J Incl Phenom Macrocycl Chem (2010) 66:107–111
DOI 10.1007/s10847-009-9658-y

ORIGINAL ARTICLE

Chiral binaphthyl receptors bearing imidazolium or urea groups for the recognition of anions

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Received: 28 June 2009 / Accepted: 26 July 2009 / Published online: 15 August 2009

Abstract Two new binaphthyl derivatives **1** and **2** bearing two imidazolium, or bisurea groups were investigated as fluorescent chemosensors for the chiral anion recognition. Receptors **1** and **2** displayed a better selectivity for (*S*)-2-phenylbutylate over (*R*)-2-phenylbutylate. Isothermal titration calorimeter methods, fluorescence as well as theoretical calculations are utilized to explain chiral selectivity.

Keywords Chiral anion recognition · Fluorescent chemosensors · Host–guest interaction · Binaphthyl imidazolium

Introduction

Anions play a fundamental role in a wide range of chemical and biological processes, and numerous efforts have been devoted to the development of abiotic receptors for anionic species [1–4]. Sensors based on anion-induced changes in fluorescence appear to be particularly attractive due to the simplicity and high detection limit of fluorescence [5–7]. Even though great effort has been devoted to chiral anion recognition [8–18], fluorescent chemosensors for chiral anions are relatively rare [8, 15–18].

In contrast to well-known type of hydrogen bonding for the anion binding such as amide, pyrrole, urea etc., imidazolium derivatives have been utilized as anion receptors via $(C–H)^{+}–X^{-}$ charged hydrogen bonding. Recently, various imidazolium derivatives have been synthesized and studied as selective anion-receptors [3, 19–23]. So far, most of the reported chiral receptors for anions are utilizing hydrogen bonding between urea, thiurea or amide groups [3, 19–22]. Recently, fluorescent chiral imidazolium receptors for the recognition of chiral guests have been reported by Yu et al. [24].

We report herein two new binaphthyl hosts bearing either bisimidazolium groups or bisurea groups as chemosensors for the chiral recognition carboxylates. Chiral recognition was confirmed by isothermal titration calorimeter (ITC) methods, fluorescence changes and ^{1}H NMR experiments. For host **2**, theoretical calculation was also performed to explain the selectivity for (*S*)-2-phenylbutylate over (*R*)-isomer.

Electronic supplementary material The online version of this article (doi:10.1007/s10847-009-9658-y) contains supplementary material, which is available to authorized users.

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Experimental

Synthesis

(*S*)-2,2′-Bis(3,3′-dimethylimidazolium-1,1′-yl)-1,1′-binaphthyl Hexafluorophosphate (1). (*S*)-2,2′-Bis(imidazol-1-yl)-1,1′-binaphthyl [25] (100 mg, 0.26 mmol) was dissolved in 10 mL of acetonitrile. CH_3I (0.8 mmol) was added, and the solution was refluxed overnight. The volatiles were removed, and the solid obtained was triturated with ether and dried in vacuo. The resulting dibromide salt was dissolved in minimum amount of DMF and added with saturated solution of ammonium hexafluorophosphate dropwise. The precipitate obtained was filtered, washed thoroughly with water and dried under vacuum to get 162 mg (82%) of hexafluorophosphate salt: mp 160–165 °C, dec.; ^{1}H NMR (CD_3CN) δ 8.36 (d, 2H, $J = 8.8$ Hz), 8.23 (d, 2H, $J = 8.2$ Hz), 8.1 (s, 2H), 7.78 (dd, 2H, $J = 8.2$ Hz & 1.2 Hz), 7.61 (dd, 4H, $J = 8.9$ Hz & 1.6 Hz), 7.31 (d, 2H, $J = 8.5$ Hz), 7.18 (t, 2H, $J = 1.8$ Hz), 6.82 (t, 2H, $J = 1.9$ Hz), 3.70 (s, 3H), 2.16 (s, 3H);^{13}C NMR (CD_3OD) δ 135.4, 133.5, 132.5, 131.8, 131.1, 129.3, 128.8, 128.5, 126.6, 126.0, 124.1, 123.3, 122.7, 36.0; MS (FAB) $m/z = 561.1$ $(M\text{-}PF_6)^+$, calc. for $[C_{28}H_{24}F_{12}N_4P_2\text{–}PF_6]^+ = 561.1$.

(*S*)-2,2′-[N,N-Bis(N′,N′-*m*-xylyl)]uredo-1,1′-binaphthyl (2). (*S*)-2,2-Diamino-1,1′-binaphthyl (200 mg, 0.7 mmol) and 1,3-Bis-isocyanatomethyl-benzene (130 mg, 0.7 mmol) were refluxed in anhydrous toluene for 5 h under inert atmosphere. The solid separated during reflux was cooled to room temperature, filtered, washed with diethyl ether and dried in vacuo to afford 250 mg (83%) of **2**: mp 166–168 °C; ^{1}H NMR (DMSO-d_6, 250 MHz) δ 8.60 (d, 2H, $J = 9.0$ Hz), 7.91 (dd, 4H, $J = 22$ & 9.1 Hz), 7.10 (m, 10H), 6.91 (d, 2H, $J = 7.6$ Hz), 6.69 (d, 2H, $J = 8.4$ Hz), 4.03 (s, 4H); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 155.0, 139.7, 137.7, 132.5, 129.5, 128.9, 128.6, 128.2, 127.9, 126.4, 125.8, 125.3, 124.0, 123.8, 120.7, 116.9, 42.6; HRMS (FAB) $m/z = 473.1980$ $[M + H]^+$, Calcd for $[C_{30}H_{25}N_4O_2] = 473.1978$.

Isothermal titration calorimeter (ITC) experiments

Microcalorimetric titrations were performed using an isothermal titration calorimeter (ITC). The ORIGIN software provided by Microcal Inc. was used to calculate the binding constant (K_a). The solvents, CH_3CN and DMSO, were purchased from Baker, Aldrich respectively. The curve shows the fit of the experimental data to 1:1 binding modes for **2**.

Preparation of fluorometric anion titration solutions

Stock solutions (1 mM) of the tetrabutylammonium salts of (*S*)-2-phenylbutylate and (*R*)-2-phenylbutylate in CH_3CN were prepared. Stock solutions of hosts (0.1 mM) were prepared either in CH_3CN or DMSO. For all measurements, excitation was at 320 nm. Both excitation and emission slit widths were 3 nm.

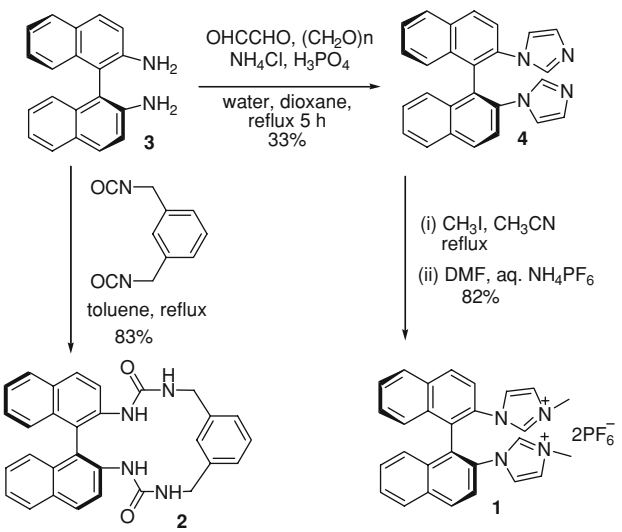
Results and discussion

Synthesis

(*S*)-2,2′-Bis(imidazol-1-yl)-1,1′-binaphthyl (**4**) was synthesized from (*S*)-2,2-diamino-1,1′-binaphthyl (**3**) following the reported procedure [25]. Treatment of **4** with CH_3I followed by the anion exchange with ammonium hexafluorophosphate to give chiral host **1** in 82% yield (Scheme 1). On the other hand, treatment of compound **3** with 1,3-bis-isocyanatomethyl-benzene gave chiral host **2** in 83% yield. The detail synthetic procedures as well as characterization data are explained in the experimental section. The ^{1}H and ^{13}C NMR spectra of host **1** and **2** are reported in the supporting information.

ITC experiments

For the chiral binding study, microcalorimetric titrations were performed using an isothermal titration calorimeter (ITC). The titration curves show the fit of the experimental data to 1:1 binding modes for host **2**. The association constants of host **2** with (*S*)-2-phenylbutylate and (*R*)-2-phenylbutylate in DMSO were calculated as 1570 and 340 M^{-1}, respectively (Fig. 1). The chiral selectivity of host **2** (K_S/K_R) was found to be ~4.6. The ITC experiment of **2** was performed in DMSO due to the solubility problem. On the other hand, the open form host **1** displayed a



Scheme 1 Synthese of host **1** and **2**

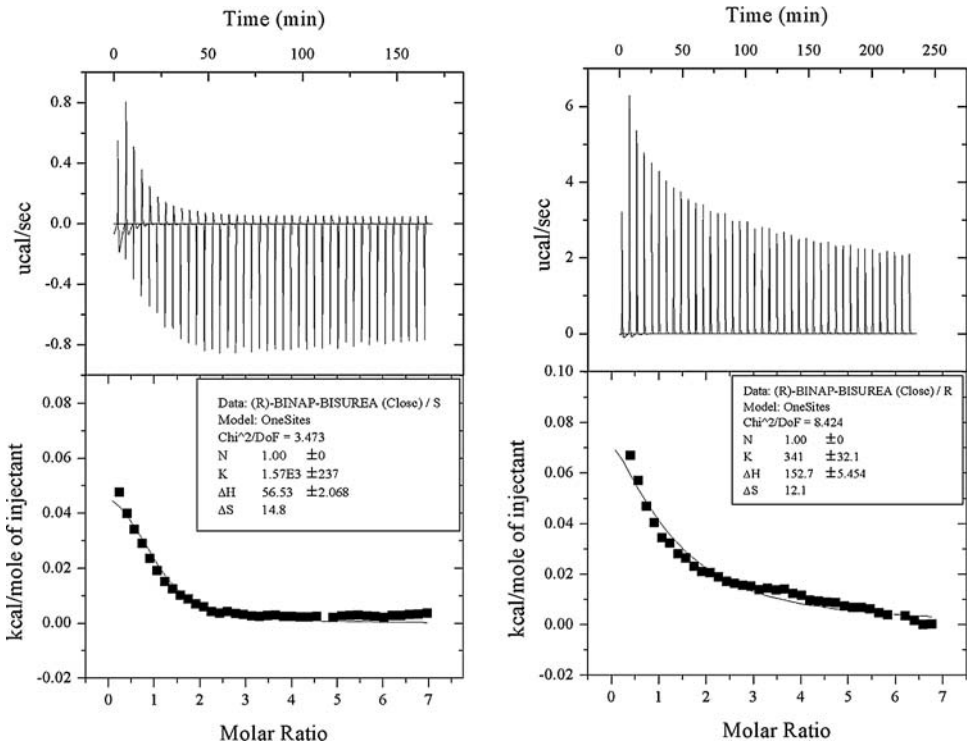


Fig. 1 ITC data of compound **2** (1.28 mM) with (*S*)-2-phenyl butylate (*left* figure) and (*R*)-2-phenyl butylate (*right* figure) (tetrabuthylammonium salts, 50.76 mM) in DMSO

mixed stoichiometry of 1:1, 1:2 and 1:3 with (*S*)-2-phenylbutylate and (*R*)-2-phenylbutylate in acetonitrile (see supporting information). The binding constants for host **1** with (*S*)-2-phenylbutylate were determined as 5890 M^{-1}, 520 M^{-2} and 14 M^{-3}, respectively, and those for host **1** with (*R*)-2-phenylbutylate were determined as 4000 M^{-1}, 559 M^{-2} and 17 M^{-3}, respectively. A slight selectivity for (*S*)-2-phenylbutylate was also observed.

NMR study

The expected strong $(C–H)^{+}–X^{-}$ hydrogen bonding between the imidazolium moieties and carboxylate was further confirmed by ^{1}H NMR (Fig. 2). Figure 2 explains the partial ^{1}H NMR spectra of open form host **1** with (*R*)- and (*S*)-madelate (tetrabutylammonium salt) in CD_3CN. As shown in Fig. 2, the imidazolium C-H displayed downfield shifts upon the addition of mandelates. Upon the addition of chiral guests (2 eq.), (*S*)-mandelate induced a larger downfield shift (δ 8.12–8.43 ppm) of imidazolium C–H in host **1** than that of (*R*)-isomer (δ 8.12–8.39 ppm).

Fluorescent study

Fluorescent experiments were done by exciting the binaphthyl moiety at 320 nm. Figure 3 explains the fluorescent titrations of chemosensor **1** (3 μM) with (*S*)-2-phenylbutylate and (*R*)-2-phenylbutylate in acetonitrile. The fluorescent titration experiments of host **2** were performed in DMSO-CH_3CN (2:8, v/v). The association constants of host **2** with (*S*)-2-phenylbutylate and (*R*)-2-phenylbutylate were calculated as 7,000 and 2,400 M^{-1}, respectively (Association constants were obtained using the computer program ENZFITTER, available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2 1LA, United Kingdom). Host **1** and **2** showed chelation enhanced quenching (CHEQ) effects with these chiral guests. These CHEQ effects can be attributed to the photo-induced electron transfer (PET) process. The PET induced quenching effects of urea anthracene derivatives as well as imidazolium derivatives with anions have been also reported [19–23].

Theoretical calculations

The selectivity of hosts **2** with (*S*)-2-phenylbutylate and (*R*)-2-phenylbutylate was further demonstrated with theoretical calculations. Density functional tight binding (DFTB) approach is used for the calculation [26]. Chiral anion selectivities on the basis of the differences on the strength π-interactions are known in literature [16, 27]. In **2**-(*S*)-2-phenylbutylate complex, the phenyl ring of the guest forms π–π interaction with the phenyl ring of host **2** and terminal alkyl hydrogen forms H–π interaction with the naphthyl ring (Fig. 4). In contrast, in **2**-(*R*)-2-phenylbutylate complex, the phenyl ring of the guest forms π–π interaction with the naphthyl ring of host **2** and terminal alkyl hydrogen forms H–π interaction with the phenyl ring.

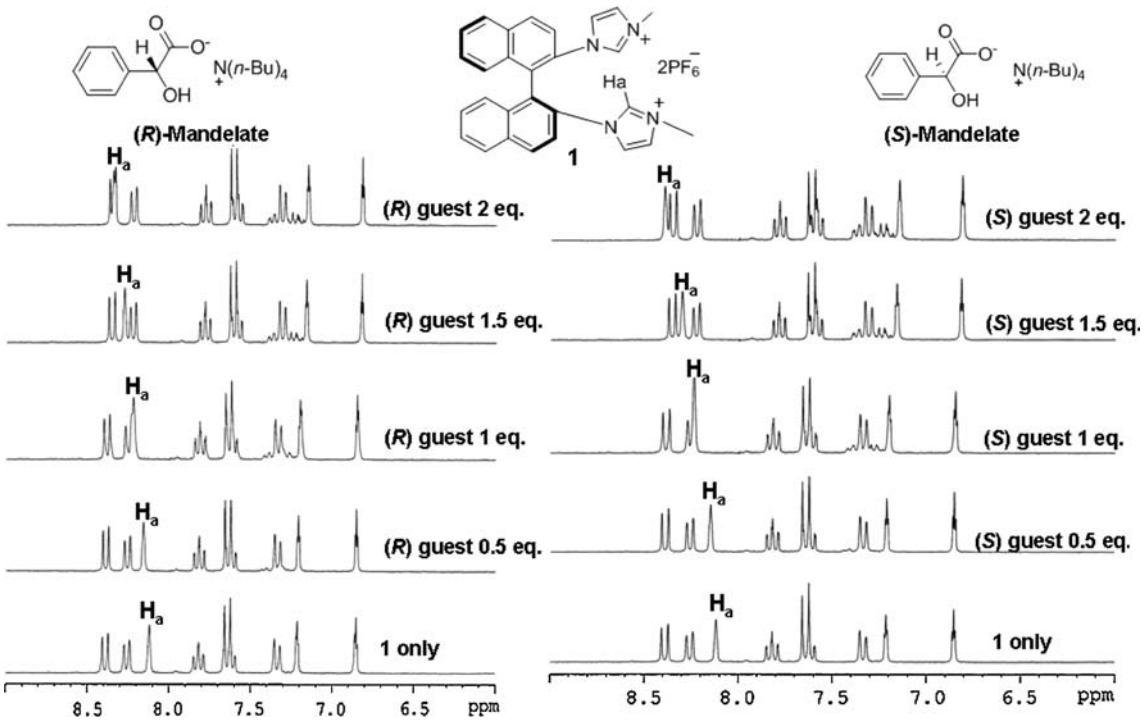


Fig. 2 Partial ^{1}H NMR (250 MHz) spectra of **1** upon the addition of (*R*)- and (*S*)-madelate (tetrabutylammonium salt) in CD_3CN

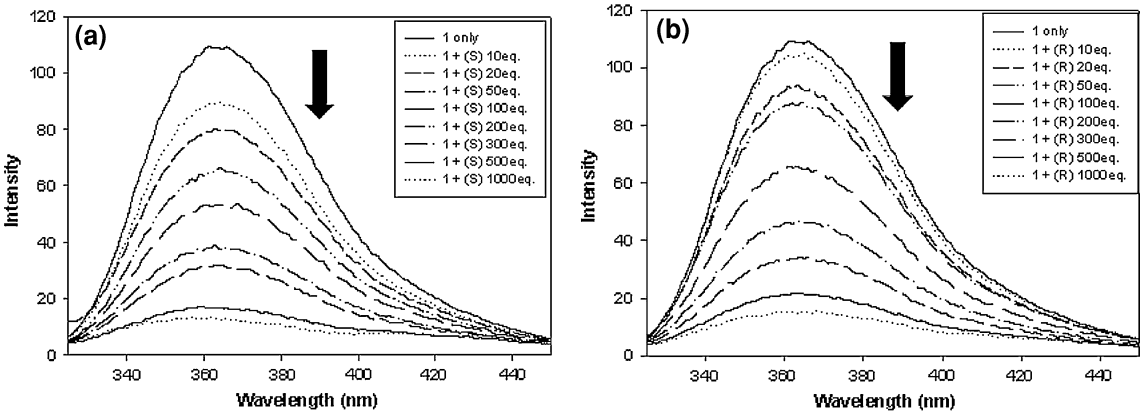


Fig. 3 Fluorescent titrations of **1** with (*S*)-2-phenyl butylate (**a**) and (*R*)-2-phenyl butylate (**b**) (tetrabuthylammonium salts) in CH_3CN

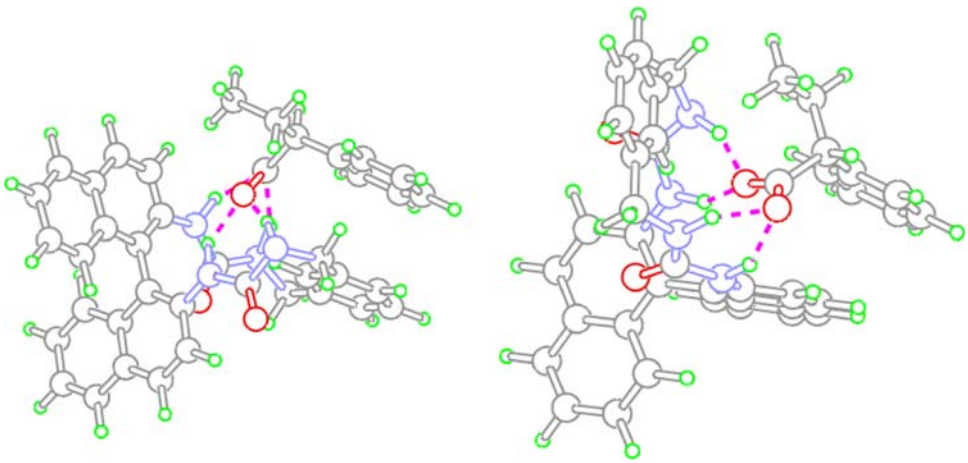


Fig. 4 DFTB optimized geometries of the **2**-(*S*)-2-phenylbutylate complex (*left*) and **2**-(*R*)-2-phenylbutylate complex (*right*)

2-(*S*)-2-Phenylbutylate complex is found to be 0.6 kcal/mol more stable than **2**-(*R*)-2-phenylbutylate complex.

Conclusion

In conclusion, two new binaphthyl derivative **1** and **2** bearing either bisimidazolium or bisurea group was investigated as fluorescent chemosensors for the chiral anion recognition. All of these two hosts displayed a better selectivity for (*S*)-2-phenylbutylate over (*R*)-2-phenylbutylate. The chiral selectivity of host **1** and **2** (K_S/K_R) were found to be $\sim$1.5 and $\sim$5 by ITC titrations, respectively. This selectivity was also confirmed by fluorescent titrations. The chiral selectivity of **2** was further confirmed by theoretical calculations.

Acknowledgements This work was supported by grants from KOSEF/MEST (SRC; R11-2005-008-02003-0) and collaboration fund between Korea and China (KOSEF; F01-2008-000-10026-0, Chinese NSFC; 50811140342). Authors also thank to Professor K. S. Kim and He Tian for helpful discussion. J.Y., S.K.K. and S-Y.C. thank to BK 21 fellowship. We also thank KBSI in Daegu, Korea, for their instrumentation assistance (FAB mass spectra).

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