A convenient route to dendritic binaphthyl-containing chiral crown ethers

Dai-Hua Tang, Xiao-Min Chen and Qing-Hua Fan*

Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, P. R. China

Novel dendritic binaphthyl-containing chiral crown ethers have been synthesised in four steps from (*R*) 2,2'-dihydroxy-1,1'-binaphthyl-3,3'-dicarboxylic acid with satisfactory yield.

Keywords: dendrimers, crown ethers, chirality, synthesis

Dendrimers are attracting increasing attention because of their unique structures and properties. A characteristic property of dendrimers is that their structure can produce localised microenvironments or internal cavities, analogous to those of found at the active sites of enzymes.[1] The combination of dendrimers and small molecular hosts thus provides a new class of hybrid macromolecules, which have increasing significance in many fields: such as biology, supramolecular chemistry, medicine and catalysis, any such hybrid macromolecules, such as dendrimer-functionalised-β-cyclodextrin,[2] calixarene-based dendrimers,[3] crowned dendrimers,[4-5] dendritic cyclophanes,[6] have been synthesised. Among them, very few are chiral supramolecular hosts.[2, 7]

Optically active binaphthyl compounds have been extensively applied in asymmetric catalysis and in molecular recognition.[8-9] Recently, BINOL- and BINAP-cored dendrimers have been synthesised as chiral ligands or as chiral sensors by others[10] and ourselves.[11-15] As an extension of our study, we report here a convenient route to dendritic binaphthyl chiral crown ethers.

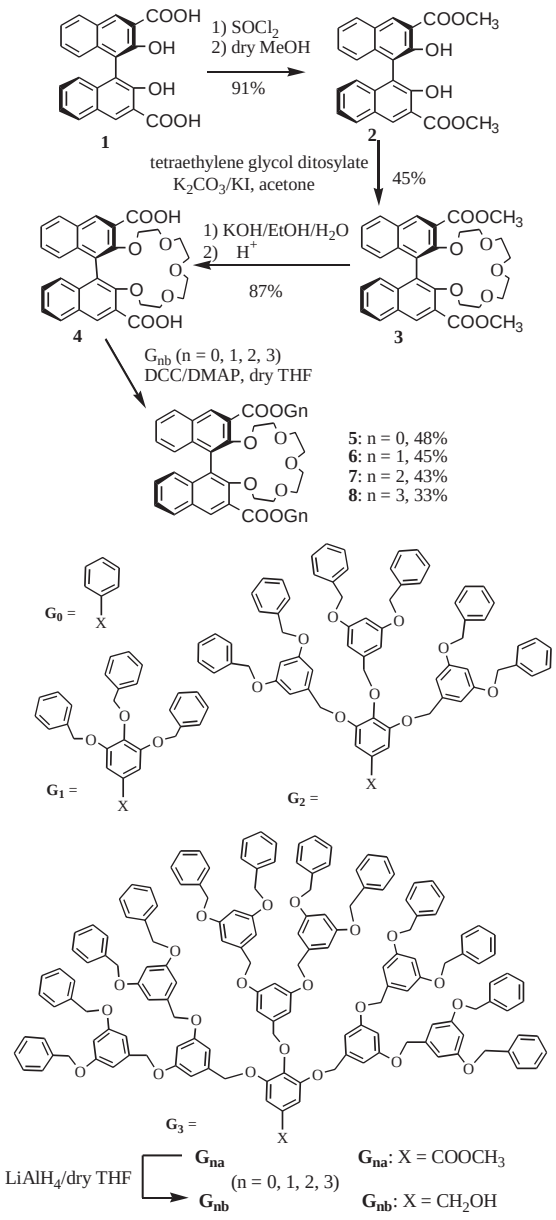
The 3,3'-positions on the binaphthyl backbone of chiral 1, 1'-binaphthyl-2,2'-crown ethers was chosen for the attachment of dendritic wedges. This choice was due to the proximity of the dendritic wedges to the crown ether, which might provide a unique opportunity to study the influence of the shape and architecture of the dendritic wedges on the chiral microenvironment built around the crown ether through systematically adjusting the generation of the dendrimer. A number of chiral BINOL derivatives with substituents at the 3,3'-positons have been reported. These provide a synthetic access to these positions for the attachment of dendritic wedges.[16] The synthetic route is outlined in Scheme 1.

(*R*)-2,2'-Dihydroxy-1,1'-binaphthyl-3,3'-dicarboxylic acid **1** was synthesised by the literature method.[17] Chlorination of **1** followed by reacting with anhydrous methanol gave the ester compound **2**.[18]

The key intermediate compound, binaphthyl-containing chiral crown ether **3**, was firstly synthesised by using a modified procedure. The synthetic route of chiral 17-crown-5 **3** is rather different from that of its analogue chiral 20-crown-6, which has been synthesised by Cram and coworkers,[18] who developed many approaches to small molecular binaphthyl crown ethers under strong basic circumstances.[19-22] Firstly, we applied Cram's methods[19-20] to synthesise **3** using *t*-BuOK as the base. This gave a low yield and very poor selectivity. Fortunately, when we used anhydrous K_2CO_3/KI instead of *t*-BuOK as the base, the reaction of **2** with tetraethylene glycol ditosylate proceeded smoothly and gave **3** with 45% yield.

The conversion of **3** into **4** was achieved by using the literature procedure.[19] AB_2–AB_3 type of Fréchet's dendrons (**Gn**) were synthesised via convergent method reported by Fréchet.[23]

Finally, the condensation reaction of **4** with the dendritic wedges with benzyl hydroxyl group at the focal point $\mathbf{G_{nb}}$ (n = 0–3) in the presence of dicyclohexylcarbodiimide (DCC) and 4-dimethyl aminopyridine (DMAP) in dry THF at room temperature gave the dendritic binaphthyl-containing chiral crown ethers in moderate yield. The reaction yields decreased slightly with increase dendrimer generation due to steric hindrance. These compounds were purified by column chromatography and characterised by ^{1}H NMR and MALDI-TOF spectra. All these dendritic chiral crown ethers give well-resolved ^{1}H NMR spectra consistent with their structures. The results of MALDI-TOF mass spectra of these dendritic chiral crown ethers match the calculated values.



Scheme 1 Synthesis of dendritic binaphthyl-containing chiral crown ethers.

* Correspondence. E-mail: fanqh@iccas.ac.cn

Experimental

The ^{1}H NMR was recorded on a Bruker DM 300 spectrometer in $CDCl_3$ with TMS as internal standard. MALDI-TOF mass spectra were obtained on an Instrum III spectrometer with α-cyano-4-hydroxy-cinnamic acid (CCA) as a matrix. Optical rotations were measured with AA-10R automatic polarimeter. Commercial reagents were used as received without further purification.

Compound **1**[17] and **2**[18] were synthesised according to published procedures. Dendrons ($\mathbf{G_{na}}$ and $\mathbf{G_{nb}}$, *n*=0–3) were synthesised by using Fréchet's method.[22]

Synthesis of **3**: A mixture of **2** (113.5 mg, 0.282 mmol), tetraethylene glycol ditosylate (141.8 mg, 0.282 mmol), anhydrous potassium bicarbonate (5.85 g, 42.3 mmol) and potassium iodide (0.47 g, 2.82 mmol) was refluxed in acetone (70 ml) for 72 h under N_2. The mixture was filtered and the filtrate was evaporated by rotary evaporator. The residue was chromatographed on silica gel using *n*-hexane/ethyl acetate (v/v = 1/1) as eluent to give **3** as a white solid (71.4 mg, 45.2 %). $[\alpha]_D^{20}$ +70.4(*c* 1.08, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.49 (s, 2H), 7.95 (d, 2H, *J*=8.2 Hz), 7.30–7.46 (m, 4H), 7.11 (d, 2H, *J*=8.4 Hz), 3.99 (s, 6H), 3.18–3.96 (m, 16H); MALDI-TOF-MS *m/z*: 582.9 $[M+Na]^+$, 598.9 $[M+K]^+$, Calcd: 560.205[M].

Synthesis of **4:** A mixture of **3** (30.5 mg, 0.0544 mmol), KOH (0.56 g, 0.01mol), H_2O (5 ml) and 95% EtOH (5 ml) was stirred under N_2 at room temperature for 48 h. The solution was acidified to pH = 2 by dropwise addition of 6 N HCl and then extracted with ethyl acetate. The extract was dried with anhydrous sodium sulfate and solvent was evaporated by rotary evaporator. The residue was chromatographed on silica gel using ethyl acetate/methanol (v/v = 1/1) as eluent to give **4** as a white solid (25.1 mg, 86.6%). $[\alpha]_D^{20}$ +92.2 (*c*=1.02, C_2H_5OH); ^{1}H NMR (300 MHz, $CDCl_3$), δ: 10.75 (s, br, 2H), 8.74 (s, 2H), 7.94 (d, 2H, *J*=8.1 Hz), 7.27–7.43 (m, 4H), 7.00 (d, 2H, *J*=8.5 Hz), 3.16–3.93 (m, 16H); MALDI-TOF-MS *m/z*: 555.3 $[M+Na]^+$, 571.2 $[M+K]^+$, Calcd: 532.173[M].

Synthesis of **5:** A mixture of **4** (21.3 mg, 0.04 mmol), benzyl alcohol (zero generation dendron, freshly distilled, 26.0 mg, 0.24 mmol), DCC (41.3 mg, 0.2 mmol), DMAP (24.4 mg, 0.2 mmol) and dry THF (10 ml) was stirred under N_2 at room temperature for 8 h. The solvent was evaporated by rotary evaporator and the residue was chromatographed on silica gel using dichloromethane/ acetone (v/v = 19/1) as eluent to give **5** as a white solid (13.6 mg, 47.7%). $[\alpha]_D^{20}$ +28.7 (*c*=0.835, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.50 (s, 2H), 7.94 (d, 2H, *J*=8.1 Hz), 7.26–7.54 (m, 14H), 7.11 (d, 2H, *J*=8.5 Hz), 5.44 (s, 4H), 3.12-3.98 (m, 16H); MALDI-TOF-MS *m/z*: 735.2 $[M+Na]^+$, Calcd: 712.27[M].

Synthesis of **6:** Prepared according to the above procedure for **5**, the resulting residue was purified by chromatography on silica gel (eluent: dichloromethane/acetone v/v = 98/2) to give **6** as a white solid (yield 44.5%). $[\alpha]_D^{20}$ +15.5 (*c*=0.905, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.37 (s, 2H), 7.85 (d, 2H, *J*=8.1 Hz), 7.18–7.35 (m, 34H), 7.05 (d, 2H, *J*=8.4 Hz), 6.76 (s, 4H), 5.23 (d, 4H, *J*=3.9 Hz), 5.03 (s, 8H), 4.98 (s, 4H), 3.02–3.84 (m, 16H). MALDI-TOF-MS *m/z*: 1371.19 $[M+Na]^+$, 1387.15 $[M+K]^+$, Calcd: 1348.52[M].

Synthesis of **7**: Prepared according to the above prodedure for 5, the resulting residue was purified by chromatography on silica gel (eluent: *n*-hexane/acetone v/v = 3/2) to give 7 as a white solid (yield 42.7%). $[\alpha]_D^{20}$ +9.4 (*c*=1.06, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.45 (s, 2H), 7.89 (d, 2H, *J*=8.1 Hz), 7.24–7.36 (m, 64H), 7.11 (d, 2H, *J*=8.4 Hz), 6.41-6.86 (m, 22H), 5.31 (d, 4H, *J*=3.8 Hz), 4.73-5.07 (m, 36H), 3.02-3.84 (m, 16H); MALDI-TOF-MS *m/z*: 2645.2 $[M+Na]^+$, Calcd: 2621.02[M].

Synthesis of **8:** Prepared according to the above procedure for **5**, the resulting residue was purified by chromatography on silica gel (eluent: *n*-hexane/acetone v/v = 1/1) to give **8** as a white solid (yield 32.5%). $[\alpha]_D^{20}$ +3.2 (*c*=0.625, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.43 (s, 2H), 7.85 (d, 2H, *J*=8.0 Hz), 7.84–7.18 (m, 124H), 7.07 (d, 2H, *J*=8.3 Hz), 6.87–6.45 (m, 58H), 5.29-4.60 (m, 88H), 3.02-3.84 (m, 16H). MALDI-TOF-MS *m/z*: 5195 $[M+Na]^+$, Calcd: 5170.05[M].

We are grateful to the National Natural Science Foundation of China (No. 203900507, 20325209 and 20102006) and Chinese Academy of Sciences.

Received 22 July 2004; accepted 30 August 2004
Paper 04/2670

References

1 M.W.P.L. Baars and E.W. Meijer, *Top. Curr. Chem.*, 2000, **210**, 131.
2 G.R. Newkome, L.A. Godínez and C.N. Moorefield, *Chem. Commun.*, 1998, 1821.
3 V. Šťastny, I. Stibor, H. Dvořáková, and P. Lhoták, *Tetrahedron*, 2004, **60**, 3383.
4 I. Gitsov and P.T. Ivanova. *Chem. Commun.*, 2000, 269.
5 J.W. Jones, W.S. Bryant, A.W. Bosman, R.A.J. Janssen, E.W. Meijer and H.W. Gibson, *J. Org. Chem.*, 2003, **68**, 2385.
6 S. Mattei, P. Wallimann, B. Kenda, W. Amrein and F. Diederich, *Helv. Chim. Acta*, 1997, **80**, 2391.
7 D.K. Smith and F. Diederich, *Chem. Commun.*, 1998, 2501.
8 R. Noyori, *Acc. Chem. Res.*, 1990, **23**, 345.
9 G. Bringmann, R. Walter and R. Weirich, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 977.
10 V.J. Pugh, Q.S. Hu and L. Pu, *Angew. Chem., Int. Ed.* 2000, **39**, 3638.
11 Q.H. Fan, Y.M. Chen, X. M. Chen, D.Z. Jiang, F. Xi and A.S.C. Chan, *Chem. Commun.*, 2000, 789.
12 Q.H. Fan, G.H. Liu, X. M. Chen, G. J. Deng and A.S.C. Chan, *Tetrahedron: Asymmetry*, 2001, **12**, 1559.
13 Q.H. Fan, R. Zhang, G.J. Deng and X.M. Chen, *J. Chem. Res.*, 2002, 318-320.
14 G.J. Deng, Q.H. Fan, X.M. Chen, D.S. Liu, and A.S.C. Chan, *Chem. Commun.*, 2002, 1570.
15 G.H. Liu, W.J and Tang, Q.H. Fan, *Tetrahedron*, 2003, **59**, 8603.
16 Y. Chen, S. Yekta and A.K. Yudin, *Chem. Rev.* 2003**, 103**, 3155.
17 H. Kitajima, K. Ito, Y. Aoki and T. Katsuki. *Bull. Chem. Soc. Jpn.*, 1997, **70**, 207.
18 J.T. Groves and P. Viski. *J. Org. Chem.*, 1990, **55**, 3628.
19 R.C. Helgeson, G.R. Weisman, J.L. Toner, T.L. Tarnowski, Y. Chao, J.M. Mayer and D.J. Cram. *J. Am. Chem. Soc.*, 1979, **101**, 4928.
20 E.P. Kyba, R.C. Helgeson, K. Madan, G.W. Gokel, T.L. Tarnowski, S.S. Moore and D.J. Cram. *J. Am. Chem. Soc.*, 1977, **99**, 2564.
21 D.J. Cram, R.C. Helgeson, S.C. Peacock, L.J. Kaplan, L.A. Domeier, P. Moreau, K. Koga, J.M. Mayer, Y. Chao, M.G. Siegel, D.H. Hoffman and G.D.Y. Sogah. *J. Org. Chem.*, 1978, **43**, 1930.
22 D.J. Cram, R.C. Helgeson, K. Koga, E.P. Kyba, K. Madan, L.R. Sousa, M.G. Siegel, P. Moreau, G.W. Gokel, J.M. Timko and G.D.Y. Sogah. *J. Org. Chem.*, 1978, **43**, 2758.
23 C.J. Hawker and J.M. J. Fréchet. *J. Am. Chem. Soc.*, 1990, **112**, 7638.