ORGANIC LETTERS

2004
Vol. 6, No. 25
4655−4658

A New Imidazolium Cavitand for the Recognition of Dicarboxylates

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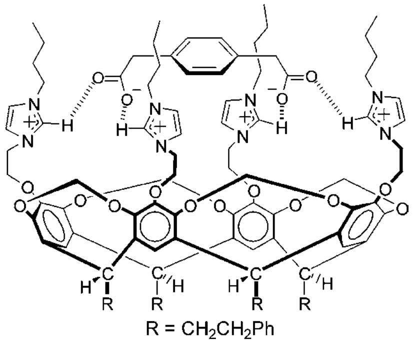
Received August 27, 2004

ABSTRACT



A new cavitand bearing four imidazolium groups was synthesized for the recognition of anions through (C-H)$^+\cdots$X$^-$ hydrogen bond formation. The binding properties toward various anions including dicarboxylates were examined on the basis of ^{1}H NMR spectroscopic experiments.

Readily available calix[4]arene derivatives have been utilized as starting materials for the synthesis of metal-selective ionophores.[1] On the other hand, it has been only a few years since cavitand derivatives have been used extensively as ionophores. Cavitands[2] are rather rigid and have enforced cavities compared with calix[4]arenes. Recently, various cavitand derivatives have been synthesized as host compounds for metal ion recognition,[3] anion recognition,[4] and organic guests.[5]

The recognition and sensing of anions has attracted considerable attention[6] owing to the important roles of anions in biological, industrial, and environmental processes. In contrast to the well-known type of hydrogen bonding for

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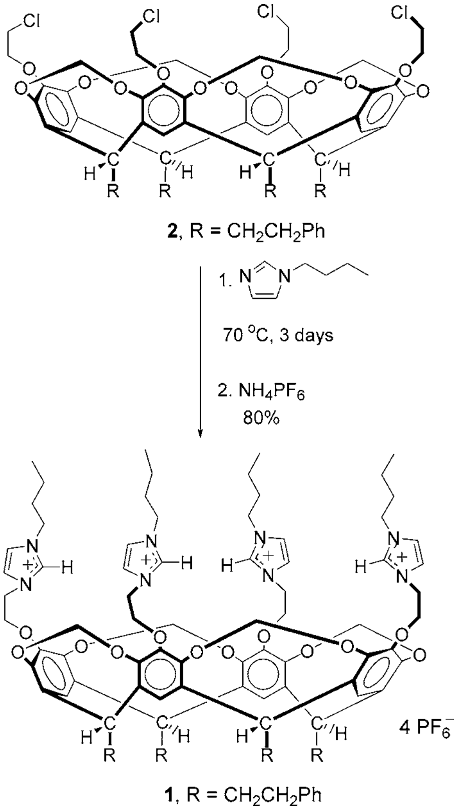
10.1021/ol048285y CCC: $27.50

Scheme 1. Synthesis of Cavitand **1**



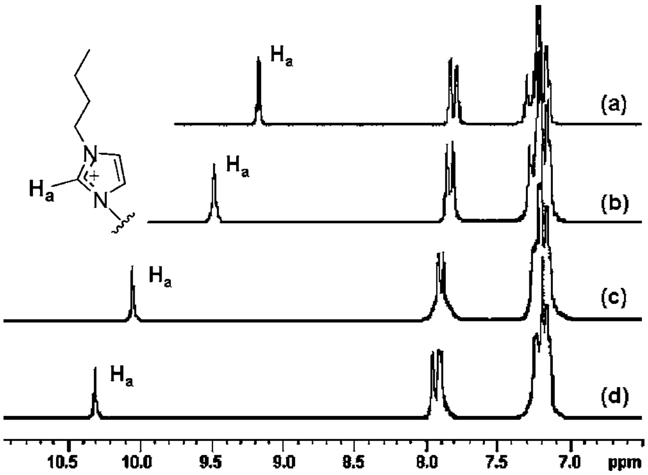


Figure 1. Partial ^{1}H NMR (250 MHz) of **1** (1 mM) in DMSO-d_6: (a) compound **1** only; (b) **1** + 0.5 equiv of bis(tetrabutylammonium) 1,3-adamantanedicarboxylate **3**; (c) **1** + 1 equiv of **3**; (d) **1** + 2 equiv of **3**.

anion binding such as amide, pyrrole, urea, etc., benzene-based tripodal imidazolium receptors and imidazolium anthracene derivatives have been employed for halide anion recognition using the strong (C-H)$^+\cdots$X$^-$ hydrogen bonding between imidazolium moieties and halide anions.[7] As far as we are aware, there has not been any report on the introduction of imidazolium groups onto the cavitand moiety. Since cavitands bear rigid and larger cavities compared to the benzene tripodal systems, a cavitand derivative may provide different binding modes with anions with four imidazolium groups.

We report herein on a new cavitand derivative bearing four imidazolium groups as a receptor for anions. The binding properties toward various anions including dicarboxylates were investigated on the basis of ^{1}H NMR spectroscopic experiments.

Our synthesis began with tetrahydroxy-cavitand, which was prepared following the published procedure.[8] It is worth mentioning that the recent report by Kaifer and co-workers regarding the improved preparation of tetrabromo-cavitand helped to increase the overall yield (up to 45%).[9] Tetrachloride **2** was synthesized by following the published procedure.[10] This intermediate was reacted with *n*-butyl imidazole at 70 °C for 3 days followed by anion exchange with NH$_4$PF$_6$, which gave the tetraimidazolium cavitand **1** in an 80% yield (see Supporting Information).

Because of the precipitate formed during the titration experiments in CD$_3$CN, the NMR data was obtained in DMSO-d_6. Upon the addition of bis(tetrabutylammonium) 1,3-adamantanedicarboxylate **3**, large downfield shifts of the C(2) proton of the imidazolium ring clearly suggest the **1**-anion complexation by CH$^+$-anion charged hydrogen bonds (Figure 1). The tetrabutylammonium salts of various anions, such as 1,3-adamantanedicarboxylate (**3**), adipate (**4**), terephthalate (**5**), 1,4-phenylenediacetate (**6**), succinate (**7**), acetate, Cl$^-$, Br$^-$, and I$^-$ were used for the binding study. Bis(tetrabutylammonium) salts of **3**−**7** were prepared by following/modifying the published procedures.[11] As shown in

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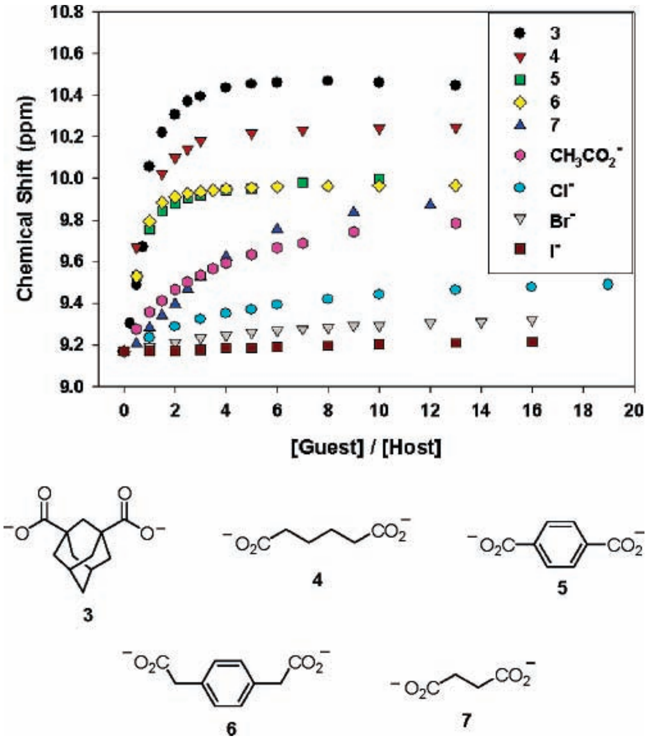

Figure 2. ^1H NMR (250 MHz) titration of **1** (1 mM) with tetrabutylammonium salts of various anions in DMSO-d_6.

Figure 2 (also see Supporting Information), downfield shifts of the CH^+ of the imidazolium ring were observed for the host **1** upon the addition of **3** ($\Delta\delta = 1.30$ ppm), **4** ($\Delta\delta = 1.08$ ppm), **5** ($\Delta\delta = 0.83$ ppm), **6** ($\Delta\delta = 0.80$ ppm), **7** ($\Delta\delta = 0.64$ ppm), $CH_3CO_2^-$ ($\Delta\delta = 0.66$ ppm), Cl^- ($\Delta\delta = 0.32$ ppm), Br^- ($\Delta\delta = 0.15$ ppm), and I^- ($\Delta\delta = 0.05$ ppm).

From the ^1H NMR titrations in DMSO-d_6, the association constants for **3**, **4**, **5**, **6**, **7**, $CH_3CO_2^-$, Cl^-, and Br^- were found to be 2100, 8100, 7300, 16200, 200, 400, 210, and 100 M^{-1} (errors <10%), respectively. Data analysis was performed using WinEQNMR[12] computer analysis.

Even though the chemical shifts in the ^1H NMR spectra were maximized with bis(tetrabutylammonium) 1,3-adamantanedicarboxylate **3**, the cavitand **1** displays a moderate selectivity for 1,4-phenylenediacetate **6** among the anions examined. The binding stoichiometry was examined using the Job plot.[13] As expected, the cavitand **1** displays 1:1 binding with **3**, **4**, **5**, and **6**. On the other hand, 1:2 complex formation was confirmed with **7**, acetate, Cl^-, and Br^-. Interestingly, instead of a 1:1 complex, the acetate and other halide anions formed a 1:2 complex with the host. In addition, the linker between dicarboxylate was found to be essential for determining the stoichiometry between host and guest.

This trend in the association constants suggests that the length of the linker between two carboxylates as well as rigidity/flexibility of the guest are important factors for the binding of the cavitand **1**.

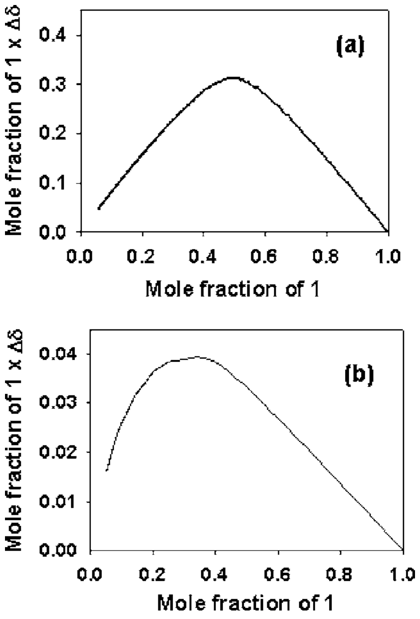

Figure 3. Job plot of **1**: (a) with **6**; (b) with Cl^-.

In the electrospray ionization (ESI) mass spectrum, a peak at m/z 906.5 that corresponds to $[\mathbf{1}\text{-}4PF_6^- + \mathbf{6}]^{2+}$ was clearly observed (see Supporting Information). Upon the addition of acetate, a peak at m/z 869.3 that corresponds to $[\mathbf{1}\text{-}4PF_6^- + 2CH_3CO_2^-]^{2+}$ was observed in the ESI mass spectrum. The association constants of cavitand **1** with **6**, acetate, and Cl^- were determined again in CD_3CN using ^1H NMR titration experiments. The calculated values were 96200, 2100, and 840 M^{-1}, respectively (errors <10%). The association constant of cavitand **1** for **6** was reported to be 96 200 M^{-1} in CD_3CN while its value in DMSO-d_6 decreased to 16 200 M^{-1}. The binding of the cavitand with these anions decreased with a more polar solvent. This was attributed to the strong interaction between DMSO and the cationic imidazolium receptor.[7d,14] In conclusion, imidazolium groups were introduced to the cavitand framework for the first time.

Table 1. Association Constants, Free Energy Changes (kcal/mol), and Chemical Shift Changes for the **1**-Anion Complexes Based on ^1H NMR Experiments

	K_a $(M^{-1})^a$	$-\Delta G^a$	K_a $(M^{-1})^b$	$\Delta\delta$ (ppm)^a
3	2100	4.77		1.30
4	8100	5.17		1.08
5	7300	5.12		0.83
6	16200	5.73	96200	0.80
7	200^c	3.04^d		0.64
$\mathbf{CH_3CO_2^-}$	400^c	3.53^d	2100^c	0.32
$\mathbf{Cl^-}$	210^c	3.14^d	840^c	0.15
$\mathbf{Br^-}$	100^c	2.93^d		0.05

^{a} In DMSO-d_6. ^{b} In CD_3CN. ^{c} K_{11}. ^{d} Based on the K_{11}.

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A new cavitand recognizes anions via $(C\text{-}H)^{+}\cdots X^{-}$ hydrogen bond formation. The binding properties of this host toward various anions were examined using ^{1}H NMR titrations. In particular, selected dicarboxylate guests were used for the binding study and among the anions examined, cavitand **1** displays a selective binding with bis(tetrabutylammonium) 1,4-phenylenediacetate.

Acknowledgment. This research was supported by a research grant from KRIBB Research Initiative Program.

Supporting Information Available: Experimental procedures and characterization data for compound **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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