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Synthesis and characterization of axially chiral enantiopure novel dendrimers

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Abstract—The synthesis of enantiopure dendrimers with axially chiral (*S*)-1,1′-bi-2-naphthol as a core unit and with *m*-terphenyl as a hydrophobic surface end group has been achieved. Chiroptical and fluorescence studies indicated the widening of the torsional angle between the two-naphthyl units with increase in the dendritic generation.

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1. Introduction

One of the most fascinating aspects of modern synthetic organic chemistry is the synthesis of chiral compounds, which play an important role in biology and material aspects such as liquid crystals. Catalytic asymmetric synthesis has attracted attention for preparing nonracemic chiral compounds. The synthesis of dendrimers with novel properties has become an active field of research in recent times.[1] Chirality in dendrimers can be used for studying interactions within the overall macromolecular system.[2] Some advanced applications for enantiopure dendrimers are biocompatibility, molecular recognition, auxiliaries and catalysts for asymmetric synthesis. Optically active (*S*)-1,1′-bi-2-naphthol is well known for the strong dependence of its optical activity due to the repulsion between the two naphthyl rings and hence a series of modifications of bridged binaphthyl diether linkage has previously been studied.[3] Although dipolar dendritic macromolecules are well known, the synthesis of optically active dendrimers has been rarely reported.[4] Optically active dendritic binaphthols were found to form metal complexes and catalyze asymmetric C–C bond formation.[5] Pu et al.[6] have reported the synthesis of structurally rigid and optically active dendrimers. The synthesis of highly effective and recyclable dendritic BINAP ligands for asymmetry hydrogenation[7] and the application of dendritic BINAP as an enantioselective catalyst[8] have been reported. Chiral dendrimers represent another important target due to their possible applications in sensor technology.[9] We have recently reported the synthesis of permanent fluorescence sensing hyperbranched dendritic architectures[10] and bactericidal efficacy of novel dendrimers.[11]

We report herein, the synthesis of enantiopure dendrimers **1a**,**b** and **1c** with axially chiral (*S*)-1,1′-bi-2-naphthol as a core unit with dendritic wedges such as *m*-terphenyl unit as a hydrophobic surface group. All the synthesized enantiopure dendrimers exhibited optical and fluorescence properties.

2. Results and discussion

Dendrimers **1a**,**b** and **1c** were prepared from (*S*)-BINOL and from the corresponding dendritic bromides **3**, **4** and **5** respectively. In ^{1}H NMR, dendrimer **1a** displayed a sharp singlet at δ 4.94 for *O*-methylene protons in addition to the aromatic protons at δ 7.06–7.79. In ^{13}C NMR, the methylene carbon appeared at δ 70.8 in addition to 16 aromatic carbons. The appearance of a molecular ion peak at *m*/*z* 770 in the FAB mass spectrum also confirmed structure **1a**.

In order to synthesize the first generation dendrimer **1b**, dendritic bromide **4** (G$_1$)-Br was prepared as reported[12] from 2.1 equiv. of bromide **3** mt-Br and methyl 3,5-dihydroxybenzoate followed by a series of functional group transformations. The reaction of 2.1 equiv. of dendritic bromide **4** (G$_1$)-Br with 1 equiv. of (*S*)-BINOL in the presence of K$_2$CO$_3$ in DMF gave (*S*)-dendrimer **1b**

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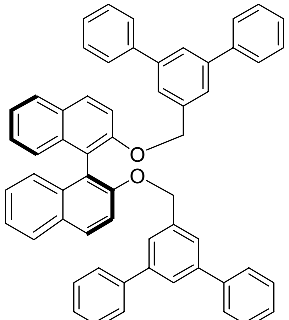
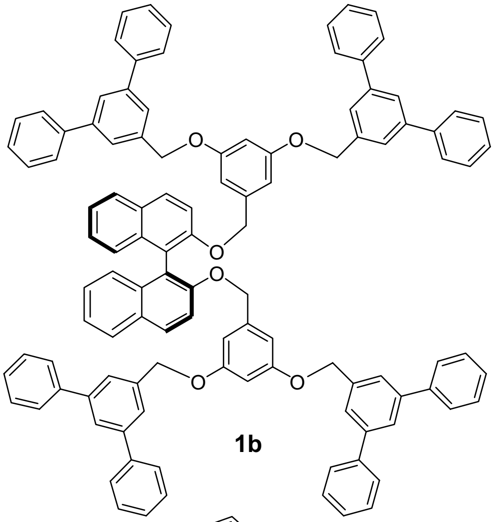
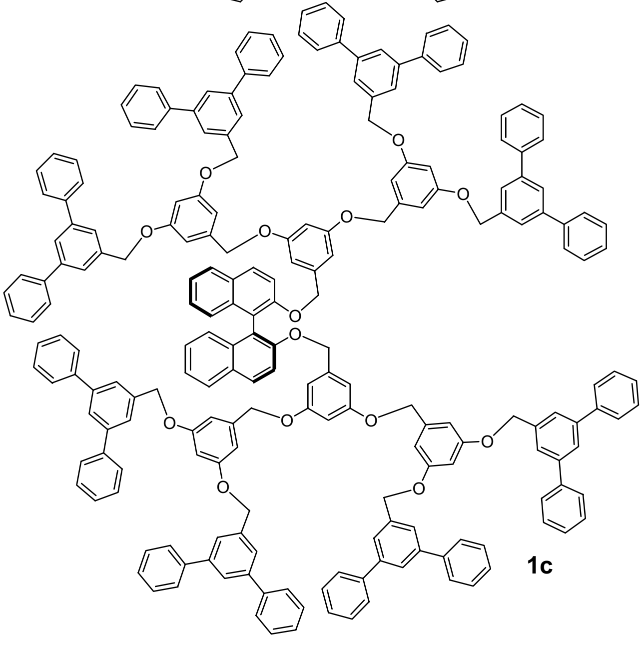


1a



1b



1c

in 36% yield. ^{1}H NMR spectrum of dendrimer **1b** displayed two singlets for two types of methylene protons at δ 4.93 and 4.59, in addition to the aromatic protons and in ^{13}C NMR methylene carbons appeared at δ 69.7 and 70.8 in addition to 17 aromatic carbons. The structure of dendrimer **1b** was further supported by the appearance of a molecular ion at *m*/*z* 1499 in the FAB mass spectrum.

Second generation (*S*)-dendrimer **1c** was obtained in 24% yield by the reaction of (*S*)-BINOL with 2.1 equiv. of dendritic bromide **5** (G_2)-Br, which was easily obtained by repeating a similar reaction sequence, as mentioned earlier, under the preparation of dendritic bromide **5** (G_2)-Br. Dendrimer **1c** was thoroughly characterized from spectral and analytical data (Scheme 1).

2.1. Chiroptical properties of enantiopure dendrimers 1a–c

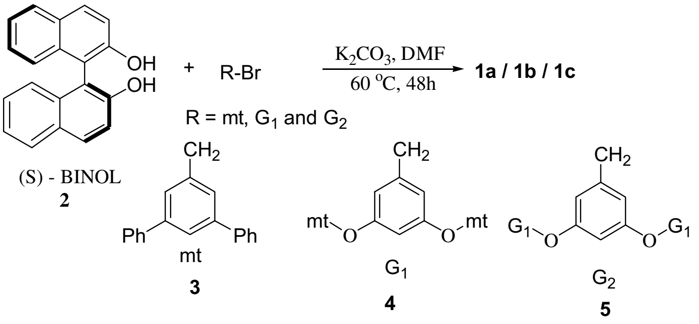
Specific rotations were determined for (*S*)-dendrimers **1a**,**b** and **1c** using $CHCl_3$ as the solvent with the results summarized in Table 1. Molar rotation was measured at 585 nm. Zero generation dendrimer **1a**, first generation dendrimer **1b** and second-generation dendrimer **1c** showed molar rotations equal to −687.45, −735.10 and −1063.44, respectively.

For dendrimers **1a**–**c**, circular dichroism (Fig. 1) studies showed a decrease in the specific rotation values from (*S*)-dendrimer **1a** to **1c** indicating a variation of the torsional angle between the two naphthyl units exceeding the orthogonal values. Further, by going from zero generation dendrimer to second generation, a larger negative value for molar optical rotation was observed due to an increase in steric hindrance by the dendritic wedges.

It is noteworthy that when Frechét type dendritic wedges were used, the value of molar rotation was not really large,[13] whereas herein, *m*-terphenyl residue gave a large negative value. This could be due to increase in steric repulsion of highly rigid and organized dendritic wedges with decreased conformational mobility, which in turn reflect in increased torsional angle and steric repulsion.

2.2. Fluorescence and optical rotational studies

The UV absorption spectra of enantiopure (*S*)-dendrimer **1a** showed λ_{max} at 370 nm in addition to shoulders at 357 and 338 nm. However, for the first generation dendrimer **1b**, λ_{max} shifted to 317 nm while in the second-generation dendrimer **1c**, λ_{max} was observed at 309 nm. The hypochromic shift observed in UV spectrum could be due to increased steric bulkiness associated with increase in conformational rigidity, which in turn results in increased torsional angle between the two naphthyl units. The change in λ_{max} from dendrimers **1a** to **1c** indicates the decreased degree of conjugation due to increased torsional angle between the naphthyl rings as a result of steric hindrance between the conformationally rigid dendritic *m*-terphenyl wedges. Similarly, molar extinction coefficient decreased from zeroth generation dendrimer to second-generation dendrimer. Dendrimer **1a** had emission maximum at 379 nm, whereas dendrimer **1b** and **1c** exhibited emission at 366 and 338 nm (**1c** emitted a weak broad band in the region of 380–440 nm), respectively. The hypsochromic shift emission observed from dendrimers **1a** to **1c** again demonstrates the widening of torsional angle between the naphthyl rings. Further, the higher generation



Scheme 1.

Table 1. Specific rotation of (*S*)-binaphthol dendrimers **1a**–**c**

Compounds	$[\alpha]_D^{25}$	Molecular weight (g/mol)	Molar rotation
(*S*)-Dendrimer **1a**	−89.3	770	−687.45
(*S*)-Dendrimer **1b**	−49.0	1499	−735.10
(*S*)-Dendrimer **1c**	−36.0	2954	−1063.44

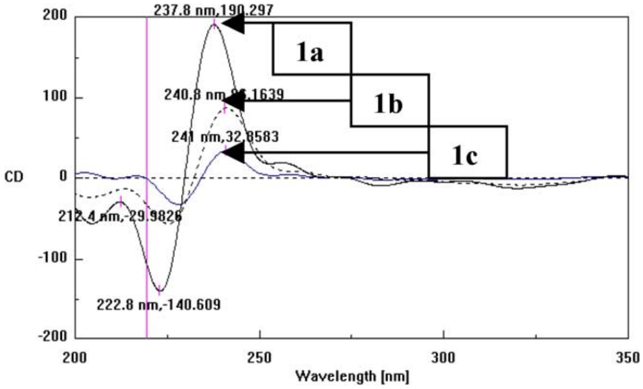


Figure 1. Circular dichroism spectrum of (*S*)-binaphthol dendrimers **1a**–**c**.

dendrimer **1c** emits nearly twice the lesser intensity than the zeroth generation dendrimer **1a**.

2.3. Decay analysis

All the dendrimers exhibited a single exponential decay with a lifetime as shown in Table 2. Higher generation dendrimer exhibited higher lifetime than zero generation dendrimer and the χ^2 values were found to be almost constant.

3. Conclusion

In conclusion, when Frechét type dendritic wedges were used the value of the molar rotation was small. However, with our *m*-terphenyl residue used as dendritic wedges, a large negative value was observed. This could be due to the increase in steric repulsion of the highly rigid and organized dendritic wedges with decreased conformational mobility, which in turn reflect in the increased torsional angle and steric repulsion. The hypsochromic shift emission observed from dendrimer **1a** to **1c** again demonstrates the widening of torsional angle between the naphthyl rings. Furthermore, the higher generation dendrimer **1c** emits nearly twice the lesser intensity than the zero generation dendrimer **1a**. All the dendrimers exhibited single exponential decay with lifetime. Higher generation dendrimers exhibited higher lifetimes than zero generation dendrimer and the χ^2 values were found to be almost constant.

Table 2. Lifetime study on (*S*)-binaphthol dendrimers **1a**–**c**

Dendrimer	Analysis	Lifetime (ns)	Amplitudes (%)	χ^2
1a	Single exp.	0.869	100	1.01
1b	Single exp.	0.897	100	1.11
1c	Single exp.	0.940	100	1.17

4. Experimental

4.1. General

All melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using Jeol GSX 400 (400 MHz) and Jeol ECA 500 (500 MHz) NMR spectrometer. Mass spectra were recorded using Jeol DX 303, Jeol SX 102 / DA–600 (6 kV, 10 mA) and MALDI-TOF LD. Column chromatography was performed using silica gel (100–200 mesh).

4.1.1. General procedure for the preparation of (*S*)-binaphthol based dendrimer 1a–c. A mixture of (*S*)-BINOL **2** (1 mmol) and bromide **3**/**4**/**5**[12] (2.1 mmol) was stirred with K_2CO_3 (5 mmol) in DMF (20 mL) at 60 °C for 48 h. The reaction mixture was then poured into H_2O and extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extract was washed with brine and dried over $MgSO_4$. Evaporation of the organic layer gave a residue, which was chromatographed over SiO_2 using hexane–$CHCl_3$ to give the corresponding dendrimer.

4.1.1.1. (*S*)-Binaphthol based dendrimer 1a. Yield: 0.86 g, 44%; hexane–$CHCl_3$ (2:8); mp 168–172 °C; $[\alpha]_D^{25} = -89.3$ (c 1, $CHCl_3$). Anal. Calcd for $C_{58}H_{42}O_2$: C, 90.38; H, 5.45. Found: C, 90.34; H, 5.42; ^1H NMR ($CDCl_3$): δ 4.94 (s, 4 H), 7.06–7.79 (m, 38H); ^{13}C NMR δ 70.8, 123.7, 124.2, 124.9, 125.3, 126.4, 127.1, 127.2, 127.9, 128.5, 129.3, 129.4, 134.1, 138.4, 140.6, 141.4, 153.9; MS: *m*/*z* 770 (M^+).

4.1.1.2. (*S*)-Binaphthol based dendrimer 1b. Yield: 0.098 g, 37%; hexane–$CHCl_3$ (1:9); mp 104–108 °C; $[\alpha]_D^{25} = -49.0$ (*c* 1, $CHCl_3$). Anal. Calcd for $C_{110}H_{82}O_6$: C, 88.11; H, 5.47. Found: C, 88.08; H, 5.42; ^1H NMR ($CDCl_3$): δ 4.93 (s, 4H), 4.59 (s, 8H), 7.11–7.77 (m, 70H); ^{13}C NMR: δ 69.7, 70.8, 101.4, 105.0, 115.6, 120.6, 123.8, 125.3, 125.7, 127.5, 127.8, 129.3, 134.1, 137.8, 140.0, 140.8, 142.0, 153.9, 159.7; MS: *m*/*z* 1499 (M^+).

4.1.1.3. (*S*)-Binaphthol based dendrimer 1c. Yield: 0.025 g, 24%; $CHCl_3$; mp 8690 °C; $[\alpha]_D^{25} = -36.0$ (*c* 1, $CHCl_3$). Anal. Calcd for $C_{214}H_{162}O_{14}$: C, 86.93; H, 5.48. Found: C, 86.88; H, 5.44; ^1H NMR ($CDCl_3$): δ 4.35 (s, 4H), 4.74 (s, 8H), 4.93 (s, 16H), 7.06–7.91 (m, 134H); ^{13}C NMR: δ 70.0, 70.2, 72.5, 101.8, 106.5, 125.2, 125.7, 127.2, 127.4, 128.7, 137.8, 140.7, 142.0, 159.9; MS (FAB): *m*/*z* 2954 (M^+).

4.1.1.4. Chiroptical measurement. Circular dichroism (CD) measurements, performed on a JASCO J-715 spectrophotometer equipped with thermostated cell holder, using a quartz cell of 1.0 mm path length. Spectra were collected over the wavelength from 200 to 350 nm with a bandwidth of 1.0 nm. For each spectrum, five scans were collected, averaged and subtracted from the solvent THF. The CD measurements were carried out at 25 °C with a concentration of 10^{-3} M of dendrimers in $CHCl_3$.

4.1.1.5. Fluorescence measurement. Fluorescence spectra were recorded using Perkin–Elmer LS 5B luminescence spectrum in $CHCl_3$. Fluorescence decay was recorded using the TCSPC method with the following setup. A diode pumped millena CW laser 532 nm was used to pump a Ti: sapphire rod in a Tsunami picosecond mode locked laser system. The 750 nm (80 MHz) output was taken from the Ti: sapphire laser and passed through a pulse picker to generate a 4 MHz pulse. The second harmonic output (375 nm) was generated by a flexible harmonic generator. The vertically polarized 375 nm laser was used to excite the sample. The fluorescence emission at the magic angle (54.7°) was dispersed in a monochromator (f/3 aperture), counted by a MCP PMT (Hamamatsu R 3809) and processed through CFD, TAC and MCA. The instrument response function for this system is ~52 ns; the fluorescence decay was analyzed by using the software provided by IBH (DAS 6) analysis software.

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