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Effect of hydroxyl groups in receptors bearing disulfonamide on anion recognition in acetonitrile-d_3

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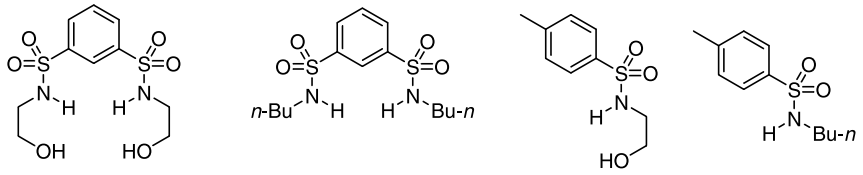
Abstract—To elucidate the roles of hydroxyl group on anion-recognition chemistry, receptors bearing disulfonamide and hydroxyl groups were prepared and their anion-binding properties were evaluated in acetonitrile.

Anion recognition by artificial receptors has been growing in the field of host–guest chemistry due to biological and environmental significance.[1] Naturally occurring anion-binding peptides for phosphate and sulfate anions are known to have amide N–H of the peptides and hydroxyl groups of serine and threonine residues in the binding sites.[2] Although hydrogen-donating effects of N–Hs of amide,[3] urea,[4] thiourea,[5] and sulfonamides[6] on anion binding have been extensively investigated in model systems, the roles of hydroxyl groups have been less studied.[7,8] Davis and co-workers have reported that rigid steroid-based anion receptors bearing hydroxyl groups bind anionic species in non-polar organic solvents such as $CDCl_3$ and hydrocarbons.[8a,b] Hamilton et al. have reported that receptors having both urethane N–Hs and hydroxyl groups exhibit considerably large binding constants for acetate anion in acetonitrile.[8c] However, it has remained whether such cooperative hydrogen bonds work on other anion species such as phosphate, sulfate, and halide anions. This prompted us to examine the effect of the cooperative hydrogen bonds on binding constants for these anions in acetonitrile by employing the receptors as shown in Scheme 1.

Receptors **1** and **2** were prepared from the corresponding disulfonyl chloride with 2-aminoethanol or 1-aminobutane in *N*,*N*-dimethylformamide, and characterized by ^{1}H NMR and elemental analysis.† Receptors **3** and **4** were prepared similarly by using tosyl chloride. Binding behavior of **1** for anion species (tetra(*n*-butyl)ammonium salts) was examined by ^{1}H NMR titration method. To eliminate higher order complexation (host:guest = 2:1 and so on), acetonitrile was used instead of less polar solvents such as chloroform. Dilution experiment of ^{1}H NMR for **1** in MeCN-d_3 ([**1**] = 10–1.67×10^{-3} mol dm^{-3}) showed no spectral



Scheme 1.

Keywords: anion recognition; hydroxyl group; sulfonamide; hydrogen bond.

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† Selected analytical data: **1**: mp 80.5°C. ^{1}H NMR (300 MHz, MeCN-d_3) δ 8.24 (*s*, 1H), 8.04 (*d*, 2H, J = 7.9 Hz), 7.75 (*t*, 1H, J = 7.9 Hz), 5.83 (*bs*, 2H), 3.46 (*q*, 4H, J = 5.6 Hz), 2.96 (*q*, 4H, J = 5.6 Hz), 2.82 (*t*, 2H, J = 5.6 Hz). Anal. calcd for $C_{10}H_{16}N_2O_6S_2$: C, 37.03; H, 4.97; N, 8.64. Found C, 37.06; H, 4.93; N, 8.26; **2**: mp 100–101°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (*t*, 1H, J = 1.6 Hz), 8.06 (*dd*, 1H, J_1 = 7.9 Hz, J_2 = 1.6 Hz), 7.69 (*t*, 1H, J = 7.9 Hz), 4.94 (*bs*, 2H), 2.97 (*q*, 4H, J = 6.7 Hz), 1.46 (*quint*, 4H, J = 7.3 Hz), 1.29 (*m*, 4H), 0.86 (*t*, 6H, J = 7.3 Hz). Anal. calcd for $C_{14}H_{24}N_2O_4S_2$: C, 48.25; H, 6.94; N, 8.04. Found C, 48.42; H, 6.92; N, 8.04%.

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change, indicating that dimerization of receptor **1** is negligible in experimental concentration range. Fig. 1 shows the result of ^{1}H NMR titration of **1** with Cl^- in MeCN-d_3. Upon addition of Cl^-, large downfield shifts of OH protons ($\Delta\delta$ 1.64 ppm), sulfonamide NH protons ($\Delta\delta$ 1.71 ppm), and 2-C-H proton of benzene ring ($\Delta\delta$ 0.51 ppm) were observed. This result strongly suggests that the hydroxyl groups are involved in hydrogen-bonding formation. Although the similar downfield shifts of OH and NH protons were observed for AcO^- and $H_2PO_4^-$, the changes of the shifts were not determined accurately because of broadening. Stoichiometry of host–guest complexation was confirmed to be 1:1 by a Job plot obtained from the chemical shift of 2-C-H of the benzene ring, as shown in Fig. 2. Negative ion mode of electron-spray ionization mass spectroscopy revealed 1:1 complex formation for **1** and **2** with all the anions used except for ClO_4^- and no higher order complex was not observed.

Binding constants of the receptors with the anion species were determined by non-linear least square calculation following the chemical shifts of 2-C-H of the benzene ring by ^{1}H NMR titration, as shown in Fig. 3. The results are summarized in Table 1. Receptor **1** is more efficient than **2** for all the anion species, indicating clearly that the hydroxyl groups involved in the complexation as hydrogen-bond donors. It is noted that receptor **1** showed good selectivity for AcO^- compared with other anions. The anion-binding ability of receptors **1** and **2** are in the order of AcO^- ($pK_a = 4.76$ in water)>$H_2PO_4^-$ (2.16)>Cl^- (−6.1)>Br^- (−9)HSO_4^- (−3.1)>I^- (−10)>ClO_4^- (−7.3). This order can be explained by both basicity and shape of the anions. The effect of the hydroxyl groups on the binding constants can be evaluated by $\Delta\Delta G$, as shown in Table 1. Much larger $\Delta\Delta G$ (9.2 kJ mol^{-1}) for AcO^- suggests the binding mode as shown in Scheme 2. Such a tendency was also observed for AcO^- binding of receptors **3** and **4**. These receptors associate with AcO^- in 1:1 complexation and K_a and ΔG values of **3** and **4** for AcO^- were 703 ($\Delta G = 16.3$ kJ mol^{-1}) and 39 dm^3 mol^{-1} ($\Delta G = 9.1$ kJ mol^{-1}), respectively.

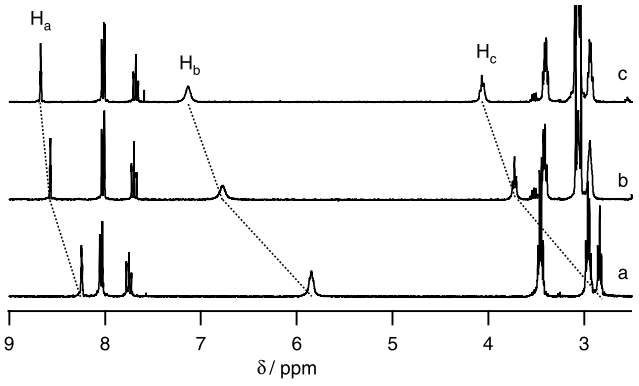


Figure 1. Partial ^{1}H NMR spectra on titration of **1** with Cl^- in MeCN-d_3 at 298 K. [**1**] = 5.0×10^{-3} mol dm^{-3}, (a) **1** only; (b) **1** and 1 equiv. of Cl^-; (c) **1** and 2 equiv. of Cl^-. The resonances corresponding to 2-CH of benzene ring (H_a), NH (H_b), and OH (H_c) are marked, respectively.

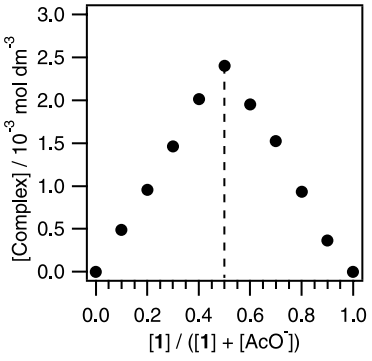


Figure 2. A Job plot for complexation of **1** with AcO^- determined by ^{1}H NMR in MeCN-d_3 at 298 K. [**1**]+[AcO^-] = 5.0×10^{-3} mol dm^{-3}.

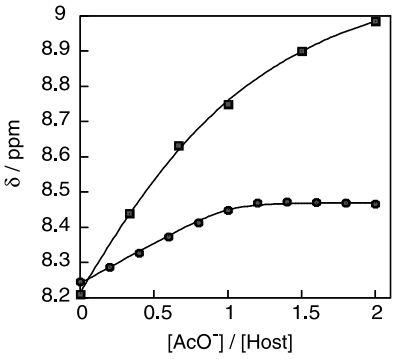
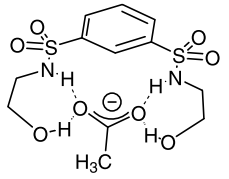


Figure 3. Plots of chemical shift (2-CH) of **1** (closed circle) and **2** (closed square) on the concentration of AcO^- in MeCN-d_3 at 298 K. [Host] = 5.0×10^{-3} mol dm^{-3}.

Table 1. Association constants and binding free energies for complexation of receptors and anions in acetonitrile-d_3

Anion	K_a/dm^3 mol^{-1} ($-\Delta G$ at 298 K/kJ mol^{-1})[a]		$\Delta\Delta G$ (kJ mol^{-1})
	1	**2**	
AcO^-	23,800 ± 1,600 (25.0)	585 ± 19 (15.8)	9.2
$H_2PO_4^-$	1,890 ± 10 (18.7)	209 ± 23 (13.2)	5.5
HSO_4^-	240 ± 13 (13.6)	62 ± 5 (10.2)	3.4
Cl^-	928 ± 35 (16.9)	124 ± 14 (11.9)	5.0
Br^-	236 ± 2 (13.5)	52 ± 2 (9.8)	3.7
I^-	2.5 (2.3)	<1[b]	
ClO_4^-	<1[b]	<1[b]	

[a] Measured by 300 MHz ^{1}H NMR at 298 K. [Receptor] = 5.0×10^{-3} mol dm^{-3}. Tetra(*n*-butyl)ammonium salts were used for all anions.
[b] Shift was too small to determine the association constant.



Scheme 2.

In conclusion, we have demonstrated that a simple disulfonamide bearing hydroxyl group **1** shows remarkable anion-binding ability in MeCN-d_3. The hydroxyl groups of the receptor act as hydrogen-bond donors in anion recognition even in such a polar solvent as MeCN-d_3. The present results are useful information for design of more sophisticated receptors. It is noteworthy that chiral recognition of optically active carboxylate such as amino acids is expected by a chiral receptor bearing hydroxyl groups, which is easily obtained from chiral aminoalcohols.

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