petroleum ether, 1:1) = 0.38. – IR ($CHCl_3$): ṽ = 2954 cm^{-1} (CH), 1726 (O−C=O), 1622 (N−C=O), 1098 (C−O). – $[\alpha]_D^{20}$ = −32.5 (*c* = 0.958, $CHCl_3$). – Mp 127−128°C. – ^{1}H NMR ($CDCl_3$): δ = −0.06 (s, 3 H, *Me*Si), 0.02 (s, 3 H, *Me*Si), 0.10 (s, 3 H, *Me*Si), 0.11 (s, 3 H, *Me*Si), 0.80 (s, 9 H, *tBu*Si), 0.89 (s, 9 H, *tBu*Si), 3.12 (d, *J* = 11.0 Hz, 1 H, C*H*N), 3.52 (d, *J* = 12.4 Hz, 1 H, C*H*N), 3,69 (dd, *J* = 10.8, 3.4 Hz, 1 H, C*H*N), 3.88 (dd, *J* = 12.6, 4.2 Hz, 1 H, C*H*N), 3.95 (br. s, 1 H, C*H*O), 4.09 (br. s, 1 H, C*H*O), 5. 39 (s, 4 H), 7.40 (m, 10 H, aromatic H), 8.38 (d, *J* = 1.4 Hz, 2 H, aromatic H), 8.80 (t, *J* = 1.5 Hz, 1 H, aromatic H). – ^{13}C NMR (CDCl3): δ = −5.0 (q, 2 C, *Me*Si × 2), −4.8 (q, 2 C, *Me*Si × 2), 17.7 (s, 1 C, *C*Si), 17.9 (s, 1 C, *C*Si), 25.5 (q, 3 H, *tBu*Si), 25.7 (q, 3 H, *tBu*Si), 52.8 (t, 1 C, *C*H_2N), 55.3 (t, 1 C, *C*H_2N), 67.3 (t, 2 C, *C*H_2Ph × 2), 75.2 (d, 1 C, *C*HOSi), 76.4 (d, 1 C, *C*HOSi), 128.4 (d, 4 C, aromatic C), 128.5 (d, 4 C, aromatic C), 128.7 (d, 2 C, aromatic C), 131.0 (d, 2 C, aromatic C), 132.1 (d, 1 C, aromatic C), 132.5 (s, 2 C, aromatic C), 135.5 (s, 2 C, aromatic C), 164.9 (s, 2 C, O*C*=O × 2), 168.2 (s, 1 C, N*C*=O). – $C_{38}H_{53}NO_7Si_2$ (692.01): calcd. C 65.96, H 7.72, N 2.02 found C 65.80, H 7.80, N 1.98.

[1] E. Buhleier, W. Wehner, F. Vögtle, *Synthesis* **1978**, 155.

[2] [2a] G. R. Newcome, C. N. Moorefield, F. Vögtle, *Dendritic Molecules: concepts, syntheses, perspectives*, VCH Verlagsgesellschaft, Weinheim, **1996**. – [2b] D. A. Tomalia, A. M. Naylor, W. A. Goddard III, *Angew. Chem*. **1990**, *102*, 119; *Angew. Chem. Int. Ed. Eng*. **1990**, *29*, 138. – [2c] F. Zeng, S. C. Zimmerman, *Chem. Rev.* **1997**, *97*, 1681. – [2d] For phosphorus-containing dendrimers: M.-L. Lartigue, M. Slany, A.-M. Caminade, J.-P. Majoral, *Chem. Eur. J.* **1996**, *2*, 1417.

[3] [3a] G. Denti, S. Campagna, S. Serroni, M. Ciano, V. Balzani, *J. Am. Chem. Soc*. **1992**, *114*, 2944. – [3b] G. R. Newkome, Z. Yao, G. R. Baker, V. K. Gupta, P. S. Russo, M. J. Saunders, *J. Am. Chem Soc.* **1986**, *108*, 849. – [3c] G. R. Newkome, C. N. Moorefield, G. R. Baker, R. K. Behera, G. H. Escamillia, M. J. Saunders, *Angew. Chem*. **1992**, *104*, 901; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 917. – [3d] K. R. Gopidas, A. R. Leheny, G. Caminati, N. J. Turro, D. A. Tomalia, *J. Am. Chem. Soc*. **1991**, *113*, 7335.

[4] [4a] P. Bhyrappa, J. K Young, J. S. Moore, K. S. Suslick, *J. Am. Chem. Soc*. **1996**, *118*, 5708. – [4b] M. R. Leduc, C. J. Hawker, J. Dao, J. M. J. Frechet, *J. Am. Chem. Soc.* **1996**, *118*, 11111. – [4c] C. Bölm, N. Derrien, A. Seger, *Synlett* **1996**, 387.

[5] [5a] H, W. I. Peerlings, E. W. Meijer, *Chem. Eur. J.* **1997**, *3*, 1563. – [5b] For the unique example of a chiral dendrimer built up from achiral building blocks see: J. A. Kremers, E. W. Meijer, *J. Org. Chem*. **1994**, *59*, 4262.

[6] D. Seebach, J.-M. Lapierre, G. Greiveldinger, K. Skobridis, *Helv. Chim. Acta* **1994**, *77*, 1673.

[7] [7a] P. Murer, D. Seebach, *Angew. Chem*. **1995**, *107*, 2297; *Angew. Chem. Int. Ed. Eng*. **1995**, *34*, 2116. – [7b] D. Seebach, D. F. Herrmann, U. D. Lengweiler, W. Amrein, *Helv. Chim. Acta* **1997**, *80*, 989. – [7c] C. C. Mak, H.-F. Chow, *J. Chem. Soc., Chem. Commun.* **1996**, 1185. – [7d] D. V. McGrath, M.-J. Wu, U. Chaudry, *Tetrahedron Lett*. **1996**, *37*, 6077. – [7e] L. J. Twyman, J. C. Beezer, J. C Mitchell, *Tetrahedron Lett*. **1994**, *35*, 4423. – [8] Most of the examples of this class are the so called "glyco-coated dendrimers" (dendrimeric molecules with carbohydrates units on the surface): [8a] T. K. Lindhorst, C. Kieburg, *Angew. Chem*. **1996**, *108*, 2075; *Angew. Chem. Int. Ed. Eng*. **1996**, *35*, 1953. – [8b] P. R. Ashton, S. E Boyd, C. L. Brown, N. Jayaraman, S. A. Nepogodiev, J. F. Stoddart, *Chem. Eur. J.* **1996**, *2*, 1115. – [8c] D. Zanini, R. Roy, *J. Org. Chem*. **1996**, *61*, 7348. – [8d] P. R. Ashton, S. E Boyd, C. L. Brown, N. Jayaraman, J. F. Stoddart, *Angew. Chem*. **1997**, *109*, 756; *Angew. Chem. Int. Ed. Eng*. **1997**, *36*, 732. [8e] For "amino acid coated dendrimers" see: J. F. G. Jansen, E. W. Meijer, E. M. M. de Brabander-van der Berg, *J. Am. Chem. Soc*. **1995**, *117*, 4417.

[9] U. Nagel, E. Kinzel, J. Andrade, G. Prescher, *Chem. Ber.* **1986**, *119*, 3326.

[10] A. Goti, F. Cardona, A. Brandi, S. Picasso, P Vogel, *Tetrahedron: Asymmetry* **1996**, *7*, 1659.

[11] [11a] C. J. Hawker, J. M. J. Frechet, *J. Chem. Soc., Chem. Commun*. **1990**, 1010. – [11b] T. M. Miller, T. X. Neenan, *Chem. Mater.* **1990**, *2*, 346.

[12] [12a] H.-F. Chow, C. C. Mak, *J. Chem. Soc., Perkin Trans. 1* **1994**, 2223. – [12b] G. R. Newkome, X. Lin, C. D. Weis, *Tetrahedron: Asymmetry* **1991**, *2*, 957. – [12c] H. T. Chang, C. T. Chen, T. Kondo, K. G. Siuzda, K. B. Sharpless, *Angew. Chem*. **1996**, *108*, 202; *Angew. Chem. Int. Ed. Engl*. **1996**, *35*, 182.

[13] S. F. Mason, *Molecular Optical Activity and Chiral Discrimination Cambridge*, University Press, Cambridge, **1982**.

[14] J. R. McElhanon, D. V. McGrath, *J. Am. Chem. Soc.* **1998**, *120*, 1647.

[15] P. Bowles, J. Clayden, M. Helliwell, C. McCarthy, M. Tomkinson, N. Westlund, *J. Chem. Soc., Perkin Trans. 1* **1997**, 2607.

[15] A. R. A. Palmans, J. A. J. M. Vekemans, E. E. Havinga, E. W. Meijer, *Angew. Chem*. **1997**, *109*, 2763; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2648.

[98289]