Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 2322–2327

Chiral Schiff base derivatives of calix[4]arene: synthesis and complexation studies with chiral and achiral amines

Mustafa Durmaz, Sabri Alpaydin, Abdulkadir Sirit and Mustafa Yilmaz*

Department of Chemistry, Selçuk University, 42031 Konya, Turkey

Received 6 July 2006; accepted 11 August 2006
Available online 20 September 2006

Abstract—Novel chiral Schiff base derivatives of calix[4]arenes **1**–**3** have been prepared from the reaction of 5,17-diformyl-25,27-dipropoxy-26,28-dihydroxycalix[4]arene **4** with (*S*)-(−)-1-phenylethylamine, (*R*)-(−)-1-cyclohexylethylamine, and (*R*)-(−)-2-heptylamine, respectively, by a convenient method in 69–80% yields. Spectrophotometric titrations have been performed in $CHCl_3$ at 20–30 °C in order to obtain the binding constants (*K*) and thermodynamic quantities (ΔH and ΔS) for the stoichiometric 1:1 inclusion complexation of various amines with these new host compounds. The molecular recognition abilities and enantioselectivity for guests (*R*)- and (*S*)-α-phenylethylamine, 3-morpholinopropylamine and *n*-butylamine are discussed from a thermodynamic point of view.

1. Introduction

Molecular recognition is one of the most fundamental processes in which functional groups of receptors form supramolecules with substrates by non-covalent interaction, such as hydrogen bonding, electrostatic interaction, and hydrophobic interaction.[1] The study of molecular recognition can provide valuable information for understanding the interactions between biological molecules, and offer new perspectives for the development of useful molecular devices in biochemical and pharmaceutical studies, separation processes, catalysis, and sensing.[2] Therefore, the design of new and efficient artificial receptors for specific target molecules is always a challenge for supramolecular chemistry and analytical techniques.[3]

Calixarenes, the third generation of supramolecules, after crown ethers and cyclodextrins, are phenol-based macrocycles,[4,5] which are able to form stable and selective complexes with cations, anions, or neutral molecules.[6] The most frequently used strategies for introducing chiral recognition ability into calixarenes are to anchor chiral subunits at either the lower or the upper rims of the calixarene macrocyclic ring.[7,8] The chiral receptors based on the calixarene platform may have potential applications in the preparation, separation, and analysis of enantiomers.[9] In this regard, investigations on the synthesis and enantiomeric recognition properties of chiral calix[4]arene derivatives have attracted considerable attention.

Amines represent either the key entity itself or a substructure of a more complex assembly in numerous, biologically important, natural, and synthetic products. The investigation of the chiral recognition of amines and substituted ammonium compounds by artificial receptors was of critical importance in the preparation, separation, and analysis of enantiomerically pure amines and disclosing the mechanism of interaction of the amines with biological systems.[10]

In our previous work,[11] various types of chiral calix[4]arene derivatives have been synthesized and tested as potential ligands for their recognition abilities. Herein, we report the synthesis of new chiral calix[4]arene Schiff base derivatives and their recognition abilities for certain chiral and achiral amines by a UV–vis titration method in $CHCl_3$.

2. Results and discussion

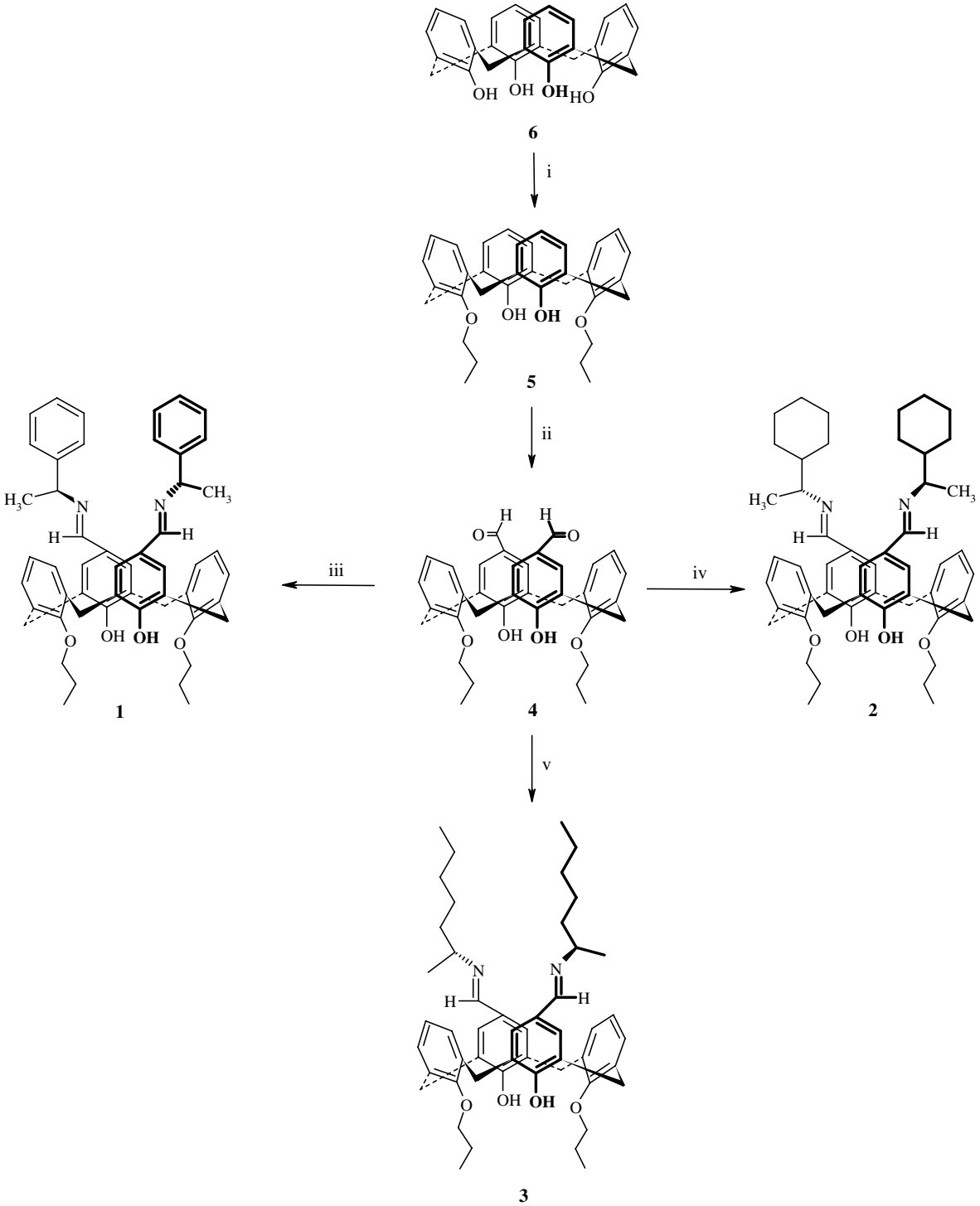
2.1. Design and synthesis of the new chiral hosts

This work is mainly focused on the design of new calix[4]-arene based ionophores, which have effective binding features for a particular set of cations, anions or neutral molecules, and could be useful for multiple applications,

* Corresponding author. Tel.: +90 332 2232774; e-mail: myilmaz@selcuk.edu.tr

0957-4166/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2006.08.008

such as environmental, laboratory, and industrial process analysis. For the desired goal, calix[4]arene **6** was chosen as the starting material,[12] and the synthetic route is shown in Scheme 1. Compounds **6**–**4** have been prepared according to the previously published procedures,[12–14] while reaction steps leading to **1**–**3** are described for the first time. Following the strategy outlined in Scheme 1, compounds **1**–**3** were obtained from compound **4** by treatment with (*S*)-(−)-1-phenylethylamine, (*R*)-(−)-1-cyclohexylethylamine, and (*R*)-2-heptylamine, respectively, in the presence of $MgSO_4$ in $CHCl_3$/MeOH under reflux. The new chiral Schiff base derivatives of calix[4]arene have been characterized by a combination of IR, ^1H and ^{13}C NMR, and elemental analysis. From ^1H NMR data, **1**–**3** exhibit a sin-



Scheme 1. Reagents and conditions: (i) *n*-PrI, MeCN, K_2CO_3; (ii) $TiCl_4$, dichloromethyl methyl ether, $CHCl_3$; (iii)–(v) (*S*)-(−)-1-phenylethylamine, (*R*)-(−)-1-cyclohexylethylamine or (*R*)-(−)-2-heptylamine, $CHCl_3$/MeOH.

glet at δ 8.13, 8.05, 8.11 ppm, respectively, which indicates the presence of HC=N. This conclusion has also been confirmed by strong C=N bands between 1637 and 1640 cm^{-1} in the FT-IR spectra of chiral Schiff base derivatives. The conformational characteristics of chiral calix[4]arenes were conveniently estimated by the splitting pattern of the $ArCH_2Ar$ methylene protons in the ^1H and ^{13}C NMR spectroscopy.

^1H and ^{13}C NMR data showed that compounds **1**–**3** are in a cone conformation. A typical AX pattern was observed for the methylene bridge $ArCH_2Ar$ protons at 3.50 ($J = 13.10$ Hz) and 4.19 ($J = 13.01$ Hz) for **1**, 3.46 ($J = 13.03$ Hz) and 4.29 ($J = 13.01$ Hz) for **2** and 3.45 ($J = 12.91$ Hz) and 4.29 ($J = 13.04$ Hz) for **3** in ^1H NMR. The high field doublets at 3.50 ppm for **1**, 3.46 ppm for **2** and 3.45 ppm for **3** were assigned to the equatorial protons of methylene group, whereas the low field signals at 4.19 ppm for **1**, 4.29 ppm for **2** and **3** were assigned to the axial protons in the ^1H NMR.

2.2. UV spectral titrations

We were interested in the search for a molecular structure that could serve as an optical sensory system for selective recognition toward biologically and chemically important amines. Optical sensors are of great interest due to their simple design and ease of handling. To date, chromogenic crown ethers[15] and calixarenes[16] have been reported as optical receptors for amines. These compounds are useful for the detection of complementary interactions between host molecules and the shape of amines, which can be easily monitored by spectroscopy. In spectroscopic titration experiments, the addition of a varying concentration of guest molecules resulted in either a gradual increase or decrease of characteristic absorptions of the host molecules. With the assumption of a 1:1 stoichiometry, the inclusion complexation of amines (G) with chiral Schiff base derivative of calix[4]arene (H) is expressed by Eq. 1:

$$H + G \overset{K}{\rightleftharpoons} H \cdot G \tag{1}$$

Under the conditions employed, the concentration of calix[4]arene derivatives (2.5×10^{-4} mol dm^{-3}) is much smaller than that of amines, that is $[H]_0 \ll [G]_0$. Therefore, the stability constant of the supramolecular system formed can be calculated according to the modified Benesi and Hildebrand equation,[17] Eq. 2, where $[G]_0$ denotes the total concentration of amine; $[H]_0$ refers to the total concentration of calix[4]arene derivative; $\Delta\varepsilon$ is the difference between the molar extinction coefficient for the free and complexed calix[4]arene derivative and ΔA denotes the changes in the absorption of the modified calix[4]arene on adding amine.

$$1/\Delta A = 1/K\Delta\varepsilon[H]_0 + 1/\Delta\varepsilon[G]_0 \tag{2}$$

For all the guest molecules examined, plots of calculated $1/\Delta A$ values as a function of $1/[G]_0$ values give good straight lines, supporting the 1:1 complex formation. The binding constants (K) of these hosts with guest molecules were calculated from the UV–vis spectra in accordance with Benesi–Hildebrand equation at three different temperatures. The UV–vis spectral changes upon the addition of (*R*)-phenylethylamine to **2** are shown in Figure 1, while typical Benesi–Hildebrand plot is shown for the complexation of **2** with (*R*)-phenylethylamine in Figure 2.

The free-energy change (ΔG) for the inclusion complexes formed by chiral calix[4]arene Schiff base derivatives and guest amines is calculated from the equilibrium constant K by Eq. 3 and is related to

$$\Delta G = -RT \ln K \tag{3}$$

the enthalpic and entropic changes (ΔH and ΔS) through the Gibbs–Helmholtz equation 4. Combining Eqs. 3 and 4, we obtain Eq. 5 which describes the temperature dependence of K. Thus, plots of the $\ln K$ values, as a function of the inverse of temperature, gave good linear relationships for a working temperature range (Fig. 3).

$$\Delta G = \Delta H - T\Delta S \tag{4}$$

$$\ln K = -\Delta H/RT + \Delta S/R \tag{5}$$

The observed K values and the thermodynamic parameters, ΔG, ΔH, and ΔS, for the complex formation are summarized in Tables 1 and 2.

From the data shown in Table 1, all hosts have greater K values toward (*R*)-phenylethylamine than (*S*)-phenylethylamine. Chiral receptors **1** and **3** showed relatively poor enantioselective recognition abilities for (*R*)- and

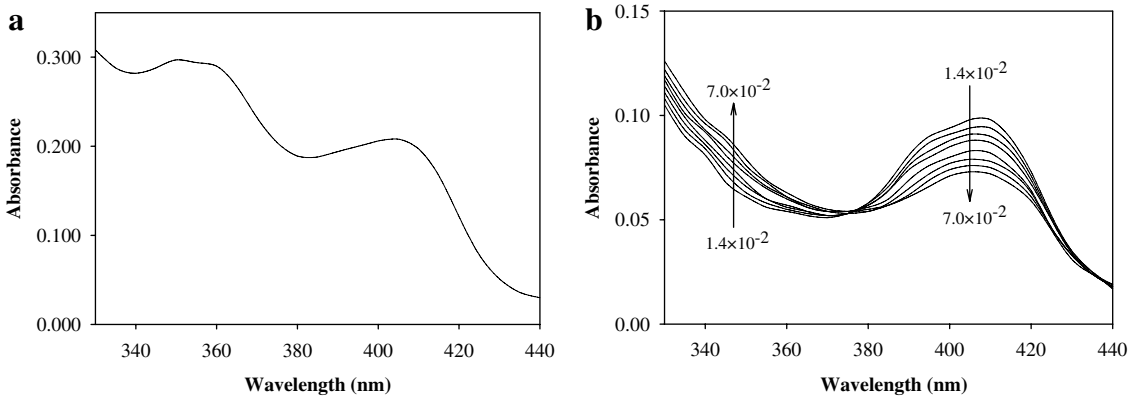


Figure 1. (a) UV–vis spectra of **2** in chloroform solution (2.5×10^{-4} mol dm^{-3}). (b) Spectral changes upon the addition of 1.4–7.0 $\times 10^{-2}$ mol dm^{-3} of (*R*)-phenylethylamine to a chloroform solution of **2** (2.5×10^{-4} mol dm^{-3}) at 25 °C.

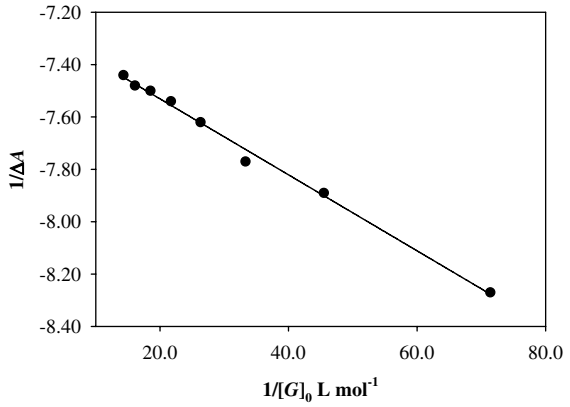


Figure 2. Typical Benesi–Hildebrand plot of $1/\Delta A$ versus $1/[G]_0$ for the host–guest complexation of **2** and (*R*)-phenylethylamine in $CHCl_3$ at 25 °C.

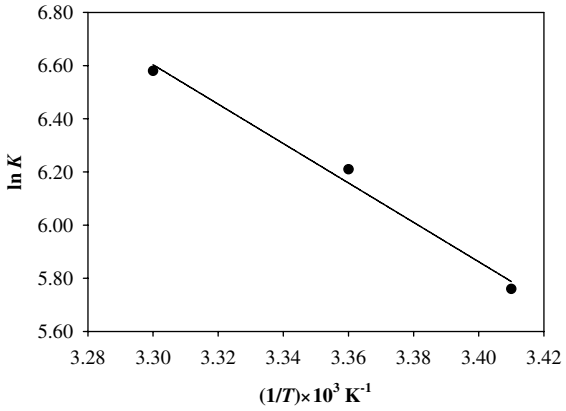


Figure 3. The plot of $\ln K$ versus $1/T$ for the host–guest complexation of **2** and (*R*)-phenylethylamine in $CHCl_3$.

(*S*)-1-phenylethylamine. On the other hand, the *K* values for **2** in the enantiomeric recognition were found to be significantly different. The calculated binding constant *K*, was 499 and 187 $dm^3\ mol^{-1}$ for the (*R*)- and (*S*)-enantiomers of phenylethylamine, respectively. Thus, the (*R*)-form is 2.67 times more stable than the (*S*)-form and $\Delta\Delta G = 2.43\ kJ\ mol^{-1}$ in $CHCl_3$. This indicates that host **2** exhibits different chiral recognition abilities toward the (*R*)- and (*S*)-forms of 1-phenylethylamine at 25 °C. This enantiodiscrimination could be due to the different interaction modes of the substituent on the guest with chiral barriers on the host.

The thermodynamic data provide information about the identification and evaluation of the relationship between the chiral ligand and guests and the degree of chiral and molecular recognition. The negative values of ΔG in each case indicate that the complexations are spontaneous. Complexation of chiral and achiral amines with all hosts was endothermic for working temperature range in each case and the ΔS values were highly positive (Tables 1 and 2). These facts indicate that ΔS favors the formation of the complexes.

Extensive studies of molecular recognition by calixarenes have revealed that the size/shape-fit concept plays a crucial role in the formation of inclusion complexes of host compounds with guest molecules of various structures. Therefore, weak intermolecular forces such as ion–dipole, dipole–dipole, dipole–induced dipole, van der Waals, electrostatic interaction, hydrogen bonding, and hydrophobic interaction are known to cooperatively contribute to the inclusion complexation of guest molecules with calixarenes according to the size/shape-fit concept. In the present case,

Table 1. Binding constants (*K*), enantioselectivities (K_R/K_S) and thermodynamic parameters for the complexation of hosts **1**–**3** with chiral guests in $CHCl_3$ at 25 °C

Host	Guest	K ($dm^3\ mol^{-1}$)	K_R/K_S	$-\Delta G$ ($kJ\ mol^{-1}$)	$-\Delta\Delta G$[a]	ΔH ($kJ\ mol^{-1}$)	$\Delta_{R-S}\Delta H$[b]	ΔS ($J\ mol^{-1}$)	$\Delta_{R-S}\Delta S$[c]
1	(*R*)-$PhCHMeNH_2$	531	1.34	15.55	0.73	55.14	15.89	236.0	54.5
	(*S*)-$PhCHMeNH_2$	396		14.82		39.25		181.5	
2	(*R*)-$PhCHMeNH_2$	499	2.67	15.39	2.43	61.62	22.01	258.2	81.8
	(*S*)-$PhCHMeNH_2$	187		12.96		39.61		176.4	
3	(*R*)-$PhCHMeNH_2$	287	1.20	14.02	0.45	78.39	14.52	310.2	50.5
	(*S*)-$PhCHMeNH_2$	239		13.57		63.87		259.7	

[a] $\Delta\Delta G = \Delta G_R - \Delta G_S$.
[b] $\Delta\Delta H = \Delta H_R - \Delta H_S$.
[c] $\Delta\Delta S = \Delta S_R - \Delta S_S$.

Table 2. Binding constants (*K*) and thermodynamic parameters for the complexation of hosts **1**–**3** with achiral guests in $CHCl_3$ at 25 °C

Host	Guest	K ($dm^3\ mol^{-1}$)	$-\Delta G$ ($kJ\ mol^{-1}$)	ΔH ($kJ\ mol^{-1}$)	ΔS ($J\ mol^{-1}$)
1	MPA	105	11.53	42.48	181.4
	n-$BuNH_2$	168	12.70	90.21	344.0
2	MPA	151	12.43	44.56	191.2
	n-$BuNH_2$	272	13.89	112.02	421.5
3	MPA	210	13.25	62.51	254.4
	n-$BuNH_2$	212	13.27	75.60	298.0

MPA = 3-morpholinopropylamine.

hydrogen bonding was considered to determine the complex stability to a large extent.

The results shown in Table 2 indicate that all hosts form more stable complexes with *n*-butylamine than that formed with 3-morpholinopropylamine. The *K* values for complexes **1**–**3** with 3-morpholinopropylamine are smaller than those for complexes with *n*-butylamine, rationalized in terms of the reduced basicity of 3-morpholinopropylamine compared with that of *n*-butylamine.

3. Conclusion

In this present study, novel chiral calix[4]arene Schiff base derivatives were synthesized as host compounds in good yields. The molecular and enantiomeric recognition capability of these new hosts toward (*R*)- and (*S*)-α-PhEt, MPA and *n*-BA by UV–vis method in $CHCl_3$ has been investigated. The results show that a relatively good enantioselective recognition ability was obtained with receptor **2** toward (*R*)- and (*S*)-phenylethylamine among all of the chiral hosts studied and more stable complexes were obtained with *n*-butylamine compared with 3-morpholinopropylamine.

4. Experimental

4.1. General information

Melting points were determined on an Electrothermal 9100 apparatus in a sealed capillary and are uncorrected. ^1H and ^{13}C NMR spectra were recorded using a Bruker 400 MHz spectrometer in $CDCl_3$ with TMS as an internal standard. IR spectra were obtained on a Perkin Elmer 1605 FT-IR spectrometer using KBr pellets. Optical rotations were measured on A-Krüss Optronic polarimeter. HPLC measurements were carried out on Agilent 1100 equipment connected with a Zorbax RX-C18 column. Elemental analyses were performed using a Leco CHNS-932 analyzer. FAB-MS spectra were taken on a Varian MAT 312 spectrometer.

Analytical TLC was performed using Merck prepared plates (silica gel 60 F_{254} on aluminum). Flash chromatography separations were performed on a Merck Silica Gel 60 (230–400 Mesh). All reactions, unless otherwise noted, were conducted under a nitrogen atmosphere. All starting materials and reagents used were of standard analytical grade from Fluka, Merck, and Aldrich and used without further purification. Toluene was distilled from CaH_2 and stored over sodium wire. Other commercial grade solvents were distilled and then stored over molecular sieves. The drying agent employed was anhydrous $MgSO_4$.

4.2. UV spectral measurement

The recognition abilities of chiral calix[4]arene derivatives with chiral and achiral amines were determined on the basis of the differential UV spectrometry in chloroform.[18] The UV–vis spectra were measured at 20, 25, and 30 °C with a thermostated cell compartment by Shimadzu 160 UV spectrometer. The same concentrations of guest solution were added to the sample cell and reference cell (light path = 1 cm). The association constants were determined at 405 nm. The concentration of the hosts is 2.5×10^{-4} mol dm^{-3} with the concentration increasing between 1.4 and 7.0×10^{-2} mol dm^{-3} of the added guest.

4.3. General procedure for the synthesis of compounds 1–3

To a solution of **4** (0.5 g, 0.89 mmol) in $CHCl_3$ (50 mL) was added a solution of appropriate chiral amine in MeOH (10 mL) and refluxed for 24 h in the presence of $MgSO_4$. The reaction mixture was allowed to cool to room temperature, and filtered. Evaporation of the solvent and subsequent purification of the mixture by recrystallization from $CHCl_3$/MeOH afforded pure **1**–**3**.

4.3.1. Compound 1. Yield 72% (0.49 g); mp: 193–196 °C; $[\alpha]_D^{20} = +54.7$ (*c* 0.5, $CHCl_3$). IR (KBr): 3239 (OH), 1637 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): δ (ppm) 8.45 (s, 2H, –O*H*), 8.13 (s, 2H, –N=C*H*), 7.42 (d, 4H, Ar*H meta*), 7.31 (d, 4H, Ar*H*), 7.22 (t, 4H, Ar*H meta*), 7.11 (t, 2H, Ar*H meta*), 6.82 (t, 4H, Ar*H para*), 6.63 (t, 2H, Ar*H meta*), 4.40 (q, 2H, –C*H*CH_3), 4.19 (d, 4H, *J* = 13.01 Hz, ArCH_2-Ar), 3.87 (t, 4H, –OC$H_2$$CH_2CH_3$), 3.50 (d, 4H, *J* = 13.10 Hz, ArCH_2Ar), 1.95 (h, 4H, –OCH$_2$C$H_2$$CH_3$), 1.50 (d, 6H, –CHC$H_3$), 1.20 (t, 6H, –OCH$_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$): δ 159.72, 156.16, 151.93, 145.41, 132.94, 129.25, 128.92, 128.42, 128.36, 127.64, 126.79, 126.75, 125.39, 78.52, 77.16, 76.84, 69.45, 50.46, 31.35, 24.49, 23.55, 10.93; FAB-MS *m*/*z*: 793.9 [M+Na]$^+$. Anal. Calcd for $C_{52}H_{54}O_4N_2$ (770.99): C, 81.01%; H, 7.06%; N, 3.63%. Found: C, 80.74%; H, 6.93%; N, 3.70%.

4.3.2. Compound 2. Yield 69% (0.46 g); mp: 221–224 °C; $[\alpha]_D^{20} = -4.5$ (*c* 0.4, $CHCl_3$). IR (KBr): 3304 (OH), 1640 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): δ (ppm) 8.52 (s, 2H, –O*H*), 8.05 (s, 2H, –N=C*H*), 7.48 (s, 4H, Ar*H*, *meta*), 6.93 (d, 4H, Ar*H meta*), 6.75 (t, 2H, Ar*H para*), 4.29 (d, 4H, *J* = 13.01 Hz, ArCH_2Ar), 4.00 (t, 4H, –OC$H_2$$CH_2$-$CH_3$), 3.46 (d, 4H, *J* = 13.03 Hz, ArCH_2Ar), 2.94 (p, 2H, –C*H*CH_3), 2.05 (h, 4H, OCH$_2$C$H_2$$CH_3$), 1.81 (m, 2H, –CH), 1.72–1.64 (m, 20H, –CH_2), 1.30 (t, 6H, –OCH$_2$CH$_2$CH_3), 1.21 (d, 6H, –CHCH_3); ^{13}C NMR ($CDCl_3$): δ 158.64, 155.83, 151.92, 132.98, 129.19, 129.04, 128.64, 128.60, 128.46, 128.25, 127.68, 125.34, 125.06, 78.33, 77.38, 77.06, 72.19, 53.32, 43.79, 32.23, 31.28, 31.24, 30.30, 29.92, 29.71, 26.66, 26.45, 26.26, 23.49, 20.03, 10.87; FAB-MS *m*/*z*: 805.94 [M+Na]$^+$. Anal. Calcd for $C_{52}H_{66}O_4N_2$ (783.08): C, 79.76%; H, 8.17%; N, 3.58%. Found: C, 79.12%; H, 8.89%; N, 3.34%.

4.3.3. Compound 3. Yield 80% (0.54 g); mp: 158–160 °C; $[\alpha]_D^{20} = -2.1$ (*c* 0.4, $CHCl_3$). IR (KBr): 3294 (OH), 1638 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): δ (ppm) 8.55 (s, 2H, –O*H*), 8.11 (s, 2H, –N=C*H*), 7.46 (s, 4H, Ar*H meta*), 6.95 (d, 4H, Ar*H meta*), 6.73 (t, 2H, Ar*H para*), 4.29 (d, 4H, *J* = 12.91 Hz, ArCH_2Ar), 3.98 (t, 4H, –OC$H_2$$CH_2$-$CH_3$), 3.45 (d, 4H, *J* = 13.04 Hz, ArCH_2Ar), 3.22 (h, 2H, –C*H*CH_3), 2.06 (h, 4H, –OCH$_2$C$H_2$$CH_3$), 1.28–1.34 (m, 26H, –$CH_2$ and –CH*C*H_3), 1.23–1.19 (m, 6H,

$-OCH_2CH_2CH_3$), 0.70 (t, 6H, $-CH_2CH_3$); ^{13}C NMR ($CDCl_3$): δ 158.68, 155.88, 151.91, 132.99, 129.72, 129.18, 128.65, 128.63, 128.30, 128.26, 127.65, 125.33, 123.21, 118.90, 78.34, 77.37, 77.05, 66.91, 37.96, 31.85, 31.27, 31.23, 29.71, 26.37, 23.50, 22.76, 22.62, 14.09, 10.87; FAB-MS m/z: 781.97 $[M+Na]^+$. Anal. Calcd for $C_{50}H_{66}O_4N_2$ (759.07): C, 79.11%; H, 8.76%; N, 3.69%. Found: C, 78.93%; H, 8.92%; N, 3.55%.

Acknowledgement

This work was supported by the Research Foundation of Selcuk University, Konya, Turkey (BAP 06101019), which is gratefully acknowledged.

References

1. (a) Marchi-Artzner, V.; Artzner, F.; Karthaus, O.; Shimomura, M.; Ariga, K.; Kunitake, T.; Lehn, J.-M. *Langmuir* **1998**, *14*, 5164–5171; (b) Bohanon, T. M.; Caruso, P.-L.; Denzinger, S.; Fink, R.; Mobius, D.; Paulus, W.; Preece, J. A.; Ringsdorf, H.; Schollmeyer, D. *Langmuir* **1999**, *15*, 174–184; (c) Russell, K. C.; Leize, E.; Van Dorsselaer, A.; Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 209–230; (d) Baudoin, O.; Gonnet, F.; Teulade-Fichou, M.-P.; Vigneron, J.-P.; Tabet, J.-C.; Lehn, J.-M. *Chem. Eur. J.* **1999**, *5*, 2762–2771.
2. (a) Reinhoudt, D. N. In *Comprehensive Supramolecular Chemistry*; Pergamon Press: New York, 1996, Vol. 10; (b) Kubo, Y.; Maeda, S.; Tokita, S.; Kubo, M. *Nature* **1996**, *382*, 522–524; (c) Murakami, Y.; Kikuchi, J.; Hisaeda, Y.; Hayashida, O. *Chem. Rev.* **1996**, *96*, 721–758; (d) Sanders, J. K. M. *Chem. Eur. J.* **1998**, *4*, 1378–1383; (e) Peczuh, M. W.; Hamilton, A. D. *Chem. Rev.* **2000**, *100*, 2479–2494; (f) Wong, W. L.; Huang, K. H.; Teng, P. F.; Lee, C. S.; Kwong, H. L. *Chem. Commun.* **2004**, 384–385.
3. Zhau, H. W.; Hua, W. T. *J. Org. Chem.* **2000**, *65*, 2933–2938.
4. (a) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161–170; (b) *Calixarenes Revisited*; Gutsche, C. D., Ed.; The Royal Society of Chemistry: Cambridge, 1998.
5. (a) Gutsche, C. D. *Calixarenes*; The Royal Society of Chemistry: Cambridge, 1989; (b) Vicence, J.; Böhmer, V. *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Kluwer Academic: Norwell, MA, 1991.
6. (a) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713–1734; (b) Liu, Y.; Zhao, B.-T.; Zhang, H.-Y.; Ju, H.-F.; Chen, L.-X.; He, X.-W. *Helv. Chim. Acta* **2001**, *84*, 1969–1975; (c) Tuntulani, T.; Thavornyutikarn, P.; Poompradub, S.; Jaiboon, N.; Ruangpornvisuti, V.; Chaichit, N.; Asfari, Z.; Vicens, J. *Tetrahedron* **2002**, *58*, 10277–10285.
7. (a) Ikeda, A.; Nagasaki, T.; Shinkai, S. *J. Phys. Org. Chem.* **1992**, *5*, 699–710; (b) Iwamoto, K.; Shimizu, H.; Araki, K.; Shinkai, S. *J. Am. Chem. Soc.* **1993**, *115*, 3997–4006; (c) Nagasaki, T.; Fujishima, H.; Shinkai, S. *Chem. Lett.* **1994**, 989–992; (d) Dondoni, A.; Marra, A.; Sherrmann, M.-C.; Casnati, A.; Sansone, F.; Ungaro, R. *Chem. Eur. J.* **1997**, *3*, 1774–1782; (e) Sansone, F.; Barboso, S.; Casnati, A.; Fabbi, M.; Pochini, A.; Ugozzoli, F.; Ungaro, E. *Eur. J. Org. Chem.* **1998**, *1998*, 897–905; (f) Sansone, F.; Barboso, S.; Casnati, A.; Sciotto, D.; Ungaro, E. *Tetrahedron Lett.* **1999**, *40*, 4741–4744.
8. (a) Castellano, R. K.; Nuckolls, C.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 11156–11163; (b) Lazzarotto, M.; Nachtigall, F. F.; Vencato, I.; Nome, F. *J. Chem. Soc., Perkin Trans. 2* **1998**, 995–998; (c) Ito, K.; Noike, M.; Kida, A.; Ohba, Y. *J. Org. Chem.* **2002**, *67*, 7519–7522.
9. (a) He, Y.; Xiao, Y.; Meng, L.; Zeng, Z.; Wu, X.; Wu, C.-T. *Tetrahedron Lett.* **2002**, *43*, 6249–6253; (b) Bitter, I.; Köszegi, É.; Grün, A.; Bakó, P.; Pál, K.; Grofcsik, A.; Kubinyi, M.; Balázs, B.; Tóth, G. *Tetrahedron: Asymmetry* **2003**, *14*, 1025–1035.
10. (a) Kubo, Y.; Maruyama, S.; Ohhara, N.; Nakamura, M.; Tokita, S. *Chem. Commun.* **1995**, 1727–1728; (b) Nachtigall, F. F.; Lazzarotto, M.; Nome, F. *J. Braz. Chem. Soc.* **2002**, *13*, 295–299; (c) Lynam, C.; Jennings, K.; Nolan, K.; Kane, P.; McKervey, M. A.; Diamond, D. *Anal. Chem.* **2002**, *74*, 59–66; (d) Zheng, Y.-S.; Zhang, C. *Org. Lett.* **2004**, *6*, 1189–1192; (e) Ito, K.; Noike, M.; Kida, A.; Ohba, Y. *J. Org. Chem.* **2002**, *67*, 7519–7522.
11. (a) Sirit, A.; Karakucuk, A.; Memon, S.; Kocabas, E.; Yilmaz, M. *Tetrahedron: Asymmetry* **2004**, *15*, 3595–3600; (b) Sirit, A.; Kocabas, E.; Memon, S.; Karakucuk, A.; Yilmaz, M. *Supramol. Chem.* **2005**, *17*, 251–256; (c) Kocabas, E.; Karakucuk, A.; Sirit, A.; Yilmaz, M. *Tetrahedron: Asymmetry* **2006**, *17*, 1514–1520.
12. Gutsche, C. D.; Levine, J. A.; Sujeeth, P. K. *J. Org. Chem.* **1985**, *50*, 5802–5806.
13. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Egberink, R. J. M.; De Song, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767–2777.
14. Arora, V.; Chawla, H. M.; Santra, A. *Tetrahedron* **2002**, *58*, 5591–5597.
15. (a) Kaneda, T.; Hirose, K.; Misumi, S. *J. Am. Chem. Soc.* **1989**, *111*, 742–743; (b) Kaneda, T.; Umeda, S.; Ishizaki, Y.; Kuo, H.-S.; Misumi, S.; Kai, Y.; Kaneshima, N.; Kasai, N. *J. Am. Chem. Soc.* **1989**, *111*, 1881–1883; (c) Yamamoto, K.; Isoue, K.; Sakata, Y.; Kaneda, T. *Chem. Commun.* **1992**, 791–793; (d) Naemura, K.; Ueno, K.; Takeuchi, S.; Tobe, Y.; Kaneda, T.; Sakata, Y. *J. Am. Chem. Soc.* **1993**, *115*, 8475–8476; (e) Naemura, K.; Takeuchi, S.; Hirose, K.; Tobe, Y.; Kaneda, T.; Sakata, Y. *J. Chem. Soc., Perkin Trans. 1* **1995**, 213–219.
16. (a) Takeshita, M.; Shinkai, S. *Chem. Lett.* **1994**, 125–128; (b) McCanick, M.; Harris, S. J.; Diamond, D. *J. Mater. Chem.* **1994**, *4*, 217–221; (c) Takeshita, M.; Shinkai, S. *Chem. Lett.* **1994**, 1349–1352; (d) Chawla, H. M.; Srinvas, K. *Tetrahedron Lett.* **1994**, *35*, 2925–2928; (e) Chawla, H. M.; Srinvas, K. *Chem. Commun.* **1994**, 2593–2594; (f) Gutsche, C. D.; Iqbal, M.; Nam, K. S.; See, K.; Alam, I. *Pure Appl. Chem.* **1988**, *60*, 483–488; (g) Kubinyi, M.; Pál, K.; Baranyai, P.; Grofcsik, A.; Bitter, I.; Grün, A. *Chirality* **2004**, *16*, 174–179.
17. (a) Polster, J.; Lachman, H. *Spectrometric Titrations*; VCH: Wienheim, 1989; (b) Connors, K. A. *Binding Constants. The Measurement of Molecular Complex*; Wiley: New York, 1987; (c) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703–2707.
18. Examples of the UV–vis titrimetric method being used in molecular recognition: (a) Ogasahara, K.; Hirose, K.; Tobe, Y.; Naemura, K. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3227–3236; (b) Mohammed-Ziegler, I.; Poór, B.; Kubinyi, M.; Grofcsik, A.; Grün, A.; Bitter, I. *J. Mol. Struct.* **2003**, *650*, 39–44; (c) Turgut, Y.; Hoşgören, H. *Tetrahedron: Asymmetry* **2003**, *14*, 3815–3818.