J Incl Phenom Macrocycl Chem (2016) 84:35–41
DOI 10.1007/s10847-015-0579-7

ORIGINAL ARTICLE

Synthesis of new chiral calix[4]arene thiourea derivatives for enantiomeric recognition of carboxylate anions

Selahattin Bozkurt[1,2] · **Mustafa Burak Turkmen**[1] · **Cengiz Soykan**[3]

Received: 18 September 2015 / Accepted: 3 November 2015 / Published online: 11 November 2015

Abstract The study of enantiomeric recognition of amino acid and carboxylic acid compounds is of significance since these compounds are basic building blocks of biological molecules. Enantiomeric recognition and separation of these compounds are among the main topics of supramolecular chemistry since they are basic building blocks of biological molecules and a number of them are known to possess potent biological activities. In this study the synthesis of novel chiral calix[4]arene thiourea derivatives has been reported. The enantioselectivity of chiral receptors was investigated by using UV–Vis spectroscopy. All the chiral calix[4]arene derivatives exhibited certain chiral recognition towards the enantiomers of α-hydroxy isovaleric acid (HIVA), mandelic acid (MA), 2-chloromandelic acid (2-ClMA) and *N*-Boc-alanine (*N*-BocAl). The receptors with hydrogen bonding sites and aromatic groups showed considerable higher stereoselectivities. As a chiral receptor, calix[4]arene 2-hydroxy-1,2 diphenyl ether thiourea derivative has enantiomeric discriminating ability for 2-chloromandelic acid (up to $K_R/K_S = 2.80$) at 25 °C. The enantiomeric recognition abilities for guests are also discussed from a thermodynamic point of view.

✉ Selahattin Bozkurt
sbozkurt420@yahoo.com; selahattin.bozkurt@usak.edu.tr

[1] Scientific Analysis Technological Application and Research Center, Usak University, 64200 Usak, Turkey

[2] Vocational School of Health Services, Usak University, 64200 Usak, Turkey

[3] Department of Materials Science and Nanotechnology Engineering, Usak University, 64200 Usak, Turkey

Keywords Chiral calix[4]arene · Enantiomeric recognition · Carboxylate anions · Thiourea · Hydrogen bonding

Introduction

Calixarenes are cyclic oligomer based on a hydroxyl alkylation product of phenols and aldehydes. Calixarenes of varying cavity size can form variety of host–guest type of inclusion complexes similar to cyclodextrins. However, calixarene host molecules have unique compositions that include benzene groups, which provide π–π interaction and hydroxyl groups for hydrogen bonding [1]. Therefore, calixarenes can be used as molecular recognition, [2–4] ion sensitive sensors, [5, 6] in HPLC stationary phases, [7] selective membranes, [8] enantiomeric recognition, [9–11] and asymmetric synthesis [12].

One of the great problems faced by the pharmaceutical industry involves the quantitation of undesirable enantiomers in drug raw material. Quite often only one enantiomer of a chiral compound is actually a bioactive therapeutic. It is therefore essential that final product be properly analyzed for enantiomeric purity [13]. Chirality is a prominent feature of most biological systems. As a consequence, metabolic and regulatory processes mediated by biological systems are sensitive to stereochemistry. Enantiomerically pure compounds such as amino acids, carboxylic acids are particularly important synthons for the preparation of pharmaceuticals because they are incorporated in a number of bioactive molecules. Therefore, a better understanding of the interactions operating in chiral recognition is helpful in developing new methods of asymmetric synthesis, chromatographic resolution of enantiomers, [14] new pharmaceutical agents [15, 16] and

separation materials [17]. Chiral receptors that are based on the calixarene platform may have potential applications in the preparation, separation, and analysis of enantiomers. In this regard, investigations conducted on the synthesis and chiral recognition properties of chiral calix[4]arene derivatives have attracted considerable attention.

Neutral receptors typically contain an N–H fragment (such as amides) which acts as an H-bond donor. Especially, thiourea contains two rigidly positioned N–H fragments suitable for the interaction with Y-shaped anions, like carboxylates [17]. Many literatures [18–20] describe the thiourea containing receptors form stable complexes with various anions [21, 22]. Therefore; in the present study, we report the synthesis of novel calix[4]arene derivatives bearing a chiral thiourea moiety at the lower rim and their recognition abilities for carboxylic acid by a UV–Vis titration method in acetonitrile.

Experimental

General

Melting points were measured on an Electro thermal 9100 apparatus and uncorrected. Elemental analyses for C, H and N were carried out using a LECO-932 CHNS -O Elemental Analyzer. ^{1}H and ^{13}C NMR spectra were recorded at room temperature on a Varian 400 MHz spectrometer in $CDCl_3$. Infrared (IR) spectra were recorded neat on a Perkin Elmer Spectrum Two FTIR-ATR spectrometer. Ultraviolet–Visible (UV–Vis) spectra were measured with a Perkin Elmer Lambda 35 spectrometer. Optical rotations were measured on an Atago AP-100 digital polarimeter.

Analytical TLC was performed using Merck prepared plates (silica gel 60 F254 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 $MgSO_4$. Analytical grade amino acid and carboxylic acids were purchased from Aldrich and employed without further purification as guest molecules.

UV spectral measurement

The recognition abilities of chiral calix[4]arenes with thiourea derivatives were determined on the basis of the differential UV spectrometry in acetonitrile. The UV–Vis spectra were measured at 20, 25, 30 and 35 °C with a thermostated cell compartment by Perkin Elmer Lambda 35 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 247 nm. The concentration of the hosts is 1.33×10^{-4} mol dm^{-3} with the increasing concentration between 0.0 and 15.0×10^{-3} mol dm^{-3} of the added guest. All anions used in this report were in the form of tetrabutylammonium salt.

Tetrabutylammonium salts

The tetrabutylammonium salts were prepared by adding 1 equiv tetrabutylammonium hydroxide in methanol to a solution of corresponding carboxylic acid (1 equiv) in methanol [21]. The mixture was stirred at room temperature for 2 h and evaporated to dryness under reduced pressure. The resulting syrup was dried at high vacuum for 24 h, stored in the desiccators.

Syntheses

*General procedure for the synthesis of compounds **5** and **6***

2.5 equiv. of amino alcohol derivatives ((*1S,2R*)-(−)-1-Amino-2-indanol or (*1S,2R*)-(+)-2-Amino-1,2-diphenylethanol) were added to a solution of 5,11,17,23-tetra-*tert*-butyl-25,27-di(isothiocyanoopropoxy)-26,28-hydroxy calix[4]arene (**4**) (87.5 mg, 0.10 mmol, 1.0 equiv.) in dry THF (20 mL). The resulting mixture was stirred at room temperature. After the completion of the reaction (TLC) the solvent was removed under vacuum. The crude product was purified by flash chromatography on silica gel (EtOAc/*n*-hexane; from 1:5 to 1:1).

*5,11,17,23-tetra-tert-butyl-25,27-bis([(1S,2R)-2-hydroxyindan-1-yl] thioureido propxy)-26,28-hydroxycalix[4]arene **(5)***

The crude product was purified by flash chromatography on silica gel to afford **5** as a white solid. Yield 72 %; white crystal; Mp 148–151 °C; $\alpha_D^{25} = -18.56$ (*c* 1.24, $CHCl_3$). IR (ATR): 1562 cm^{-1}; ^{1}H NMR (400 MHz,) δ 7.85 (s, 2H), 7.60 (s, 2H), 7.28–7.16 (m, 4H), 7.13–6.97 (m, 4H), 6.94 (t, $J = 1.9$ Hz, 4H), 6.80 (t, $J = 2.3$ Hz, 4H), 5.79 (s, 2H), 4.68 (q, $J = 5.9$ Hz, 2H), 4.01 (d, $J = 12.0$ Hz, 3H), 3.97–3.85 (m, 3H), 3.69 (d, $J = 13.2$ Hz, 2H), 3.39 (s, 2H), 3.23 (d, $J = 13.2$ Hz, 2H), 3.13 (d, $J = 13.2$ Hz, 2H), 2.96 (dd, $J = 16.2$, 6.4 Hz, 2H), 2.48 (dd, $J = 16.2$, 5.3 Hz, 2H), 2.28 (q, $J = 6.3$ Hz, 4H), 1.75 (s, 3H), 1.26 (s, 18H), 0.98 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm):

181.7, 151.4, 149.8, 149.5, 148.5, 139.5, 138.2, 132.2, 127.9, 127.7, 127.4, 126.1, 126.0, 125.3, 124.6, 74.7, 73.7, 61.9, 41.9, 40.3, 34.1, 33.9, 32.1, 31.4, 27.9; Anal. Calcd for $C_{70}H_{88}N_4O_6S_2$ (1145.60): C, 73.39 %; H, 7.74 %; N, 4.89 %; S, 5.60 %. Found: C, 73.41 %; H, 7.72 %; N, 4.91 %; S, 5.58 %.

5,11,17,23-tetra-tert-butyl-25,27-bis([(1S,2R)-2-hydroxy-1,2-diphenylethyl] thioureido propxy)-26,28-hydroxycalix[4]arene ***(6)***

The crude product was purified by flash chromatography on silica gel to afford **6** as a white solid. Yield 78 %; white crystal; Mp 174–177 °C; $\alpha_D^{25} = -11.49$ (*c* 0.86, $CHCl_3$). IR (ATR): 1548 cm^{-1}; ^1H NMR (400 MHz,) δ 8.12 (s, 2H), 7.38–6.78 (m, 29H), 5.88 (s, 2H), 5.36–5.01 (m, 2H), 4.02 (ddd, $J = 61.7$, 13.2, 8.9 Hz, 14H), 3.36 (dd, $J = 13.1$, 7.9 Hz, 4H), 2.04 (s, 2H), 1.67 (s, 2H), 1.30 (s, 18H), 1.04 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 180.2, 150.7, 149.5, 149.4, 148.3, 143.4, 142.1, 132.4, 130.4, 129.5, 128.9, 127.9, 127.6, 127.4, 127.3, 126.0, 125.9, 76.9, 74.8, 64.9, 42.1, 34.3, 33.6, 32.1, 31.8, 27.6; Anal. Calcd for $C_{80}H_{96}N_4O_6S_2$ (1273.77): C, 75.43 %; H, 7.60 %; N, 4.40 %; S, 5.03 %. Found: C, 75.45 %; H, 7.56 %; N, 4.38 %; S, 5.04 %.

Result and discussion

Design and synthesis of the new hosts

Calix[4]arene based chiral thiourea receptors **5** and **6** were synthesized from known precursors 2, [23] 3, [24] and 4, [25] respectively. Condensation of 2.5 equiv. (*1S*,*2R*)-(+)-2-Amino-1,2-diphenylethanol or (*1S*,*2R*)-(−)-1-Amino-2-indanol with 1.0 equiv. of *p-tert*-butylcalix[4]arene dipropoxy isothiocyanate **4** in dichloromethane gave thiourea **5** and **6** in 72 and 78 % yields, respectively (Scheme 1) The structures of all the compounds **5** and **6** were confirmed from their spectroscopic and analytical data. The IR spectra of **5** and **6** showed characteristic C=S stretching bands at 1562 and 1548 cm^{-1}, respectively. The conformational characteristics of calix[4]arenes were conveniently estimated by way of 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 newly synthesized *p-tert*-butylcalix[4]arene derivatives **5** and **6** are in a cone conformation. The cone conformation of all compounds were reflected in the characteristic AB system for the methylene groups bridging the aromatic rings in the ^1H and ^{13}C NMR spectra. In addition, $ArCH_2Ar$ methylene groups showed four doublets instead of two doublets.

UV spectral titrations

Molecular recognition, and in particular chiral recognition, is a fundamental characteristic in the biochemical systems. The study of synthetic model systems could contribute to the understanding of these processes and, at the same time, offer new perspectives for the development of pharmaceuticals, enantioselective sensors, catalysts, and other molecular devices [21]. To evaluate the binding abilities of calix[4]arene receptors **5**–**6** towards different carboxylic acids and N-protected amino acid (Fig. 1), we carried out UV–Vis experiments.

The binding constants (*K*) of inclusion complexes of above-mentioned chiral calix[4]arene receptors with carboxylate were determined on the basis of the differential UV spectrometry in acetonitrile. Acetonitrile was chose as the solvent considering the solubility of anions. The titration experiments showed that the absorption maximum of all hosts gradually decreased with the addition of various concentrations of carboxylic acid derivatives (Fig. 2).

With the assumption of a 1:1 stoichiometry, the complexation of carboxylic acid derivatives (G) with chiral 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 (1.33×10^{-4} mol dm^{-3}) is much smaller than that of guest molecules, *i.e.* $[H]_0 \ll [G]_0$. Therefore, the stability constant of the supramolecular system formed can be calculated according to the modified Hildebrand–Benesi equation [26], Eq. (2), where $[G]_0$ denotes the total concentration of guest, $[H]_0$ 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, ΔA denotes the changes in the absorption of the modified calix[4]arene on adding guest molecules.

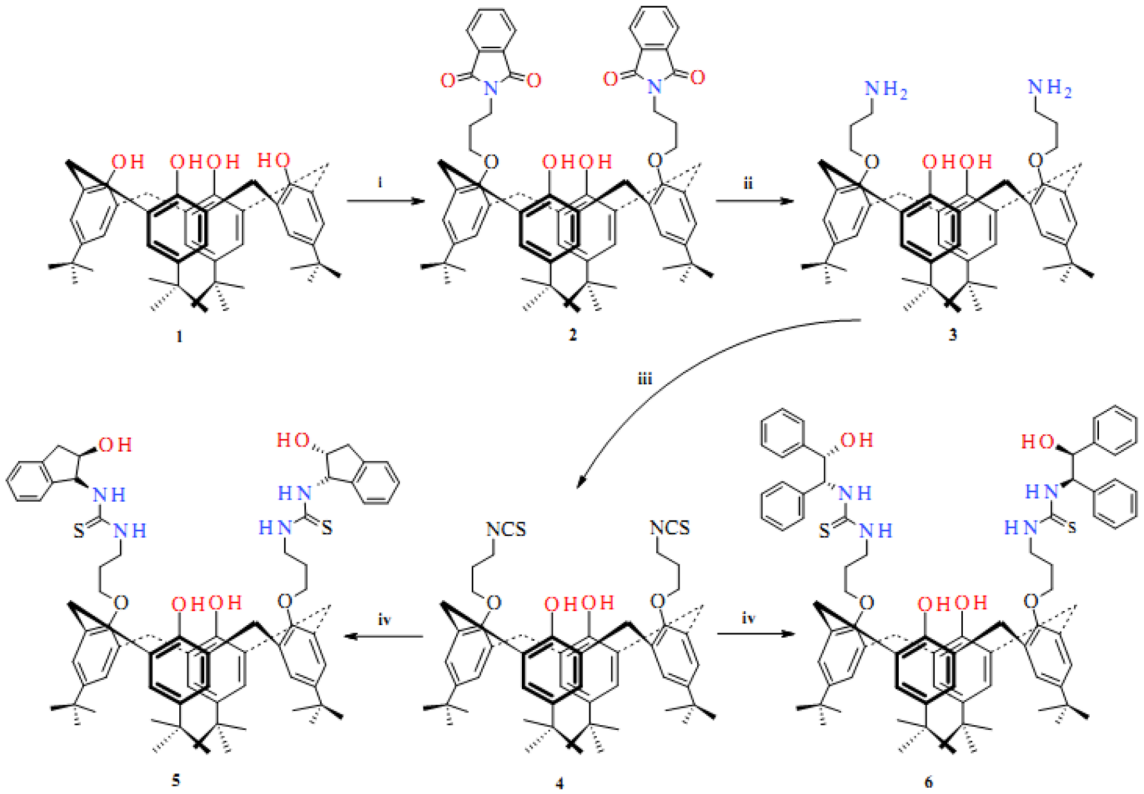
$$1/\Delta A = 1/K\Delta\varepsilon[H]_0[G]_0 + 1/\Delta\varepsilon[H]_0 \tag{2}$$

For all 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. Typical plots are shown for the complexation of compound **6** with *R*-2-chloromandelic acid in Fig. 3.

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

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

the enthalpic and entropic changes (ΔH and ΔS) through the Gibbs–Helmholtz Eq. (4). Combining Eqs. (3) and (4),



Scheme 1 (*i*) K_2CO_3, N-(bromopropyl)phtalaimide, acetone, reflux; (*ii*) hydrazine hydrate, ethanol, reflux; (*iii*) $BaCO_3$, Cl_2CS, DCM, rt; (*iv*) (*1S*,*2R*)-(+)-2-Amino-1,2-diphenylethanol or (*1S*,*2R*)-(−)-1-Amino-2-indanol, DCM

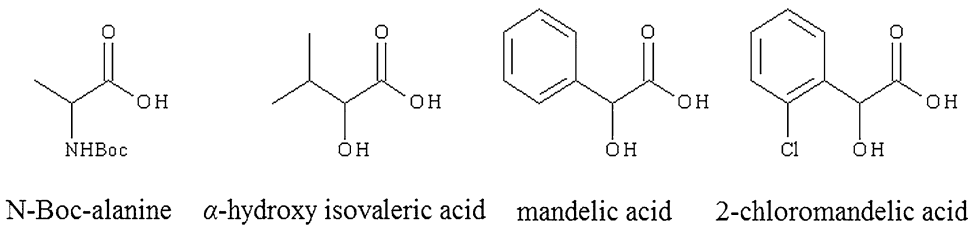


Fig. 1 Chemical structures of chiral *N*-protected amino acid and carboxylic acids

N-Boc-alanine α-hydroxy isovaleric acid mandelic acid 2-chloromandelic acid

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 working temperature range.

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

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

The association constants (*K*), the free-energy change ($\Delta\Delta G_0$) calculated from the slope and the intercept, and the thermodynamic parameters are summarized in Table 1, along with the enantioselectivity K_L/K_D for the complexation of *D*/*L* *N*-protected amino acid and *R*/*S* carboxylic acids by these hosts **5** and **6**.

From the data shown in Table 1, all hosts have greater *K* values toward the enantiomers of 2-ClMA and MA than HIVA. This may be due to the fact that the chiral calix[4]arene with an aromatic group attached to the nitrogen of the thiourea units could have π–π interaction with that of 2-ClMA and MA as an additional binding force. As a result, stronger binding was realized in all cases.

UV–Vis spectroscopic studies indicate that chiral selector **5** and **6** show strong binding and good recognition ability for the enantiomers of 2-ClMA and MA.

Table 1 also shows the enantiomeric discrimination of a pair of guest molecules, characterized by the value of K_D/K_L, which are 1.11–2.80 or $\Delta\Delta G_0$ of −0.26 to −2.55 kJ mol^{-1} for chiral calix[4]arene receptors **5** and **6**. It was found that chiral host **6** gave stronger binding and better recognition ability for carboxylic acids containing an aromatic group than for those possessing an aliphatic group. This is presumably due to multiple hydrogen bonding and π–π stacking interaction between the receptor

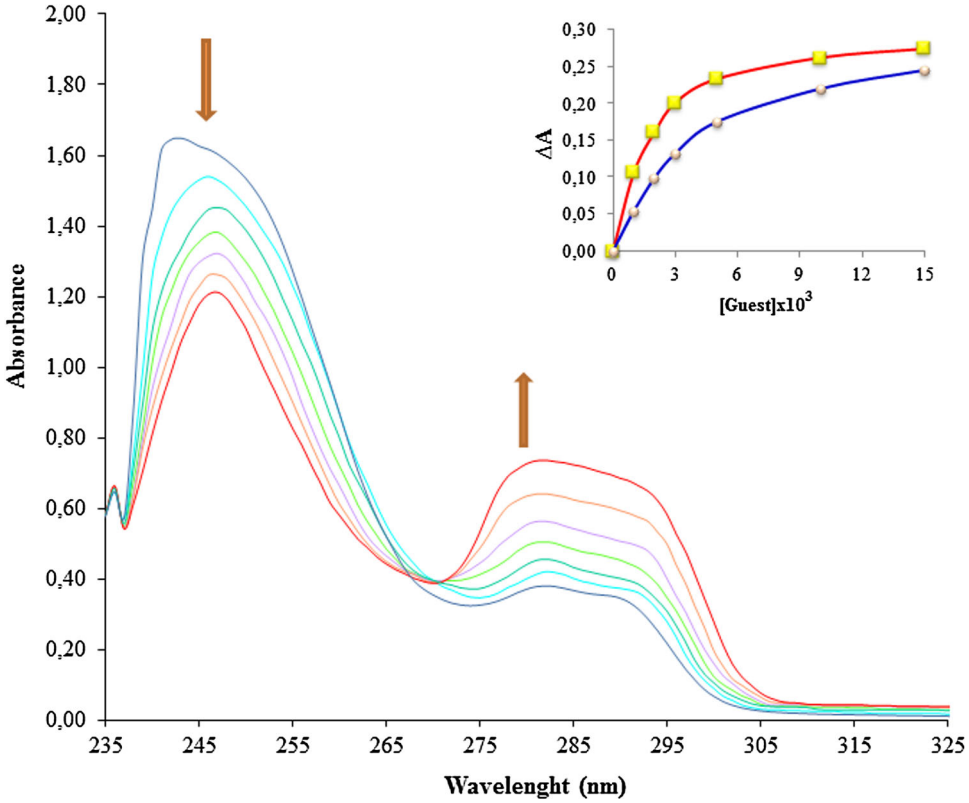


Fig. 2 UV–Vis spectra of 6 (1.33×10^{-4} mol dm^{-3}) in the presence of *R*-2-chloromandelic acid ($0.0–15.0 \times 10^{-3}$ mol dm^{-3}) in acetonitrile solution and the plot of ln K versus 1/T for the host–guest complexation

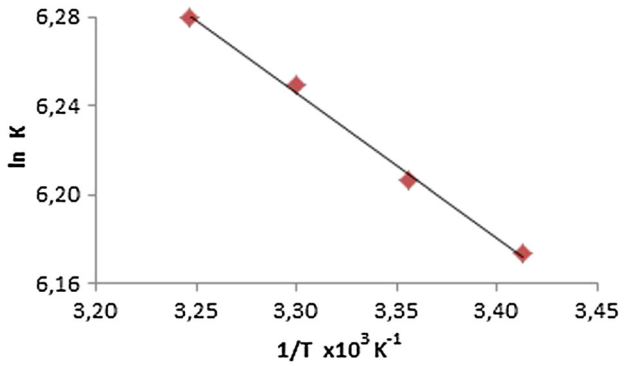


Fig. 3 The plot of ln *K* versus 1/T for the host–guest complexation of **6** and *R*-2-chloromandelic acid

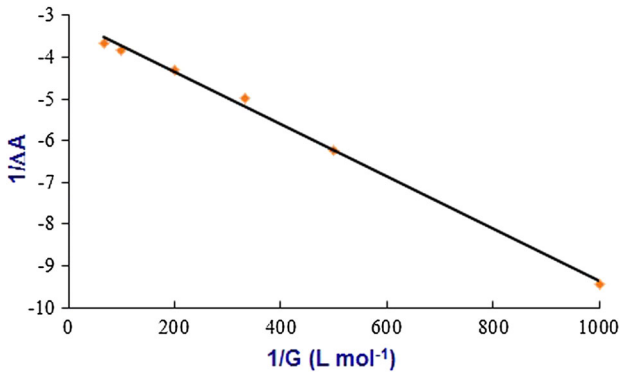


Fig. 4 Typical Benesi–Hildebrand plot of $1/\Delta A$ versus $1/[G]_0$

and the aromatic side chain of carboxylic acid. Also, it is important that thiourea contains two rigidly positioned N–H fragments suitable for the interaction with carboxylates. Mandelic acid and 2-chloromandelic acid have aromatic group, which can bind a guest by hydrogen bonding and π–π stacking interactions. Other guests are capable of complexing aromatic hosts by hydrogen bonding interactions only. The steric hindrance between the benzene ring and aromatic moieties around the stereogenic centers of the host may also play an important role in chiral recognition. Therefore, the *R* or *D*-isomers of carboxylic acid form more favourable complexes with the chiral selectors than the *S* or *L*-isomers.

The complexation of chiral calix[4]arene thiourea derivatives with carboxylic acids possibly occurs through interaction of the hydrogen atom in the thiourea loop and the oxygen atoms in the carboxylates. Noncovalent interactions between the guests and hydrogen bonding sites defined by phenolic oxygen contribute to the stabilization of these complexes as well as π–π interactions

Table 1 Binding constants (K), enantioselectivities (K_L/K_D) and thermodynamic parameters for the complexation of *L/D-N*-protected amino acid and *R/S* carboxylic acid with the chiral receptors **5–6** in acetonitrile at 25 °C

Entry	Host	Guest	K (M^{-1})	K_L/K_D	$-\Delta G$ (kJ mol^{-1})	$-\Delta\Delta G^a$	ΔH (kJ mol^{-1})	$\Delta\Delta H^b$	ΔS (J mol^{-1})	$\Delta\Delta S^c$
1	**5**	*R*-2-ClMA	392.1 ± 0.6	1.53	14.81 ± 0.22	1.07	5.13 ± 0.20	1.87	66.92 ± 0.92	9.87
2	**5**	*S*-2-ClMA	256.3 ± 0.5		13.74 ± 0.11		3.26 ± 0.11		57.05 ± 0.11	
3	**5**	*R*-HIVA	77.1 ± 0.4	1.11	10.76 ± 0.08	0.26	9.40 ± 0.07	1.53	67.62 ± 2.12	5.97
4	**5**	*S*-HIVA	69.4 ± 0.3		10.50 ± 0.18		7.87 ± 0.19		61.65 ± 2.04	
5	**5**	(*D*)-MA	95.9 ± 0.4	1.22	11.32 ± 0.19	0.48	13.06 ± 0.20	5.17	81.82 ± 4.66	18.96
6	**5**	(*L*)-MA	78.9 ± 0.2		10.84 ± 0.08		7.89 ± 0.07		62.86 ± 0.30	
7	**5**	(*D*)-N-Boc-Al	92.7 ± 0.1	1.16	11.22 ± 0.76	0.36	8.59 ± 0.76	3.49	66.47 ± 0.86	12.91
8	**5**	(*L*)-N-Boc-Al	80.1 ± 0.1		10.86 ± 0.77		5.10 ± 0.77		53.56 ± 1.54	
9	**6**	*R*-2-ClMA	495.9 ± 10.2	2.80	15.38 ± 0.24	2.55	5.43 ± 0.13	4.03	69.85 ± 0.20	22.12
10	**6**	*S*-2-ClMA	177.0 ± 4.1		12.83 ± 0.10		1.40 ± 0.10		47.73 ± 0.11	
11	**6**	*R*-HIVA	85.8 ± 0.3	1.17	11.03 ± 0.11	0.37	15.68 ± 0.11	4.08	89.61 ± 1.03	4.94
12	**6**	*S*-HIVA	73.2 ± 0.2		10.66 ± 0.16		11.59 ± 0.08		74.67 ± 1.28	
13	**6**	(*D*)-MA	140.8 ± 0.1	1.86	12.28 ± 0.11	1.51	16.24 ± 0.10	2.31	95.68 ± 1.03	12.79
14	**6**	(*L*)-MA	76.2 ± 0.2		10.77 ± 0.16		13.93 ± 0.16		82.89 ± 1.28	
15	**6**	(*D*)-N-Boc-Al	76.8 ± 0.3	1.36	10.79 ± 0.12	1.02	8.85 ± 0.11	1.97	65.92 ± 1.21	9.36
16	**6**	(*L*)-N-Boc-Al	56.4 ± 0.2		9.77 ± 0.27		6.88 ± 0.27		56.56 ± 5.65	

2-ClMA 2-chloromandelic acid, *MA* mandelic acid, *HIVA* α-hydroxy isovaleric acid, *N-Boc-Al* N-Boc-Alanine

[a] $\Delta\Delta G = \Delta G_L - \Delta G_D$

[b] $\Delta\Delta H = \Delta H_L - \Delta H_D$

[c] $\Delta\Delta S = \Delta S_L - \Delta S_D$

Conclusion

In conclusion, novel calix[4]arene thiourea compounds were synthesized by the reaction of diisothiocyano derivatives of *p-tert*-butylcalix[4]arene with chiral amino alcohols. The enantioselective recognition of these receptors has been studied by UV–Vis spectroscopy. Chiral selectors **5** and **6** show strong binding and good recognition ability for the enantiomers of 2-chloromandelic acid and mandelic acid. The results indicate that the multiple hydrogen bonding, steric hindrance, structural rigidity or flexibility and π–π stacking between the aromatic groups may be responsible for the enantiomeric recognition.

Acknowledgments This work was supported by the Research Foundation of Usak University (UBAP 2014/SB001). We also thank Usak University Scientific Analysis Technological Application and Research Center (UBATAM) for support of this work.

References

1. Agrawal, Y.K., Pancholi, J.P., Vyas, J.M.: Design and synthesis of calixarene. J. Sci. Ind. Res. **68**, 745–768 (2009)
2. Kurzatkowska, K., Sayin, S., Yilmaz, M., Radecka, H.: Calix[4]arene derivatives as dopamine hosts in electrochemical sensors. Sens. Actuators B **218**, 111–121 (2015)
3. Bayrakci, M., Yigiter, S.: Synthesis of tetra-substituted calix[4]-arene ionophores and their recognition studies towards toxic arsenate anions. Tetrahedron **69**, 3218–3224 (2013)
4. Sap, A., Tabakci, B., Yilmaz, A.: Calix[4]arene-based Mannich and Schiff bases as versatile receptors for dichromate anion extraction: synthesis and comparative studies. Tetrahedron **68**, 8739–8745 (2012)
5. Chawla, H.M., Goel, P., Munjal, P.: A new metallo-supramolecular sensor for recognition of sulfide ions. Tetrahedron Lett. **56**, 682–685 (2015)
6. Marcos, P.M., Teixeira, F.A., Segurada, M.A.P., Ascenso, J.R., Bernardino, R.J., Brancatelli, G., Geremia, S.: Synthesis and anion binding properties of new dihomooxacalix[4]arene diurea and dithiourea receptors. Tetrahedron **70**, 6497–6505 (2014)
7. Erdemir, S., Yilmaz, M.: Preparation and chromatographic performance of calix[4]crown-5 macrocycle-bonding silica stationary phase. J. Sep. Sci. **34**, 393–401 (2014)
8. Adhikari, B.B., Fujii, A., Schramm, M.P.: Calixarene-madiated liquid-membrane transport of choline conjegates. Eur. J. Org. Chem. 2971–2979 (2014)
9. Botha, F., Budka, J., Eigner, V., Hudecek, O., Vrzal, L., Cisarova, I., Lhotak, P.: Recognition of chiral anions using calix[4]arene-based ureido receptor in the 1,3-alternate conformation. Tetrahedron **70**, 477–483 (2014)
10. Bozkurt, S., Yilmaz, M., Sirit, A.: Chiral calix[4]arenes bearing amino alcohol functionality as membrane carriers for transport of chiral amino acid methylesters and mandelic acid. Chirality **24**, 129–136 (2012)
11. Tanaka, K., Tsuchitani, T., Fukuda, N., Masamoto, A., Arakawa, R.: Highly enantiosele active florescent recognition of mandelic derivatives chiral salen macrosycles. Tetrahedron Asymmetry **23**, 205–208 (2012)

12. Durmaz, M., Sirit, A.: Calixarene-based highly efficient primary amine–thiourea organocatalysts for asymmetric Michael addition of aldehydes to nitrostyrenes. Supramol. Chem. **25**, 292–301 (2013)
13. McMahon, G., O'Malley, S., Nolan, K., Diamond, D.: Important calixarene derivatives—their synthesis and applications. Arkivoc **7**, 23–31 (2003)
14. Zhang, X.X., Bradshaw, J.S., Izatt, R.M.: Enantiomeric recognition of amine compounds by chiral macrocyclic receptors. Chem. Rev. **97**, 3313–3361 (1997)
15. Beddell, C.R.: The design of drugs to macromolecular targets. Wiley, Chichester (1992)
16. Jinno, K.: Chromatographic separations based on molecular recognition. VCH, Weinheim (1996)
17. Smith, P.J., Reddington, M.V., Wilcox, C.S.: Ion pair binding by a urea in chloroform solution. Tetrahedron Lett. **33**, 6085–6088 (1992)
18. Martinez-Manez, R., Sancenon, F.: New advances in fluorogenic anion chemosensors. J. Fluoresc. **15**, 267–285 (2015)
19. Gomez, D.E., Fabbrizzi, L., Licchelli, M., Monzani, E.: Urea vs. thiourea in anion recognition. Org. Biomol. Chem. **3**, 1495–1500 (2005)
20. Pfeffer, F.M., Lim, K.F., Sedgwick, K.J.: Indole as a scaffold for anion recognition. Org. Biomol. Chem. **5**, 1795–1799 (2007)
21. Qing, G., Sun, T., Chen, Z., Yang, X., Wu, X., He, Y.: 'Naked-Eye' enantioselective chemosensors for N-protected amino acid anions bearing thiourea units. Chirality **21**, 363–373 (2009)
22. Zhou, E., Zhang, J., Lu, Y., Dong, C.: Design and synthesis of novel C-2-symmetric chiral shift reagents derived from squaramide and their recognition of anions and chiral carboxylate anions. Arkivoc **5**, 351–364 (2014)
23. Chrisstoffels, L.A.J., Jong, F., Reinhoudt, D.N., Sivelli, S., Gazzola, L., Casnati, A., Ungaro, R.: Facilitated transport of hydrophilic salts by mixtures of anion and cation carriers and by ditopic carriers. J. Am. Chem. Soc. **121**, 10142–10151 (1999)
24. Bozkurt, S.: Calixarene based chiral solvating agents for a-hydroxy carboxylic acids. J. Mol. Struct. **1048**, 113–120 (2013)
25. Santoyo-Gonzalez, F., Torres-Pinedo, A., Barria, C.S.: An efficient synthesis of bis(calix[4]arenes) bis(crown ether)-substituted calix[4]arenes, aza-crown calix[4]arenes, and thiaza-crown calix[4]arenes. Eur. J. Org. Chem. **21**, 3587–3593 (2000)
26. Benesi, H.A., Hildebrand, J.H.: A spectrophotometric investigation of the interaction of iodine with aromatic hydrocarbons. J. Am. Chem. Soc. **71**, 2703–2707 (1949)