4-(*N*,*N*-Dimethylamino)benzoic Acid as a New Class of Simple Chromogenic and Fluorogenic Anion Host Exhibiting High Selectivity to HPO_4^{2-} and SO_4^{2-}

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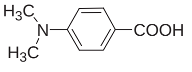
Commercially available 4-(*N*,*N*-dimethylamino)benzoic acid (**1**) was directly applied for anion recognition in CH_3CN. It showed remarkable affinity and selectivity to divalent anions HPO_4^{2-} and SO_4^{2-} over monovalent anions such as $H_2PO_4^-$, HSO_4^-, ClO_4^-, BF_4^-, PF_6^-, and NO_3^- in terms of UV–vis and fluorescence titrations. The combination of the basicity and charge density of guest anions played an important role in the selectivity of host **1** toward anions.

Anions are ubiquitous throughout chemical, analytical, biological, and environmental systems. A great deal of effort has gone into designing and synthesizing anion hosts for the specific recognition of anions, which resulted in not simple but quite massive and complicated molecular features of the hosts to accomplish such selective recognition and sensitive signaling on the specific anions.[1]

Thus, we have embarked on developing simple, efficient, and, if possible, commercially available reagents for anion hosts. One candidate suitable for this purpose is the aromatic acid derivative, since it has an acidic hydrogen atom to be transferred to guest anions as well as an aromatic moiety to show spectral response upon complexation with guest anions. If the aromatic acid interacts with the guest anion whose conjugate acid is less acidic than the host acid (i.e., the basicity of the guest anion is stronger than that of the conjugate base of the host acid), the host acid would easily *transfer* a proton to the guest anion to give the corresponding carboxylate anion, which would cause notable spectral changes. In the case of the guest anion whose conjugate acid is more acidic than the host acid (i.e., the basicity of the guest anion is weaker than that of the conjugate base of the host acid), proton exchange between the host acid and the guest anion would be quite difficult. However, even in this case, if the structure of the guest anion is complementary to the host acid, *complexation* between the host acid and the guest anion could occur to give a partially anionic species of the acid concomitant with spectral changes as reported by Wu et al.[2] Charge densities on guest anions would also play a crucial role in effective interaction between the host acid and the guest anion.

These considerations led us to utilize 4-(*N*,*N*-dimethylamino)benzoic acid (**1**) (Scheme 1) as a preliminary experiment for the methodology, since we have applied a 4-(*N*,*N*-dimethylamino)benzoate subunit tethered to the cyclic guanidinium ion derivative as a probe for anion recognition.[3] On the other hand, divalent anion HPO_4^{2-} is selected as a target anion, because it has the highest basicity among typical inorganic anions which frequently appear in the environment (Table 1). In this paper, we report the complexation behavior of *commercially available* acid **1** with divalent anions, HPO_4^{2-} and SO_4^{2-}, as well as monovalent anions, $H_2PO_4^-$, HSO_4^-, ClO_4^-, BF_4^-, PF_6^-, and NO_3^-, studied by means of UV–vis and fluorescence spectroscopy.



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Scheme 1.

Table 1. Acid dissociation constants (pK_a) of a variety of acids and base dissociation constants (pK_b) of their conjugate bases

Acid	pK_a	Conjugate base	pK_b[a]
H_2SO_4	ca. 3[b]	HSO_4^-	ca. 17
HNO_3	−1.64[c]	NO_3^-	15.6
$HClO_4$	−1.6[d]	ClO_4^-	15.6
HBF_4	0.5[d]	BF_4^-	13.5
HSO_4^-	1.99[b]	SO_4^{2-}	12.0
H_3PO_4	2.16[d]	$H_2PO_4^-$	11.8
C_6H_5COOH	4.19[d]	$C_6H_5COO^-$	9.81
$H_2PO_4^-$	7.21[d]	HPO_4^{2-}	6.79

[a] Calculated by equation $K_b = K_w/K_a$. [b] ref 4. [c] ref 5. [d] ref 6.

The complexation behavior of host **1** toward a variety of anions was investigated by UV–vis titrations in CH_3CN. All anions were used as tetrabutylammonium (TBA) salts. Acid **1** showed an absorption maximum at 309 nm ($\mathcal{E} = 2.8 \times 10^4$ [$L \cdot mol^{-1} \cdot cm^{-1}$] in CH_3CN). Gradual addition of HPO_4^{2-}, whose basicity ($pK_b = 6.79$) is stronger than that of the conjugate base of **1** (pK_b of benzoate itself is 9.81), led to substantial decrease of the absorbance at 309 nm along with obvious increase of new absorption at 275 nm (Figure 1a). When equimolar amounts of host acid **1** and tetrabutylammonium hydroxide ((TBA)OH) were mixed together in CH_3CN in a separate experiment, similar absorption around 275 nm appeared. This result clearly indicates that the new absorption at 275 nm should be ascribed to the absorption of the conjugate base (4-(*N*,*N*-dimethylamino)benzoate anion) of host acid **1** generated by simple proton exchange between acid **1** and base HPO_4^{2-}.[7] The existence of clear inflection points around $[HPO_4^{2-}]/[\mathbf{1}] = 0.5$ in titration profiles (Figure 2) as well as the observation of a maximum at $[\mathbf{1}]/([\mathbf{1}] + [HPO_4^{2-}]) = 0.65$ in Job's plot[8] apparently indicates that the stoichiometry of the complex is 2:1 (host **1**:anion) in the case of HPO_4^{2-}. On the other hand, titrations by monovalent anions ($H_2PO_4^-$, HSO_4^-, ClO_4^-, BF_4^-, and NO_3^-), whose basicity is weaker ($pK_b > 11$) than that of the conjugate base of host **1** (pK_b of benzoate itself is 9.81), resulted in quite limited changes both at 275 and 309 nm (Figure 2). Interestingly, however, in the case of divalent anion SO_4^{2-}, whose basicity is weaker than HPO_4^{2-}, the titration profile was similar to that of the latter, showing large spectral changes as well as rapid saturation during titration.[8]

The UV–vis titration data monitored at 309 nm (Figure 2b) were subjected to curve fitting to determine binding constants of host **1** with the anions.[3] Monotonic changes were observed in the cases of monovalent anions ($H_2PO_4^-$, HSO_4^-, ClO_4^-,

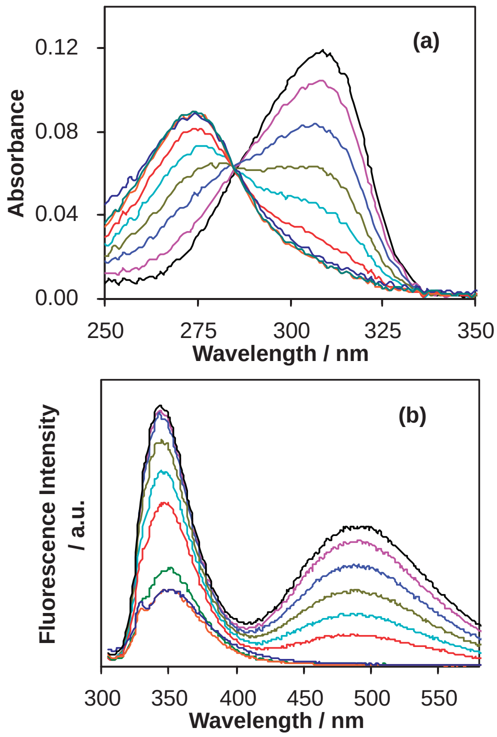

Figure 1. Absorption (a) and fluorescence (b) spectra of host **1** in CH_3CN (4.46×10^{-6} M) in the absence (—) of and in the presence of 0.1 (—), 0.2 (—), 0.3 (—), 0.4 (—), 0.5 (—), 1.0 (—), 2.0 (—), and 10.0 (—) equivalent of $(TBA)_2HPO_4$, respectively.

BF_4^-, PF_6^-, and NO_3^-), whereas slightly sigmoidal change was observed in the case of divalent anion SO_4^{2-} (Figure 2). Taking into account of the charge balance between host acid **1** and guest anions as well as the above titration profiles, 1:1 (host **1**:anion) and 2:1 complexation models were applied for the calculations in the cases of monovalent and divalent anions, respectively. K_1 denotes 1:1 complexation constants for monovalent anions and K_2 denotes 2:1 complexation constants for divalent anions. As a result, monovalent anions showed almost equal binding affinities to host **1** ($\log K_1 = 4.3$ for $H_2PO_4^-$, 3.6 for HSO_4^-, 4.2 for ClO_4^-, 3.4 for BF_4^-, 3.4 for PF_6^-, and 3.5 for NO_3^-), while divalent anions showed higher affinities to host **1** (HPO_4^{2-} and SO_4^{2-}: $\log K_2 > 10$) than the monovalent anions.[9] Interestingly, when the basicity of anions is weaker than that of the conjugate base of **1**, the basicity of the anions is not related to the strength of complexation. While anions, $H_2PO_4^-$ and SO_4^{2-}, have nearly the same basicity ($pK_b = 11.8$ and 12.0, respectively), the latter exhibited much higher affinity to host **1** than the former. These results indicate that the charge density on anion is the most important factor influencing the complexation ability between host **1** and anions with weaker basicity than the conjugate base of host **1**.

Fluorescence titrations in CH_3CN were also performed in order to estimate the complexation behavior of host **1** with the anions. Host **1** exhibited dual fluorescence at 343 nm (locally excited state, LE) and 491 nm (twisted intramolecular charge transfer state, TICT) at excitation wavelength 300 nm. Gradual fluorescence quenching of host **1** was observed by stepwise addition of divalent HPO_4^{2-} in CH_3CN (Figure 1b). Titration profiles of host **1** monitored at TICT emission (491 nm)[8] turned out to be quite similar to those observed in UV–vis titrations (Figure 2b).[10]

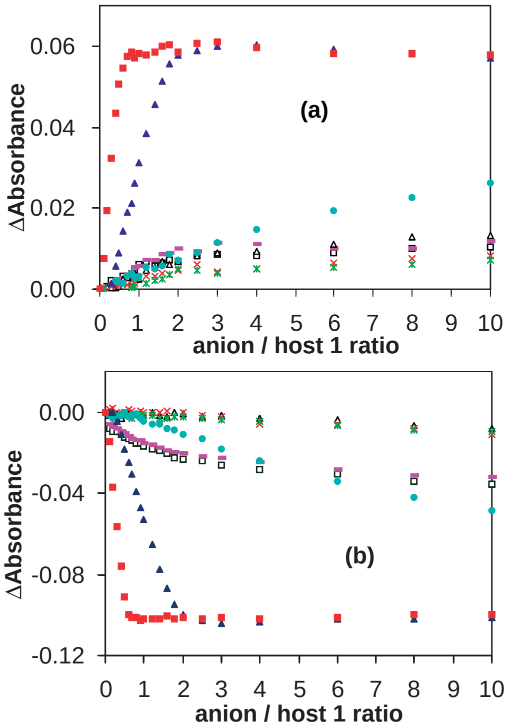

Figure 2. Absorbance changes of host **1** (4.46×10^{-6} M) monitored at 275 nm (a) and 309 nm (b) upon addition of $(TBA)_2HPO_4$ (■), $(TBA)_2SO_4$ (▲), $(TBA)H_2PO_4$ (●), $(TBA)HSO_4$ (□), $(TBA)ClO_4$ (—), $(TBA)BF_4$ (△), $(TBA)PF_6$ (×), and $(TBA)NO_3$ (*) in CH_3CN.

In conclusion, we have directly applied simple and *commercially available* acid **1** as an anion host to recognize a variety of anions. Host **1** exhibits strong binding affinity and high selectivity toward divalent anions (HPO_4^{2-} and SO_4^{2-}) over the monovalent anions. The observation will induce a new methodology on anion recognition. Studies on other aromatic acid systems are in progress.

References and Notes

1 For example, see: K. A. Schug, W. Lindner, *Chem. Rev.* **2005**, *105*, 67, and references are cited therein.
2 F.-Y. Wu, Y.-B. Jiang, *Chem. Phys. Lett.* **2002**, *355*, 438.
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5 A. J. Gordon, R. A. Ford, *The Chemist's Companion: A Handbook of Practical Data, Techniques, and References*, Wiley-Interscience, New York, **1972**.
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7 We suppose that the resulting host carboxylate and conjugate acid of anion would not be separated by the solvent fully to give a complete ion species but would make a pair through hydrogen bonding in CH_3CN, because titrations of host **1** by the strongest base (OH^-), a strong base (HPO_4^{2-}), and a weak base (SO_4^{2-}) gave similar spectra finally.
8 See Supporting Information.
9 The binding constants K_2 for divalent anions (HPO_4^{2-} and SO_4^{2-}) are too large to be calculated accurately. However, we believe that the binding constant for HPO_4^{2-} is larger than that for SO_4^{2-} judging from the titration profile as shown in Figure 2b.
10 The titration profiles by divalent anions (HPO_4^{2-} and SO_4^{2-}) monitored at LE emission (343 nm) exhibited completely different features from those by the monovalent anions, suggesting the chemical species generated by interaction of host **1** with the divalent anions were quite different from those with the monovalent anions.[8]

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