Chiral Poly(aromatic amide ester) Dendrimers Bearing an Amino Acid Derived C_3-Symmetric Core − Synthesis and Properties

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The effect of hyperbranched macromolecular architectures (dendrimers) upon chirality has received significant attention in recent years in the light of the proposal of amplification of chirality. In particular, several studies have been carried out on the chiroptical properties of dendrimers that contain a chiral core and achiral branches in order to determine if the chirality of the central core can be transmitted to the distal region of the macromolecule. In addition to interest of a pure academic nature, the presence of such chiral conformational order would be extremely useful in the development of asymmetric catalysts. In this paper, a novel class of chiral dendrimers is described – these perfect hyperbranched macromolecules have been prepared by a convergent route by the coupling of a chiral central core based upon tris(2-aminoethyl)amine and poly(aromatic amide ester) dendritic branches. The chiral properties of these dendrimers have been investigated by detailed optical rotation studies and circular dichroism analysis; the results of these studies are described herein.

Introduction

Dendrimers constitute a novel class of polymers[1] that possess regular highly branched, well-defined structures. One aspect of dendrimer chemistry that has attracted significant attention is the introduction of chirality within dendritic architectures.[2] As a consequence of their well-defined branched macromolecular structures,[3] the study of chiral dendrimers should enable detailed insights into the impact of chirality in macromolecular systems and also provide valuable data on the relationship between chirality at molecular and macroscopic levels. It is essential to understand the relationship between macroscopic and nanoscopic chirality in polymers in order to access new materials whose properties and functions depend on the expression of chirality at a macromolecular level.[4] Indeed, one of the most promising developments of dendrimer research is the preparation of novel and efficient catalytically active hyperbranched macromolecules.[5] Dendrimers combine the main advantages of both homogeneous and heterogeneous catalysts, i.e. excellent solubility in common organic solvents (an advantage of homogeneous catalysts) and ease of removal from the reaction media by membrane and ultrafiltration techniques as a direct result of their large size in comparison to the products (an advantage of heterogeneous catalysts).[6]

As part of a programme studying the properties and potential applications of chiral dendrimers, we herein report the synthesis of a novel class of chiral poly(aromatic amide ester) dendrimers which incorporates a chiral C_3-symmetric core unit that is analogous to the tris(2-aminoethyl)amine (TREN) ligand.[7] Two multifunctional chiral C_3-symmetric core systems have been prepared by reductive alkylation of ammonia with either of the enantiomeric D- or L-Garner aldehyde precursors which in turn are derived from the amino acids D- or L-serine, respectively. The first and second generation poly(aromatic amide ester) dendrons have been synthesized by a convergent approach[8] using 1,3-diamino-2-hydroxypropane and 4-carboxybenzaldehyde as the building blocks.[9] Coupling of the poly(aromatic amide ester) dendrons bearing carboxylic acid functionalities at the focal points to the enantiomeric C_3-symmetric core systems has enabled two series of chiral dendrimers to be constructed.[7] This paper describes the synthesis and chiral properties of this type of poly(aromatic amide ester) dendrimers.

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Results and Discussion

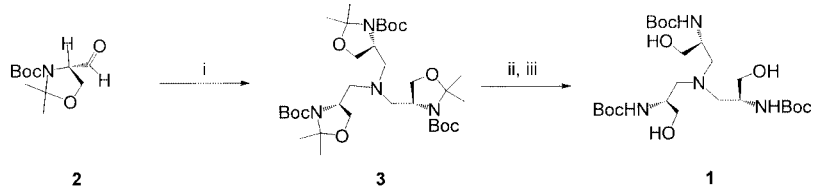
Synthesis

Synthesis of the Chiral Core

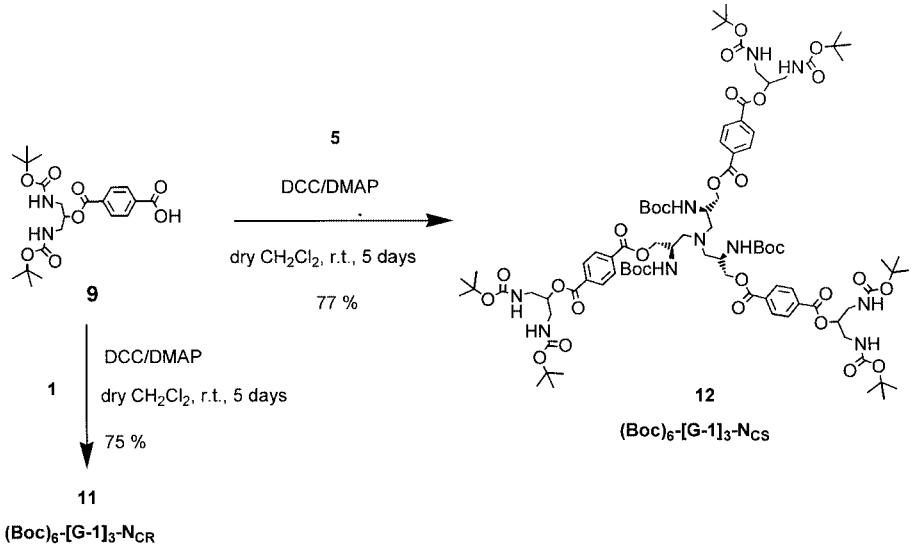
In a parallel study to the work of Raymond et al.,[10] a novel chiral C_3-symmetric core unit **1** was prepared in an efficient manner (Scheme 1) from the so-called L-Garner aldehyde **2**. L-Garner aldehyde **2** was synthesized from L-serine using a modification of the efficient four-step route described by Taylor and co-workers.[11] Reductive alkylation of ammonium acetate with the Garner aldehyde in the presence of $NaBH(OAc)_3$ led to the formation of the trialkylated system **3** in 90% yield. The latter was then exposed to HCl (6 N) to effect complete deprotection of the oxazolidine and Boc protecting groups in order to afford the corresponding triamino-triol **4**. Subsequent selective protection of the three amino functionalities in the form of the corresponding Boc derivatives then afforded the desired optically pure C_3-symmetric (*RRR*)-core system **1** in an overall yield of > 90% from the trialkylated system **3**. The enantiomeric (*SSS*)-core derivative **5** was prepared from the D-Garner aldehyde derivative **6** (in turn obtained from D-serine) in an equally efficient manner using the same synthetic approach via the corresponding trialkylated and triamino-triol derivatives **7** and **8**, respectively.

Synthesis of the First and Second Generation Chiral Dendrons and Dendrimers

A convergent approach[8] was chosen in order to avoid formation of structural defects during dendrimer construction. Commercially available 1,3-diamino-2-hydroxypropane was selected as the AB_2-type monomer and 4-carboxybenzaldehyde has been used as the rigid "linker" between the branched points. After initial protection of the amino groups in the form of the Boc analogues of the branching unit to form the peripheral surface of the resultant dendrimers, coupling with 4-carboxybenzaldehyde using dicyclohexylcarbodiimide (DCC) as the coupling agent afforded the first generation dendron featuring an aldehyde at the focal point. Subsequent oxidation of the aldehyde functionality with $KMnO_4$ yielded the corresponding first generation dendron with a carboxylic acid at the focal point $(Boc)_2$-[G-1]-COOH **9**.[9] Selective coupling with the amino functionalities of a further equivalent of 1,3-diamino-2-hydroxypropane led to the formation of the second generation dendron that featured a secondary hydroxy moiety at the focal point. Repetition of the esterification and oxi-



Scheme 1. Synthesis of the chiral C_3-symmetric core unit derived from L-serine; i) $NaBH(OAc)_3$, NH_4OAc, CH_3OH, 4 h, room temp., 90%; ii) HCl (6 N), > 99%; iii) $(Boc)_2O$, THF/water, > 90%

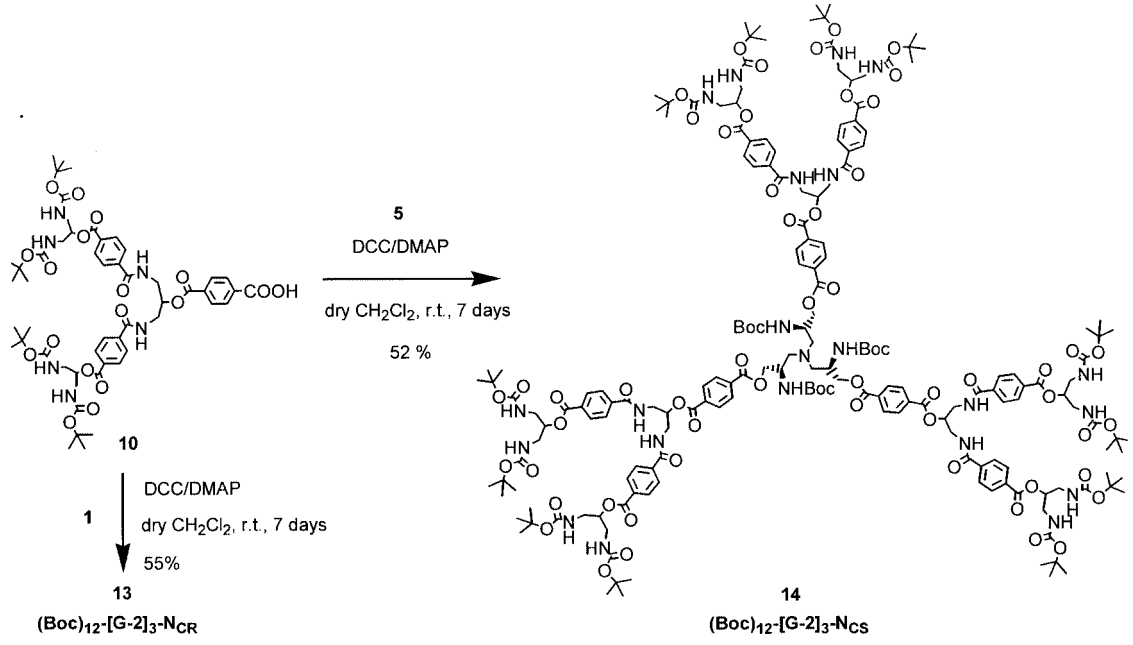


Scheme 2. Synthesis of the first generation dendrimer $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11** and $(Boc)_6$-$[G\text{-}1]_3$-N_{CS} **12**

dation steps led to the desired second generation dendron $(Boc)_4$-[G-2]-COOH **10**.

The preparation of both series of enantiomeric chiral dendrimers was carried out by coupling the carboxylic acid at the focal point of the first and second generation poly(aromatic amide ester) dendrons[9] to the three hydroxy functionalities of the chiral core systems **1** and **5**. Several coupling approaches were examined in order to generate the desired chiral dendrimers. Routes examined included conversion of the carboxylic acid functionalities to the corresponding acid chlorides or activation with DCC in presence of non-nucleophilic bases such as dimethylaminopyridine (DMAP) or its derivatives such as 4-(dimethylamino)pyridinium toluene-*p*-sulfonate (DPTS) prior to addition of the chiral core systems **1** and **4**. In keeping with the studies of Taylor and co-workers,[12] with our dendrimer systems it was observed that use of acid chlorides was only applicable in the case of the lower generation dendrimers and that detrimental formation of numerous by-products occurred in higher order systems. In the light of these observations, coupling of the first generation $(Boc)_2$-[G-1]-COOH dendron **9** and the chiral core system **1** was carried out using DCC as the coupling agent in the presence of a catalytic amount of DMAP (Scheme 2). Purification by column chromatography afforded the first generation chiral dendrimer $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **10** in a moderate yield of 40%. In order to improve this disappointing yield, an excess of $(Boc)_2$-[G-1]-COOH dendron **9** with respect to the chiral core system was used (1.5 equiv. of dendron per hydroxy group) in conjunction with prolonged reaction times as described[12] by Taylor and co-workers. After stirring for 5 d under argon, a higher yield (75%) was thus obtained, but problems arose during the purification of the desired product $(Boc)_6$-$[G\text{-}1]$-N_{CR} **11** by silica gel column chromatography as a result of the presence of a by-product possessing a very similar R_f value to that of **11** (0.7 and 0.68, respectively, using $CHCl_3$/EtOH, 90:10 as the eluent). Interestingly, MALDI-TOF mass spectrometric analysis revealed that this by-product possessed a molecular weight corresponding to an "adduct" between the excess of dendron $(Boc)_2$-[G-1]-COOH **9** and dicyclohexylurea formed from DCC used during the coupling step. As a consequence of the comparable solubility properties of this by-product with the desired dendritic material, it was impossible to separate it completely from the chiral dendrimer **11** even after repetitive filtrations of a concentrated solution containing the mixture. Purification using gel permeation chromatography (GPC) was used to afford the pure chiral dendrimers − slow elution employing THF as the eluent afforded the desired pure dendrimer $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11**. Coupling of the $(Boc)_2$-[G-1]-COOH dendron **9** and the enantiomeric (*SSS*)-core system **5** was carried out using the same coupling conditions and the desired first generation dendrimer $(Boc)_6$-$[G\text{-}1]_3$-N_{CS} **12** (Scheme 2) was obtained in comparable yield (77%) to that of the opposite enantiomer **11**.

The second generation dendrimer $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** was prepared in a similar way by using DCC and DMAP in anhydrous CH_2Cl_2 by coupling the second generation dendron $(Boc)_4$-[G-2]-COOH **10** and the core system **1** (Scheme 3). After 7 d of stirring at room temperature under argon, the desired second generation dendrimer $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** was isolated in 55% yield. Use of THF as the solvent did not lead to an improvement of the reaction yield (53%) and heating the reaction mixture at 60 °C for several days led to the formation of a larger amount of by-products with concomitant lower isolated yield (30%) of the chiral dendrimers. Usefully, the second generation chiral dendrimer $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** revealed very low solubility in CH_2Cl_2 and therefore, when this solvent was employed in the coupling reaction, the product precipitated and could



Scheme 3. Synthesis of the second generation dendrimer $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CS} **14**

be filtered off without an aqueous workup. However, the reaction mixture contained other insoluble materials such as dicyclohexylurea and by-products, including an adduct between the dendron $(Boc)_4$-[G-2]-COOH **10** and dicyclohexylurea (the molecular weight of this by-product corresponded to the mass of the dendron **10** plus 225 a.m.u. as revealed by MALDI-TOF mass spectrometric analysis). The DCC by-product could be eliminated by repeated filtration of the concentrated mixture suspended in THF (as the dendrimer **13** was completely soluble in this solvent) and silica gel column chromatography. It was observed that, on passing from the first to the second generation dendrimer of this type, removal of the dicyclohexylurea by-product proved more difficult, probably as a result of the enhanced ability of the dendrimers to encapsulate[13] impurities (and solvent) within the dendritic structure. This behaviour could also be observed from MALDI-TOF mass spectrometric analysis which revealed the presence of peaks of higher mass with respect to the dendrimer of first and second generation corresponding to the encapsulation of one and two molecules of dicyclohexylurea (vide infra). As described for the corresponding first generation chiral dendrimers **11** and **12**, the dendritic by-product deriving from the excess of dendron **10** and dicyclohexylurea could only be eliminated by size exclusion column chromatography in THF as a result of its very similar R_f value with respect to the desired dendrimer **13**. The preparation of the second generation dendrimer with opposite configuration $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CS} **14** (Scheme 3) was carried out under similar conditions and it was isolated in a comparable yield of 52%. The decrease in yield of the higher generation dendrimers is consistent with the findings of other convergent dendrimer syntheses.[14]

Characterization of the Dendrimers

Solubility Properties and NMR Spectroscopic Studies

These novel chiral poly(aromatic amide ester) dendritic systems exhibited slightly different solubility properties with respect to the analogous achiral systems that have been described elsewhere.[9] In particular, the first and second generation dendrimers **11** and **13** and the opposite enantiomers **12** and **14**, respectively, were soluble in CH_3CN, THF, DMF and DMSO but exhibited very low solubility (ca. 5 mg/mL) in halogenated solvents such as $CHCl_3$ and CH_2Cl_2. This feature was considered quite surprising considering that the only difference between the two series of achiral and chiral dendrimers is the structure of the core system, whereas the dendritic branches and peripheral surface (that are believed to control the bulk solubility properties of dendrimers) are identical.[9] In addition, the second generation chiral dendrimers $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CS} **14** did not exhibit the gelation properties of the analogous achiral counterpart, even when dissolved at the same concentration (ca. 20 mg/mL).

^1H and ^{13}C NMR spectra of the first and second generation dendrimers of both enantiomers were recorded using $[D_6]$DMSO and did not reveal any particular difference with respect to the spectra of the analogous achiral series apart from the presence of additional proton resonances relating to the chiral core system.[9] However, some interesting features were observed when comparing the ^1H NMR spectra of the first and second generation dendrimers, respectively. In the ^1H NMR spectrum of the dendrimers $(Boc)_6$-$[G\text{-}1]$-N_{CR} **11** and $(Boc)_6$-$[G\text{-}1]$-N_{CS} **12** the proton resonances of the additional three carbamate groups at the central chiral core were separated and at lower field with respect to the signal of the peripheral carbamate groups (δ = 7.10 and 6.95 ppm, respectively). A similar situation was observed for the proton resonances of the Boc groups at the central core and peripheral surface as two singlets were present at δ = 1.35 and 1.30 ppm, respectively. This result indicates the presence of a more electronically shielded environment at the central core with respect to that at the peripheral surface. However, a different situation was exhibited by the second generation chiral dendrimers $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CS} **14**. The resonances of the carbamate protons of the central core system and of the peripheral surface unit almost overlapped (δ = 7.01 and 6.98 ppm, respectively) and the protons of the Boc groups resonated with only one singlet in evidence for the two different groups. This result suggests that a similar electronic environment is present at the central core and peripheral surface in the case of the second generation dendrimers. Furthermore, these dendritic systems − especially the second generation − revealed the tendency to encapsulate solvents and resonance peaks assigned to THF could be observed even after prolonged exposure to high-vacuum conditions.

MALDI-TOF Mass Spectrometric, HPLC, GPC and DSC Analyses

The molecular weights of the chiral dendrimers were determined by MALDI-TOF mass spectrometric analysis using *trans*-2-indoleacrylic acid as the matrix. The mass spectra of the first and second generation dendrimers **11** and **13**, respectively, as the sodium and potassium adducts are shown in Figure 1 (molecular weights 1819.1 $[M + Na]^+$, 1835.2 $[M + K]^+$ and 3740.2 $[M + Na]^+$, 3756.3 $[M + K]^+$, respectively).

As observed in the MALDI-TOF mass spectra of the achiral dendrimers,[9] fragmentation of the dendritic structure by loss of one Boc group was observed, especially when high laser powers were used. This fragmentation was also evident in the MALDI-TOF spectrum of the second generation dendrimer $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** [see (b) in Figure 1] as indicated by the presence of smaller peaks possessing lower mass differing by ca. 55−57 and 101 a.m.u. from the peaks corresponding to the chiral dendrimers. From the spectrum of the first generation dendrimer $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11** [see (a) in Figure 1] it is still possible to observe the presence of the peaks corresponding to an encapsulated dicyclohexylurea dendrimer adduct. However, extensive NMR spectroscopic, HPLC and elemental analysis revealed that the sample was > 98% pure thus indicating that only negligible amounts of these impurities were still present.

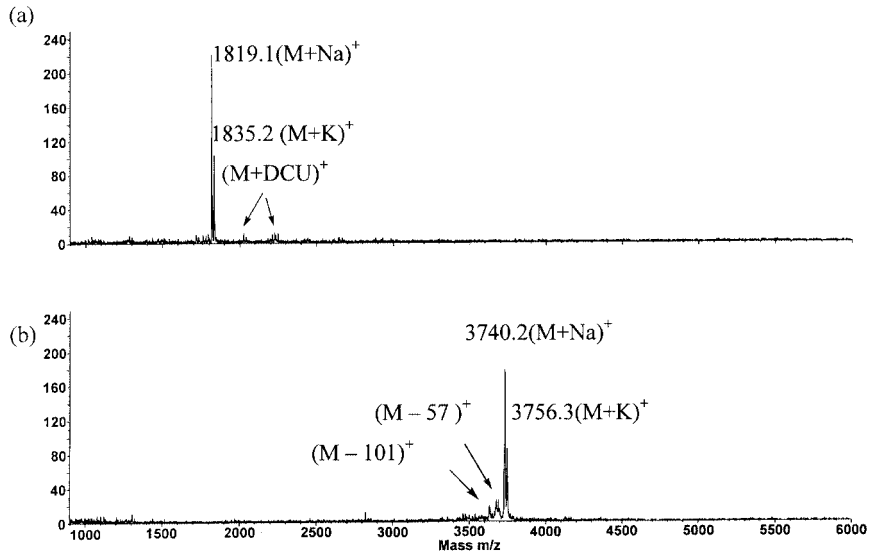


Figure 1. MALDI-TOF mass spectra of the first (a) and second (b) generation dendrimers **11** and **13**, respectively

The purity of the first and second generation dendrimers has also been confirmed by reverse phase HPLC analysis. Optimum results were obtained using a combination of CH_3CN and CH_3OH either in isocratic or gradient elution modes. Both the first and second generation dendrimers (in the two enantiomeric forms) eluted as single narrow peaks with a purity of 98.76 and 98.77%, respectively for the dendrimers $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** [see HPLC chromatograms (a) and (b), respectively, in Figure 2] and 98.13 and 100.0% for the corresponding enantiomers $(Boc)_6$-$[G\text{-}1]_3$-N_{CS} **12** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CS} **14**. As observed with the analogous achiral series,[9] the first generation chiral dendrimers eluted later then the corresponding higher generation systems in the solvent systems used indicating higher affinity of the latter with the polar eluting solvent, probably as a result of the formation of hydrogen bonds between the amide linkages of the dendritic structure and the polar solvent.

GPC analysis of the two series of chiral dendrimers was carried out employing narrow molecular weight polystyrenes as the calibrants and THF as the mobile phase; the same conditions as used for the analysis of the achiral dendrimers.[9] Symmetrical peaks were obtained with polydispersity values (PDI) of 1.04 and 1.05 for the first and second generation chiral dendrimers of both configurations, respectively {the GPC traces of $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** are shown in Figure 3}. Interestingly, both the first and second generation chiral dendritic systems exhibited a similar overestimation of the molecular weight by ca. 300 a.m.u. In addition, the overestimation values were comparatively higher then those obtained when the corresponding achiral dendrimers were analysed. These results suggested that a more extended shape was adopted by the chiral dendritic systems of first and second generation, probably as a consequence of a more efficient solv-

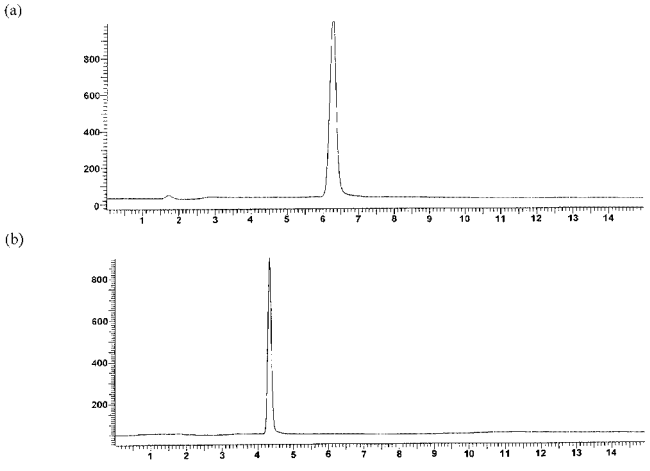


Figure 2. HPLC traces of the first (a) and second (b) generation chiral dendrimers $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** using a reverse phase column C_{18} and CH_3CN/MeOH (90:10) as the eluent

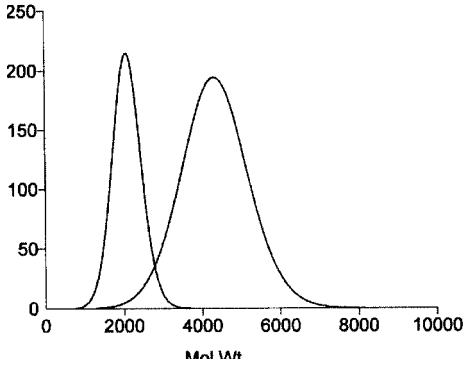


Figure 3. GPC trace (THF) of the first and second generation chiral dendrimers, $(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13**, respectively

ation effect in comparison to the corresponding achiral systems.[9]

The thermal stability of these poly(aromatic amide) chiral dendrimers was investigated by differential scanning calorimetry (DSC) analyses and, as with the achiral dendrimers, showed an absence of glass transition temperatures. However, broad melting endotherms were also observed with melting peaks at 252.11 and 252.72 °C for the first generation dendrimers **11** and **12** and 246.81 and 248.38 °C for the second generation dendrimers **13** and **14**, respectively.

Study of the Chiroptical Properties

The chiroptical properties of these dendritic systems have been studied by determination of the specific rotation $[\alpha]_D^{20}$ and molar rotation $[\Phi]_D^{20}$ in addition to circular dichroism analysis. A decrease of the specific rotation was observed on passing from the core systems **1** and **5** to the first (**11** and **12**) and second (**13** and **14**) generation of the corresponding dendrimers as shown in Table 1. In particular, whereas the $[\alpha]_D^{20}$ values were −44.6 (c = 1.03, $CHCl_3$) and +45.7 (c = 1.05, $CHCl_3$) for the core molecules **1** and **5**, the specific rotations for the first generation dendrimers (**11** and **12**) were −11.9 (c = 1.05, $CHCl_3$) and +11.7 (c = 1.01, $CHCl_3$) and for the second generation dendrimers (**13** and **14**) −10.8 (c = 1.05, $CHCl_3$) and +10.4 (c = 1.02, $CHCl_3$), respectively. These results are not surprising considering that the concentration of the solution for the calculation of the specific rotation is expressed in g per 100 mL. In fact, a decreasing number of stereogenic centres is present passing from a solution of the core molecules **1** and **5** to a solution of the corresponding first and second generation dendrimers when the same concentration of the chiral compounds (ca. 10.00−10.50 mg/mL) is employed. Therefore, the determination of the molar rotation $[\Phi]_D^{20}$ values was considered necessary since the specific rotation values are normalised for the number of mol of the compound in solution. As shown in Table 1, a decrease of the molar rotation values was observed on passing from **1** and **5** ($[\Phi]_D^{20}$ = −2322.9 and +2343.6, respectively) to the corresponding first generation dendrimers **11** and **12** ($[\Phi]_D^{20}$ = −2040.1 and +2082.9, respectively). However, the most interesting result was obtained when examining the molar rotation of the second generation dendrimers **13** and **14** ($[\Phi]_D^{20}$ = −3826.4 and +3811.8, respectively) as these values not only increased with respect to the core systems **1** and **5** but almost doubled with respect to the values obtained when the smaller dendritic systems were analysed. A similar result has been reported by Seebach et al.[15] when the chiroptical properties of chiral dendrimers incorporating a tris(hydroxymethyl)methane core unit coupled to poly(aromatic ether) or to poly(amide aromatic) dendrons were studied. These findings might be related to the presence of a chiral substructure in the dendritic branches induced by the chiral central core and probably favoured by the formation of intramolecular hydrogen bonding. However, "anomalies" of the optical activity behaviour can also be caused by other factors such as constitutional changes of the chiral units by incorporation in the dendritic systems as demonstrated[16] by McGrath and co-workers.

In order to further investigate the origin of this difference in optical rotation, UV and circular dichroism (CD) spectroscopic analysis of the series of chiral dendrimers was undertaken. Several key absorption bands can be observed in the UV spectra of the different dendrimers **11**−**14** (see Figure 4). A strong band at 240 nm corresponds to the n → π* transition of the carbamate functionality. Adjacent to this strong absorption band is a shoulder at 255 nm that corresponds to the n → π* transition of the carbonyl functionality adjacent to the phenyl group {this shoulder is most apparent in the UV spectrum of $(Boc)_6$-$[G\text{-}1]_3$-N_{CS} **12**}. In addition, an absorption band at 280 nm is evident that corresponds to the π → π* transition of the phenyl functionalities within the dendrimers.

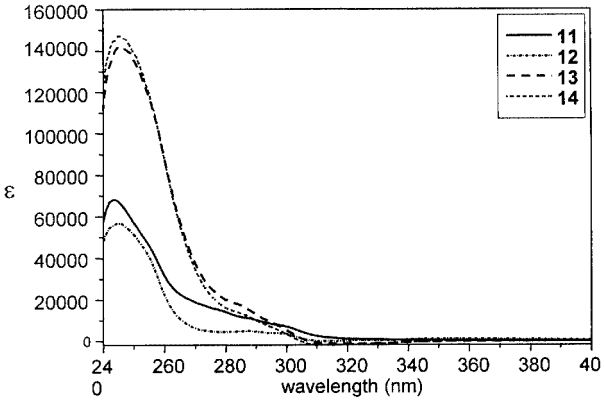


Figure 4. UV spectra of the chiral dendrimers **11**−**14**

Table 1. Specific rotation and molar rotation values of the chiral core molecules and of the corresponding first and second generation dendrimers

Compound	c in $CHCl_3$	$[\alpha]_D^{20}$	Mol. wt. [Da]	$[\Phi]_D^{20}$
1	1.03	−44.6	536.34	−2322.9
5	1.05	+45.7	536.34	+2343.6
11	1.05	−11.9	1798.03	−2040.1
12	1.01	+11.7	1798.03	+2082.9
13	1.05	−10.8	3720.07	−3826.4
14	1.02	+10.4	3720.07	+3811.8

Close examination of the circular dichroism spectra reveals a Cotton Effect at approximately 256 nm (see Figure 5). This absorption corresponds to the n → π* transition of the carbonyl functionality adjacent to the phenyl group.

In order to compare the CD spectra of the different molecules, g values ($\Delta\varepsilon/\varepsilon$) were determined (see Figure 6). Surprisingly, the g value at $\lambda \approx 258$ nm (assumed to be the n → π* transition of the carbonyl functionality adjacent to the phenyl group) was not related directly to the number of stereocenters present in the chiral dendrimers.

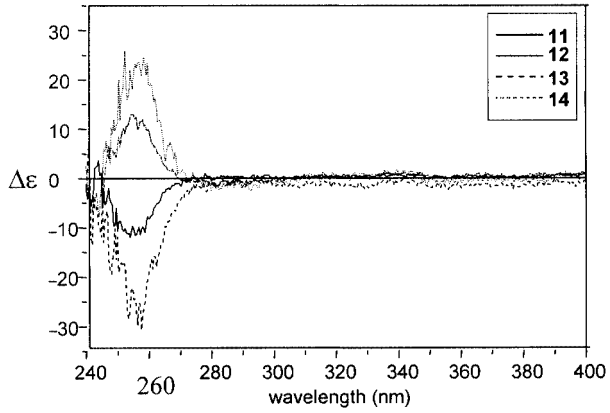


Figure 5. Circular dichroism spectra of the chiral dendrimers **11**−**14**

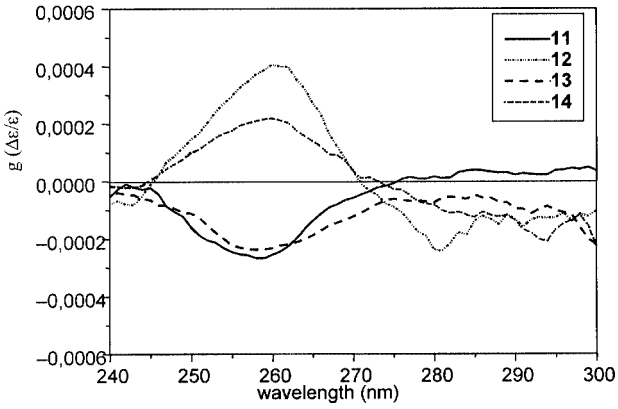


Figure 6. *g* values of the chiral dendrimers **11**−**14**

Both generation dendrimers contain three stereocenters per molecule; however, the ratio of stereocenters vs. carbonyl functionalities adjacent to a phenyl group was 3:6 and 3:18 for the first and second generation dendrimers, respectively. Therefore, based on the CD results obtained, it is not possible to produce a rationale for the chiral nature of these dendrimers based upon consideration of the structures of the two short series of chiral dendrimers. However, it is evident that the intrinsic chirality for the large dendrimers was much higher than expected based on the structures. In this respect, the CD data are in full agreement with the specific rotations described (vide supra).

Molecular Modelling Studies of the Chiral Core

The potential binding properties of these novel chiral core moieties was evident from molecular modelling studies of the (*RRR*) enantiomer **1**. These theoretical studies[17,18] have shown (Figure 7) that the three amino functionalities (represented by the black spheres) are resident on the same face, thereby forming a cavity that should favourably accommodate transition metals. In addition, the molecular model also reveals that, in contrast to the three amino groups, the three hydroxy functionalities are arranged in a divergent manner from the central amino moiety. It is envisaged that this conformation should favour the coupling between the hydroxy groups of the chiral TREN ligand with the hindered dendritic branches in order to minimize the steric strain.

Conclusions

The preparation of a novel class of chiral dendrimers incorporating a chiral C_3-symmetric core in both enantiomeric forms [(*RRR*) and (*SSS*), **1** and **5**, respectively] based on the structure of tris(2-aminoethyl)amine has been described. The two core systems possessing (*RRR*) and (*SSS*) configurations have then been coupled to poly(aromatic amide ester) dendrons leading to two series of enantiomerically pure dendrimers of first {$(Boc)_6$-$[G\text{-}1]_3$-N_{CR} **11** and $(Boc)_6$-$[G\text{-}1]_3$-N_{CS} **12**, respectively} and second generation {$(Boc)_{12}$-$[G\text{-}2]_3$-N_{CR} **13** and $(Boc)_{12}$-$[G\text{-}2]_3$-N_{CS} **14**, respectively}. Interesting chiroptical properties have been observed for the two series of chiral dendrimers as the molar rotation values decreased slightly from the core system to the corresponding first generation dendrimer, but it almost doubled upon progressing to the larger dendritic system. This result could be an indication of the presence of chiral substructures within the dendritic macromolecule induced by the stereogenic centres at the core. The chiroptical properties of the chiral dendrimers were also analysed in more detail by circular dichroism studies in order to establish if the "anomalous behaviour" of the molar rotation values were related to an induced chiral conformational order or more simply to constitutional changes of the chiral centres (with consequent changes of their specific rotation) determined by the presence of the large dendritic substituents. Although it is not possible to draw a final conclusion of the chiroptical behaviour of this novel series of chiral

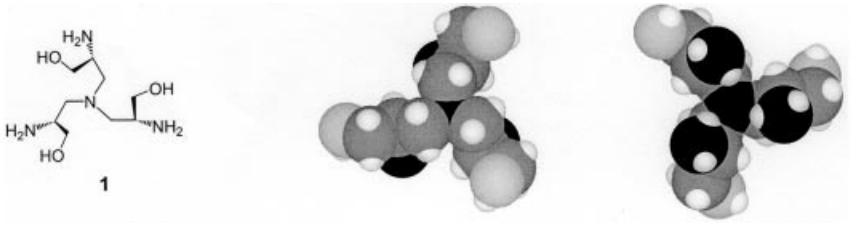


Figure 7. Two opposite faces of the molecular model representing the (*RRR*) enantiomer **1**

dendrimers, from these investigations it was found that the intrinsic chirality for the larger dendrimers was much higher than expected based on the structure. This result might indicate the presence of an induced chiral conformation from the core to the achiral dendritic branches. Further studies are required in order to establish the potential uses of these chiral macromolecules as potential catalysts in asymmetric reactions.

Experimental Section

General Remarks: Reagents were purchased from Aldrich Chemical Company and Acros Chimica, and were used as received without purification. Solvents were used as supplied, with the exception of the following: dichloromethane (CH_2Cl_2) was distilled from calcium hydride under reduced pressure, tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone, and methanol (CH_3OH) was distilled from anhydrous calcium sulfate under reduced pressure. Thin-layer chromatography (TLC) was performed on aluminium sheets coated with Merck 5735 Kieselgel 60F. Developed plates were air-dried, scrutinised under a UV lamp (254 nm) and, if necessary, by staining with potassium permanganate solution. Sorbsil 60 (0.040−0.063 mm mesh, Merck 9385) was used to perform column chromatography. Preparative size exclusion chromatography (GPC) was performed on Bio-Beads® S-X1 beads (BIO-RAD), 200−400 mesh, with THF as the mobile phase. Analytical GPC was performed with a PL-GPC 220 coupled with a refractive index detector, with THF as the eluent at a flow rate of 1.0 mL min^{-1} and a temperature of 40 °C. HPLC analysis of the dendrimers was carried out using a Perkin−Elmer series 200 LC pump in conjunction with an Applied Biosystems 785A programmable absorbance detector (operating at a single wavelength of 254 nm). The sample concentration employed in analytical scale separations was 0.05 mg mL^{-1} with an injection volume (20 μL) introduced onto a LiChrosorb RP18 column (15 cm × 4.6 mm i.d.). The flow rate of the mobile phase (CH_3CN/CH_3OH, 90:5) was 1 mL min^{-1}. Microanalyses were performed by MEDAC Ltd., Egham, Surrey UK. Melting points were determined with an Electrothermal digital melting point apparatus and are uncorrected. Differential Scanning Calorimetry (DSC) was performed using a Mettler DSC 20 System. Chemical ionization mass spectra (CIMS) were obtained using Fisons VG Autospec instrument employing ammonia as the impact gas. MALDI-TOF mass spectra were obtained with a SAI LT3 LaserTof or with a Bruker Biflex IV Mass Spectrometer using *trans*-2-indoleacrylic acid as matrix. A typical sample preparation is described as follows: 3 μL of a solution of the analyte in THF (1−10 mg/mL) was combined with 10−20 μL of the freshly prepared matrix (0.1 or 0.2 M in THF) in a mini-vial, and from the mixture was taken a 2 μL aliquot which was carefully transferred onto a sample plate and left to air-dry prior to analysis. ^1H nuclear magnetic resonance (NMR) spectra were recorded with Bruker DPXC250 (250 MHz) or Bruker AMX400 (400 MHz) spectrometers (using the deuterated solvent as lock and residual protic solvent or tetramethylsilane as the internal reference). ^{13}C nuclear magnetic resonance (NMR) spectra were recorded with Bruker DPX250 (62.8 MHz) or Bruker AMX400 (100 MHz) spectrometers. Chemical shifts are quoted in ppm. The coupling constants (J) are given in Hz. Specific rotation determinations ($[\alpha]_D^{20}$) were performed with a Perkin−Elmer 341 polarimeter and were recorded at the sodium D line (589.3 nm) in chloroform or water and the values are given in $degcm^2g^{-1}$. Circular dichroism measurements were carried out using a Jasco J600 spectropolarimeter. Ultraviolet (UV) spectroscopic analyses were carried using a Perkin−Elmer Lambda40 spectrometer. In the case of both the CD and UV spectroscopic analyses, the concentration of the dendrimers in chloroform (p.a. grade) was ca. 0.04 mg mL^{-1}. Infrared (IR) spectroscopic analyses were performed with a Perkin−Elmer 881 and 1720-X Infrared Fourier Transform spectrometer using either Nujol mull or thin film methods for sample preparation.

Molecular Modelling Calculations: The minimum energy conformations of the chiral core were generated by combining molecular mechanics and molecular dynamics techniques using the Cerius2 v4.2 programme.[17] The Universal Force-Field v1.02[18] and QEq charges[19] was used in each case. Initially, structures were constructed using the Cerius2 graphical user interface and the energies of these structures minimised initially by the steepest-decent method followed by a truncated Newton−Raphson method. In order to obtain the low-energy conformations of the chiral core, a molecular dynamics simulation for the chiral core were carried out using an NVT ensemble. The simulation was performed with a single molecule in the gas phase at 1000 K for a period of 50 ps using a time-step of 1 fs and trajectory files containing the atomic coordinates were saved after every 50 iterations. Ten structures that had a low potential energy were then extracted from the trajectory file and these were then energy-minimised as described above. The resulting set of 10 conformers was then ranked according to their minimised energy level and the conformer with the lowest energy was selected and this is the conformer shown in the results.

***tert*-Butyl (4*R*)-4-{Bis[(4*R*)-3-(*tert*-butyloxycarbonyl)-2,2-dimethyl-1,3-oxazol-4-ylmethyl]aminomethyl}-2,2-dimethyl-1,3-oxazole-3-carboxylate (3):** A solution of L-Garner aldehyde **2** (0.50 g, 2.18 mmol), ammonium acetate (0.05 g, 0.62 mmol), $Na(OAc)_3BH$ (0.42 g, 2.0 mmol) and dry triethylamine (0.27 mL, 2.0 mmol) in dry CH_3CN (5 mL) was stirred at room temp. for 2 h. Water was added to the reaction mixture and the aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried with $MgSO_4$, filtered and the solvents evaporated under vacuum to afford a crude product that was purified by column chromatography (CH_2Cl_2/EtOAc, 8:2). The pure product was isolated as a white solid (0.36 g, 90%). R_f = 0.8 (CH_2Cl_2/ EtOAc, 5:5); m.p. 177−178 °C. $[\alpha]_D^{20}$ = −126.3 (c = 1.05, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.48 [s, 27 H, 3 × $C(CH_3)_3$], 1.51 [m, 9 H, 3 × $(CH_3)C(CH_3)$], 1.57 [m, 9 H, 3 × $(CH_3)C(CH_3)$], 2.46 (m, 6 H, 3 × CH_2N), 3.70 (m, 6 H, 3 × CH_2O), 3.90 (m, 3 H, 3 × CHN). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 23.6, 24.6, 27.3, 28.1, [$C(CH_3)_2$], 28.8, 28.9, [$C(CH_3)_3$], 55.2, 55.4 (CH_2N), 56.1, 56.2 (CHN), 65.9, 66.3 (OCH_2), 80.2, 80.7 [$C(CH_3)_3$], 93.9, 94.4 [$C(CH_3)_2$], 151.8, 152.4 [$NCOOC(CH_3)_3$]. IR $\tilde{\nu}$ = 1701, 1459, 1386, 1073, 845 cm^{-1}. MS (CI): m/z: 657.4454 [M + H]$^+$. $C_{33}H_{60}N_4O_9 \cdot 0.5H_2O$ (668.44): calcd. C 59.53, H 9.23, N 8.41; found C 59.21, H 9.08, N 8.32.

***tert*-Butyl (4*S*)-4-{Bis[(4*S*)-3-(*tert*-butyloxycarbonyl)-2,2-dimethyl-1,3-oxazol-4-ylmethyl]aminomethyl}-2,2-dimethyl-1,3-oxazole-3-carboxylate (7):** Employing an identical procedure to that used to produce **3**, the (*SSS*) compound **7** was obtained as a white solid (0.45 g, 88%) from D-Garner aldehyde **6** (0.54 g, 2.38 mmol) and ammonium acetate (0.06 g, 0.78 mmol). R_f = 0.8 (CH_2Cl_2/EtOAc, 5:5); m.p. 178−179 °C. $[\alpha]_D^{20}$ = +123.7 (c = 1.03 $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.40 [s, 27 H, 3 × $C(CH_3)_3$], 1.44 [m, 9 H, 3 × $(CH_3)C(CH_3)$], 1.50 [m, 9 H, 3 × $(CH_3)C(CH_3)$], 2.42 (m, 6 H, 3 × CH_2N), 3.62 (m, 6 H, 3 × CH_2O), 3.84 (m, 3 H, 3 × CHN). $C_{33}H_{60}N_4O_9$ (656.44): calcd. C 60.34, H 9.21, N 8.53; found C 59.96, H 9.27, N 8.40.

(*RRR*)-2-Amino-3-[bis(2-amino-3-hydroxypropyl)amino]-1-propanol (4): A solution of **3** (0.1 g, 0.156 mmol) and 6 N HCl (6 mL) was stirred at room temperature for 4 h. The solvent was evaporated under reduced pressure to afford the product as a yellowish solid (0.037 g, > 99.9%); m.p. > 250 °C. $[\alpha]_D^{20}$ = +18.6 (*c* = 1.06, $CHCl_3$). ^{1}H NMR (250 MHz, D_2O): δ = 2.68 [dd, *J* = 7.6, 14.0 Hz, 3 H, 3 × N(C*H*H)], 2.74 [dd, *J* = 6.3, 14.0 Hz, 3 H, 3 × N(CH*H*)], 3.46 (m, 3 H, 3 × C*H*NH_2), 3.60 [appt. dd, *J* = 5.3, 12.3 Hz, 3 H, 3 × C(H*H*)OH], 3.75 [appt. dd, *J* = 3.6, 12.3 Hz, 3 H, 3 × C(*H*H)OH]. ^{13}C NMR (62.8 MHz, D_2O): δ = 50.8 (*C*HNH_2), 53.8 (*C*H_2N), 59.7 (*C*H_2OH). MS (CI): *m*/*z* = 237.1939 $[M + H]^+$. IR $\tilde{\nu}$ = 3442, 3352, 1573, 1461, 722 cm^{-1}. $C_9H_{27}N_4O_3 \cdot 2HCl \cdot 1.9H_2O$ (352.43): calcd. C 30.48, H 7.96, N 15.80; found C 30.64, H 7.87, N 15.60.

(*SSS*)-2-Amino-3-[bis(2-amino-3-hydroxypropyl)amino]-1-propanol (8): Employing an identical procedure to that used to produce **4**, (*SSS*) compound **8** was obtained as a yellowish solid (0.10 g, > 99.9%) from **5** (0.28 g, 0.42 mmol); m.p. > 250 °C; $[\alpha]_D^{20}$ = −20.8 (*c* = 1.08, $CHCl_3$). ^{1}H NMR (250 MHz, D_2O): δ = 2.67 [dd, *J* = 7.6 and 14.0, 3 H, 3 × N(C*H*H)], 2.75 [dd, *J* = 6.3, 14.0 Hz, 3 H, 3 × N(CH*H*)], 3.46 (m, 3 H, 3 × C*H*NH_2), 3.60 [appt. dd, *J* = 5.3, 12.3 Hz, 3 H, 3 × C(H*H*)OH], 3.75 [appt. dd, *J* = 3.6, 12.3 Hz, 3 H, 3 × C(*H*H)OH]. $C_9H_{27}N_4O_3 \cdot 2HCl \cdot 0.6H_20$ (345.38): calcd. C 31.27, H 7.87, N 16.20; found C 30.86, H 7.92, N 15.88.

(*RRR*)-[({Bis[2-(*tert*-butoxycarbonylamino)-3-hydroxypropyl]-amino}methyl)(2-hydroxyethyl)amino](*tert*-butoxy)methanone (1): To a solution of **4** (0.15 g, 0.43 mmol) and triethylamine (0.39 mmol, 0.55 mL) in THF/water (10 mL, 9:1), di-*tert*-butyl dicarbonate (1.43 g, 6.5 mmol), dissolved in THF (4 mL), was added dropwise. After 4 h of stirring at room temperature, the solvent was evaporated to afford the crude product as a yellowish oil that was subsequently purified by column chromatography ($CHCl_3$/EtOH, 90:10) to yield the pure product as a white solid (0.21 g, 90%); R_f = 0.6 ($CHCl_3$/EtOH, 85:15); m.p. 119−120 °C; $[\alpha]_D^{20}$ = −44.6 (*c* = 1.03 $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.37 [s, 27 H, 3 × C(CH_3)$_3$], 2.49 [dd, 3 H, *J* = 5.7, 13.1 Hz, 3 × (CH*H*)N], 2.63 [dd, *J* = 7.1, 13.1 Hz, 3 H, 3 × (C*H*H)N], 3.42 (br. s, 3 H, 3 × CH_2OH), 3.62 (m, 9 H, 3 × C*H*NH, 3 × CH_2OH), 5.10 (d, *J* = 6.3 Hz, 3 H, 3 × CHN*H*). ^{13}C NMR (62.8 MHz, $[D_6]$DMSO): δ = 28.6 [C(*C*H_3)$_3$], 50.9 (*C*HNH), 56.4 (*C*H_2N), 61.9 (*C*H_2OH), 77.8 [*C*(CH$_3$)$_3$], 155.5 [NH*C*OOC(CH$_3$)$_3$]. MS (CI): *m*/*z* = 537.3517 $[M + H]^+$. IR $\tilde{\nu}$ = 3388, 3340, 1716, 1677, 1536, 1367, 759 cm^{-1}. $C_{24}H_{48}N_4O_9$ (536.34): calcd. C 53.71, H 9.01, N 10.43; found C 53.29, H 9.14, N 10.32.

(*SSS*)-[({Bis[2-(*tert*-butoxycarbonylamino)-3-hydroxypropyl]-amino}methyl)(2-hydroxyethyl)amino](*tert*-butoxy)methanone (5): Employing an identical procedure to that used to produce **1**, the (*SSS*) compound **5** was obtained as a white solid (0.29 g, 95%) from **8** (0.20 g, 0.57 mmol); R_f = 0.6 ($CHCl_3$/EtOH, 85:15); m.p. 119−120 °C; $[\alpha]_D^{20}$ = +45.7 (*c* = 1.05, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.38 [s, 27 H, 3 × C(CH_3)$_3$], 2.50 [dd, *J* = 5.7, 13.1 Hz, 3 H, 3 × (CH*H*)N], 2.62 [dd, *J* = 7.1, 13.1 Hz, 3 H, 3 × (C*H*H)N], 3.42 (br. s, 3 H, 3 × CH_2OH), 3.63 (m, 9 H, 3 × C*H*NH, 3 × CH_2OH), 5.10 (d, *J* = 6.3 Hz, 3 H, 3 × CHN*H*). $C_{24}H_{48}N_4O_9 \cdot 0.7H_2O$ (548.95): calcd. C 52.48, H 9.07, N 10.2; found C 52.33, H 8.90, N 9.97.

First Generation Chiral Dendrimer (Boc)$_6$-[G-1]$_3$-N$_{CR}$ (11): A solution of **9** (0.25 g, 0.56 mmol), the chiral core **1** (0.07 g, 0.12 mmol) and a catalytic amount of dimethylaminopyridine (DMAP) in dry CH_2Cl_2 (10 mL) was cooled to 0 °C under argon. Dicyclohexylcarbodiimide (DCC) (0.12 g, 0.56 mmol) in dry CH_2Cl_2 (5 mL) was then added dropwise to the stirred solution. The mixture was stirred at room temperature for 5 d and then filtered. The organic solution was concentrated under vacuum and the residue dissolved in EtOAc (10 mL) and then washed with 5% $NaHCO_3$ (aq.) (10 mL) and water (10 mL). The organic phase was dried with $MgSO_4$, filtered and then concentrated under vacuum to afford the crude product that was purified by size exclusion chromatography (THF) to yield the pure product as a white powder (0.16 g, 75%); R_f= 0.68 ($CHCl_3$/EtOH, 90:10). HPLC (CH_3CN/CH_3OH, 90:10): retention time 6.2 min, 98.76%; GPC (THF): PDI = 1.036. $[\alpha]_D^{20}$ = −11.9 (*c* = 1.05 $CHCl_3$). ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.30 [s, 54 H, 6 × C(CH_3)$_3$], 1.35 [s, 27 H, 3 × C(CH_3)$_3$], 2.45 [br. m, 3 H, 3 × (CH*H*)N], 2.80 [br. m, 3 H, 3 × (C*H*H)N], 3.17 [br. m, 12 H, 6 × CH_2NHCOOC(CH$_3$)$_3$], 3.92 [br. m, 3 H, 3 × C*H*NHCOOC(CH$_3$)$_3$], 4.19 [br. m, 3 H, 3 × C(H*H*)OCO], 4.40 [br. m, 3 H, 3 × C(*H*H)OCO], 4.96 (br. m, 3 H, 3 × C*H*OCO), 6.95 [br. m, 6 H, 6 × N*H*COOC(CH$_3$)$_3$], 7.10 [br. m, 3 H, 3 × N*H*COOC(CH$_3$)$_3$], 7.90 (br. m, 12 H, AA′XX′ system, 12 × *H*-ArCOO). ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 28.1 [C(*C*H$_3$)$_3$], 28.2 [C(*C*H$_3$)$_3$], 40.7 [*C*H_2NHCOOC(CH$_3$)$_3$], 47.8 [*C*HNHCOOC(CH$_3$)$_3$], 56.0 [(*C*H$_2$)N], 65.2 (*C*H_2OCO), 73.4 (*C*HOCO), 77.9 [*C*(CH$_3$)$_3$], 79.2 [*C*(CH$_3$)$_3$], 129.2, 129.5 (H-*Ar*-COO), 133.3, 133.9 (*Ar*COO), 155.3 [NH*C*OOC(CH$_3$)$_3$], 155.8 [NH*C*OOC(CH$_3$)$_3$], 164.7 (CH$_2$O*C*O), 164.9 (CHO*C*O). MS (MALDI-TOF): *m*/*z* = 1819.1 $[M + Na]^+$, 1835.2 $[M + K]^+$. IR $\tilde{\nu}$ = 3366, 1711, 1529, 1269, 1172, 730 cm^{-1}. $C_{83}H_{132}N_{10}O_{30}$ (1796.91): calcd. C 58.12, H 7.40, N 7.79; found C 57.67, H 7.55, N 7.67.

First Generation Chiral Dendrimer (Boc)$_6$-[G-1]$_3$-N$_{CS}$ (12): Employing an identical procedure to that used to produce **11**, compound **12** was obtained as a white solid (0.29 g, 77%) from compound **5** (0.11 g, 0.21 mmol) and **9** (0.41 g, 0.95 mmol); R_f= 0.68 ($CHCl_3$/EtOH, 90:10). HPLC (CH_3CN/CH_3OH, 90:10): retention time 6.2 min, 98.13%; GPC (THF): PDI = 1.037. $[\alpha]_D^{20}$ = +11.7 (*c* = 1.01, $CHCl_3$). ^{1}H NMR (250 MHz, $[D_6]$DMSO): δ = 1.31 [s, 54 H, 6 × C(CH_3)$_3$], 1.37 [s, 27 H, 3 × C(CH_3)$_3$], 2.49 [br. m, 3 H, 3 × (CH*H*)N], 2.80 [br. m, 3 H, 3 × (C*H*H)N], 3.21 [br. m, 12 H, 6 × CH_2NHCOOC(CH$_3$)$_3$], 3.95 [br. m, 3 H, 3 × C*H*NHCOOC(CH$_3$)$_3$], 4.20 [br. m, 3 H, 3 × C(H*H*)OCO], 4.40 [br. m, 3 H, 3 × C(*H*H)OCO], 4.97 (br. m, 3 H, 3 × C*H*OCO), 6.99 [br. m, 6 H, 6 × N*H*COOC(CH$_3$)$_3$], 7.10 [br. m, 3 H, 3 × N*H*COOC(CH$_3$)$_3$], 7.99 (br. m, 12 H, AA′XX′ system, 12 × *H*-ArCOO). $C_{83}H_{132}N_{10}O_{30} \cdot 1H_2O$ (1814.92): calcd. C 57.54, H 7.44, N 7.71; found C 57.48, H 7.41, N 7.61.

Second Generation Chiral Dendrimer (Boc)$_{12}$-[G-2]-N$_{CR}$ (13): A solution of **10** (0.36 g, 0.34 mmol), the chiral core **1** (0.04 g, 0.08 mmol) and a catalytic amount of DMAP in dry CH_2Cl_2 (5 mL) was cooled to 0 °C under nitrogen. DCC (0.07 g, 0.34 mmol) in dry CH_2Cl_2 (3 mL) was then added dropwise to the stirred solution. The mixture was stirred for 7 d and then filtered to isolate the crude product which was purified by size exclusion column chromatography (THF) to afford the pure product in 55% yield (0.05 g); R_f = 0.7 ($CHCl_3$/EtOH, 90:10). HPLC (CH_3CN/CH_3OH, 90:10): retention time 4.2 min, 98.77%; GPC (THF): PDI = 1.055. $[\alpha]_D^{20}$ = −10.8 (*c* = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.30 [s, 135 H, 15 × C(CH_3)$_3$], 2.45 [br. m, 3 H, 3 × (CH*H*)N], 2.80 [br. m, 3 H, 3 × (C*H*H)N], 3.17 [br. m, 24 H, 12 × CH_2NHCOOC(CH$_3$)$_3$], 3.65 [br. m, 12 H, 6 × CH_2CONH), 3.92 [br. m, 3 H, 3 × C*H*NHCOOC(CH$_3$)$_3$], 4.19 [br. m, 3 H, 3 × C(H*H*)OCO], 4.40 [br. m, 3 H, 3 × C(*H*H)OCO], 4.90 (br. m, 6 H, 6 × C*H*OCO), 5.40 (br. m, 3 H, 3 × C*H*OCO), 6.98 [br. m, 12 H, 12 × N*H*COOC(CH$_3$)$_3$], 7.01 [br. m, 3 H, 3 ×

N*H*COOC$(CH_3)_3$], 7.90 (m, 12 H, 12 × *H*-ArCONH), 7.99 (m, 24 H, 24 × *H*-ArCOO), 8.80 (br. m, 6 H, 6 × CH_2N*H*CO). ^{13}C NMR (100 MHz, [D$_6$]DMSO); δ = 27.9 [C(*C*$H_3)_3$], 40.5 [CH_2NHCOOC(C*H*$_3)_3$], 40.6 (*C*H_2NHCO), 47.8 [*C*HNHCOOC$(CH_3)_3$], 56.0 [(*C*H_2)N], 65.2 (*C*H_2OCO), 73.0 (*C*HOCO), 73.2 (*C*HOCO), 77.8 [*C*$(CH_3)_3$], 79.2 [*C*$(CH_3)_3$], 127.1 (H-*Ar*CONH), 129.5 (H-*Ar*COO), 132.4 (*Ar*CONH), 133.4 (*Ar*-COO), 133.5 (*Ar*COO), 138.1 (*Ar*COO), 155.3 [NH*C*OOC$(CH_3)_3$], 155.7 [NH*C*OOC$(CH_3)_3$], 164.8 (CH_2O*C*O and CHO*C*O), 166.0 (CH_2NH*C*O). MS (MALDI-TOF): *m*/*z* = 3740.2 [M + Na]$^+$, 3756.3 [M + K]$^+$. IR $\tilde{\nu}$ = 3357, 1711, 1536, 1268, 1107, 730 cm^{-1}.

Second Generation Chiral Dendrimer (Boc)$_{12}$-[G-2]$_3$-N$_{CS}$ (14): By employing an identical procedure that was used to produce **13**, **(Boc)$_{12}$-[G-2]$_3$-N$_{CS}$ 14** was obtained as a white solid (0.30 g, 52%) from compound **5** (0.08 g, 0.16 mmol) and **10** (0.78 g, 0.72 mmol); R_f = 0.7 ($CHCl_3$/EtOH, 90:10). HPLC (CH_3CN/CH_3OH, 90:10): retention time 4.3 min, 100.0%; GPC (THF): PDI = 1.051. $[\alpha]_D^{20}$ = +10.4 (*c* = 1.02, $CHCl_3$).

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