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Synthesis and anion recognition properties of 8,8′-dithioureido-2,2′-binaphthalene

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Abstract—A novel artificial receptor based on 2,2′-binaphthalene skeleton bearing two thiourea groups was prepared via nickel(II)-catalyzed homocoupling of the corresponding bromide. The receptor showed high binding ability for F^- and AcO^- in acetonitrile.
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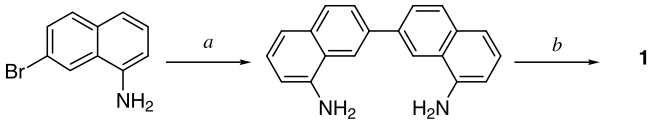
Artificial receptors based on molecular recognition have attracted considerable attention in host–guest chemistry.[1] Recently, considerable attention has focused on the design of anion receptors because of their medicinal and environmental utilities.[2] For construction of anion receptors, it would be crucial to select spacer molecules bearing anion binding sites. Such receptors are also required to display dynamic structural changes through anion binding, in which information of the binding process could be detected, as optical signals, by simple spectroscopic methods. It is known that receptors bearing two thiourea groups at suitable positions bind anions through hydrogen bondings.[3] Although the binding strength and anion selectivity are considered to depend on acidity of H-donors, structure of the spacers, and solvents, it may be difficult to design anion-selective receptors probably because of different shape and size of anions, which are tetrahedral for oxoanions such as $H_2PO_4^-$ and HSO_4^-, planar for AcO^- and NO_3^-, and spherical for halide ions. For example, Umezawa et al. have reported that highly preorganized xanthene derivatives bearing two thiourea groups strongly and selectively bind $H_2PO_4^-$ in DMSO, whereas 1,3-bisthioureidomethylbenzene shows lower anion selectivity in 1,2-dichloroethane.[3d] Hong et al. have reported that 2,2′-(bisthioureidomethyl)biphenyl shows a high selectivity for F^- in $CHCl_3$.[3n] However, indoaniline spacers have been reported to show much smaller selectivities for oxoanions and halide ions in MeCN.[3o]

A skeleton of 2,2′-binaphthalene is expected to strong fluorescence properties rather than biphenyl moiety.[4] However, as far as we know, no receptors based on 2,2′-binaphthalene were reported. These prompted us to examine a 2,2′-binaphthalene derivative directly connected with two thiourea groups at 8- and 8′-positions, since the receptor could provide a convergent binding site on anion binding and the anion-induced changes of absorption and fluorescence spectra due to two naphthyl moieties (Scheme 1). In this letter, we describe the synthesis of 8,8′-di(3-butylthioureido)-2,2′-binaphthalene (**1**) and its binding abilities for various anions in comparison with those of 1-(3-butylthioureido)naphthalene (**2**) in MeCN (Chart 1).

Synthetic route of **1** is illustrated in Scheme 1. 1-Amino-7-bromonaphthalene (**3**) was prepared from bromobenzene in five steps according to the literature.[5] Homocoupling of **3** by a catalytic amount of nickel(II) chloride with a stoichiometric amount of zinc as a reducing metal in the presence of 2,2′-bipyridine and triphenylphosphine in *N*,*N*-dimethylacetamide at 70°C gave 8,8′-diamino-2,2′-binaphthalene (**4**) in 70% yield as yellow crystals.[6] Reaction of **4** with butyl isothio-



3 **4**

Scheme 1. *Reagents and conditions*: (a) Zn, $NiCl_2$ (cat.), bpy, PPh_3, DMAc, 60°C, 70%; (b) BuNCS, EtOH, reflux, 64%.

Keywords: 2,2′-binaphthalene; anion recognition; hydrogen bond; thiourea.

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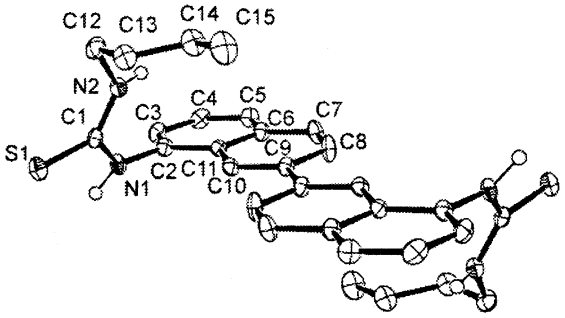


Figure 1. An ORTEP view of the crystal structure of receptor **1** (50% probability ellipsoids). Hydrogen atoms except for NH's are omitted for clarity.

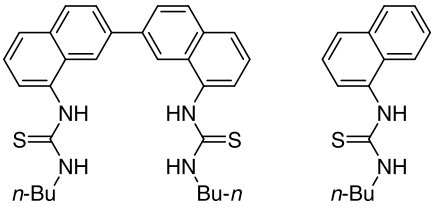


Chart 1.

cyanate in EtOH in reflux gave receptor **1** in 64% yield. The product was characterized by ^{1}H NMR spectroscopy, ESI-MS and elemental analysis.[7] Receptor **2** was also prepared from 1-aminonaphthalene with butyl isothiocyanate in EtOH in 92% yield.[3m] UV–vis spectra of **1** and **2** in MeCN showed λ_{max} at 314.5 nm ($\varepsilon = 1.9\times 10^4$ M^{-1} cm^{-1}) and 292.5 nm ($\varepsilon = 8.7\times 10^3$ M^{-1} cm^{-1}), respectively.

Single crystals of **1** for X-ray crystallographic structure analysis were obtained by recrystallization from MeCN. The result showed that two naphthyl rings are placed in the same plane and two thiourea groups are located in *anti*-position as shown in Figure 1.[8] The thiourea functionalities are *syn–anti* conformation due to formation of intermolecular hydrogen bonds in solid state.

Titration experiments for anion recognition of **1** and **2** were performed by UV–vis spectroscopy in MeCN. As shown in Figure 2, a bathochromic shift was observed passing through isosbestic points at 292.5 and 334.0 nm upon addition of AcO^- (tetra(*n*-butyl)ammonium was used for counter cation) into the solution of **1**. The addition of F^- (isosbestic points at 293 and 333 nm) and $H_2PO_4^-$ (301 and 333 nm) showed similar spectral changes and the addition of Cl^- showed small spectral changes. However, addition of Br^-, I^-, HSO_4^-, and NO_3^- virtually showed no spectral changes. ESI-MS (negative ion mode) of **1** in the presence of 1 equiv. of F^-, AcO^-, and $H_2PO_4^-$ showed peaks corresponding to 1:1 complex in good agreement of the isotope patterns, and no higher order complexes (receptor:guest = 1:2 and so on) were observed. Job's plots of **1** and guests (F^-, AcO^-, and $H_2PO_4^-$) in MeCN showed maxima at a mole fraction of 0.5 in each cases. These results indicate

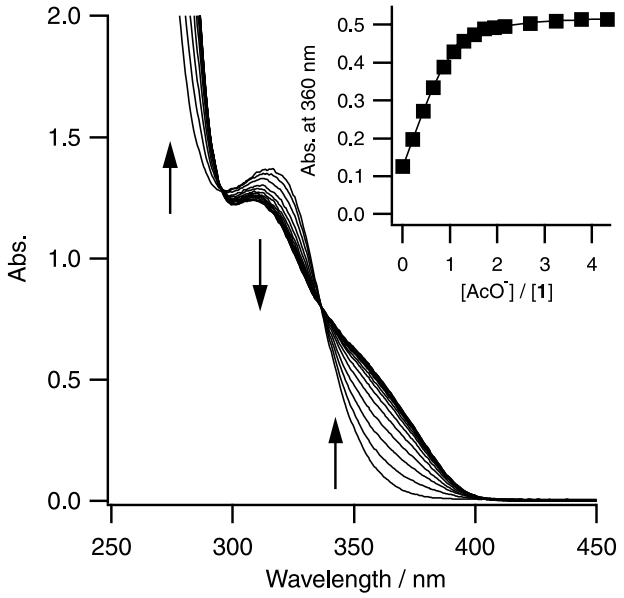


Figure 2. UV–vis spectral titration of **1** with AcO^- in MeCN at 298 K. [**1**] = 6.67×10^{-5} mol dm^{-3}. [AcO^-] = 0–2.88×10^{-4} mol dm^{-3}. Inset: Change of absorbance of **1** at 360 nm upon addition of AcO^-.

that host **1** binds anionic guests for 1:1 ratio. Binding constants of **1** and **2** for anionic species were calculated by non-linear curve fitting of UV–vis titrations and the results are summarized in Table 1. Binding constants of **1** for F^-, AcO^-, $H_2PO_4^-$, and Cl^- were larger than those of **2**, indicating that two thiourea groups of **1** act as cooperative binding sites. Unfortunately, ^{1}H NMR titration was not able to be performed due to low solubility of **1** in MeCN-d_3.

Fluorescence titrations of **1** excited at 333 nm were also performed in MeCN and typical spectral changes are shown in Figure 3. Upon addition of AcO^- into the solution of **1**, the emission at 459 nm was decreased and a weak broad emission at around 650 nm was increased. Similar spectra were observed upon addition of F^- and $H_2PO_4^-$. Binding constants were calculated by non-linear curve fitting of I/I_0 at 650 nm, giving 1.2×10^5, 1.4×10^6, and 1.5×10^4 dm^3 mol^{-1} for AcO^-, F^-,

Table 1. Binding constants of **1** and **2** for various anions

Anion	K_a/dm^3 mol^{-1} ($-\Delta G$/kJ mol^{-1})[a]	
	1	**2**
AcO^-	1.1×10^5 (29)	3.7×10^3 (20)
$H_2PO_4^-$	5.5×10^4 (27)	2.4×10^3 (19)
HSO_4^-	$<10^2$[b]	$<10^2$[b]
NO_3^-	$<10^2$[b]	$<10^2$[b]
F^-	2.1×10^6 (36)	7.7×10^3 (22)
Cl^-	1.1×10^4 (23)	6.4×10^2 (16)
Br^-	$<10^2$[b]	$<10^2$[b]
I^-	$<10^2$[b]	$<10^2$[b]

[a] Measured by UV–vis spectroscopy in MeCN at 298 K. The errors in the binding constants were at less than 10%.
[b] No spectral change was observed.

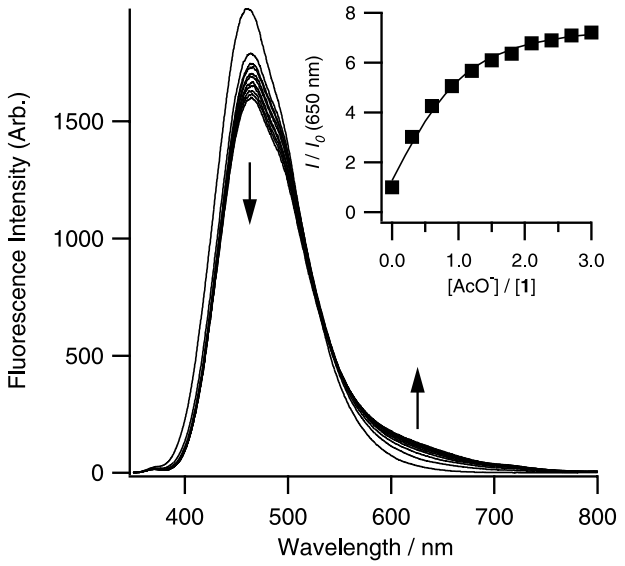
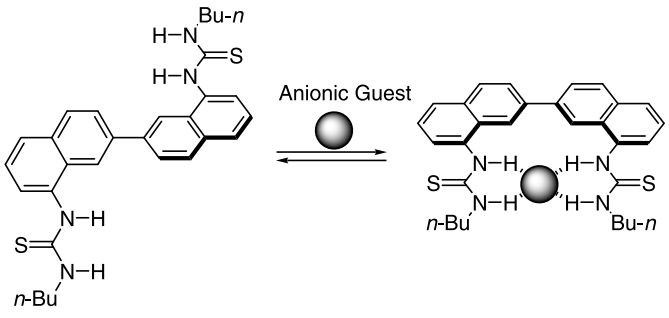


Figure 3. Fluorescence titration of **1** with AcO^- in MeCN excited at 333 nm at 298 K. [**1**] = 3.33×10^{-5} mol dm^{-3}. [AcO^-] = 0–1.00×10^{-4} mol dm^{-3}. Inset: Change of I/I_0 of **1** at 650 nm upon addition of AcO^-.

and $H_2PO_4^-$, respectively, which are in fairly good agreement with those calculated from UV–vis titrations (Table 1). In the case of **2**, decrease of the emission at 410 nm (λ_{ex} = 308 nm) was only observed and no emission at longer wavelength was observed upon addition of AcO^- into the solution of **2**. In solution state, two naphthyl rings of **1** are freely rotatable, however, the complexation with a guest anion by two thiourea groups of **1** restricted the rotation to form the more planar conformer as illustrated in Scheme 2. The emission at the longer wavelength is explained by the planar structure of the complex.

As can be seen in Table 1, the anion binding abilities of **1** and **2** are in the order of F^->AcO^->$H_2PO_4^-$>Cl^-, whereas a high F^- selectivity for 2,2′-(bisthioureidomethyl)biphenyl,[3n] and $H_2PO_4^-$>AcO^->Cl^- for 1,3-bisthioureidomethylbenzene system.[3d] This suggests that the spacer units are responsible for anion-selectivity. To clarify the factors which control the selectivity, further experimental efforts on the spacer molecules may be necessary.



Scheme 2.

The present study demonstrated that 2,2′-binaphthalene bearing two thiourea groups strongly binds anionic species, such as F^- and AcO^- in MeCN and the binding constants are simply determined by UV–vis spectroscopy. We believe that the 2,2′-binaphthyl scaffold is quite useful for construction of various types of receptors by introducing functional groups at 8- and 8′-positions. Further studies on this line are in progress.

Acknowledgements

We acknowledge Professor Hideyuki Matsumoto and Professor Masafumi Unno at Gunma University for valuable discussions and technical supports of X-ray crystal analysis. This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

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4. The skeleton of 2,2′-binaphthalene is found in natural products such as gossypol (1,1′,6,6′,7,7′-hexahydroxy-3,3′-dimethyl-5,5′-bis(1-methylethyl)[2,2′-binaphthalene]-8,8′-di-

carboxaldehyde) which is a natural toxin present in the cotton (*Gossypium* sp.) seed. See: Adams, R.; Geissman, T. A.; Edwards, J. D. *Chem. Rev.* **1960**, *60*, 555.

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7. Selected data for **1**: Mp 198–199°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (t, 6H, $J=7.3$ Hz), 1.17 (sex, 4H, $J=7.3$ Hz), 1.43 (quit, 4H, $J=7.3$ Hz), 3.56 (q, 4H, $J=7.3$ Hz), 5.77 (bs, 2H), 7.50 (d, 2H, $J=7.6$ Hz), 7.56 (t, 2H, $J=7.6$ Hz), 7.92 (dd, 2H, $J_1=8.5$ Hz, $J_2=1.8$ Hz), 7.93 (d, 2H, $J=7.6$ Hz), 7.99 (d, 2H, $J=8.5$ Hz), 8.02 (bs, 2H), 8.25 (s, 2H). Anal. calcd for $C_{30}H_{34}N_4S_2$: C, 70.00; H, 6.66; N, 10.88. Found C, 70.08; H, 6.69; N, 10.76. ESI-MS (negative ion mode) calcd for $C_{30}H_{34}N_4S_2$-H^+: m/z 513.2; found: 513.3.
8. Crystal data for **1**: $C_{30}H_{34}N_4S_2$, $M=514.75$, triclinic, space group P-1, $a=5.5969(8)$, $b=9.6783(13)$, $c=13.1903(13)$ Å, $\alpha=72.868(10)$, $\beta=78.45(2)$, $\gamma=89.34(2)°$, $V=668.1(2)$ Å^3, $Z=1$, $\rho_{calcd}=1.279$ g/cm^3, $T=113$ K. Reflections measured: 5258, unique data: 3394. The structure was refined on F^2 to $R_1=0.065$, $wR_2=0.150$ (2796 reflections) and GOF = 0.98 for 172 parameters. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 217176. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].