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Specific naked eye sensing of cyanide by chromogenic host: studies on the effect of solvents

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ABSTRACT

We have synthesized receptor **1**, which showed high selectivity toward CN^- over other competitive anions in protic solvents. In addition, it distinguished CN^- from other anions by color changes. Furthermore, its detection limit is far below the WHO guidelines of drinking water. However, in aprotic solvents such as acetonitrile, the unique selectivity for CN^- disappeared, and the nonselective color change was observed for strongly basic anions such as F^-, AcO^-, and $H_2PO_4^-$. These results suggest that receptor **1** interacts with cyanide with different mechanisms depending on solvents. The interaction mechanisms between **1** and cyanide in protic and aprotic solvents were investigated.

There have been considerable efforts to develop efficient artificial receptors for anion recognition and sensing as anions play a major role in biological, medical, environmental, and chemical sciences.[1] In recent years, artificial receptors specific for cyanide have been of particular interest[2] due to the extreme toxicity of cyanide in physiological systems[3] and environment.[4] Despite its toxicity, cyanide is still widely used in gold mining, electroplating, polymer production such as nitriles, nylon, and acrylic plastics.[5] Among various cyanide sensing strategies, optical sensors which allow selective naked eye detection of cyanide are attractive. Cyanide anion receptors based on hydrogen bonding usually showed limitations such as poor selectivity over fluoride or acetate.[6] In addition, many of them are reported to work only in aprotic organic media. Therefore the search for effective cyanide sensing systems in aqueous environments or protic solvents is still a great challenge. For the recognition of cyanide in aqueous or protic solvents, many researchers adopted a chemodosimetric approach. This reaction based recognition takes advantage of the good nucleophilicity of the cyanide ion.[7] It is well known that the cyanide anion is a strong nucleophilic reagent, and the nucleophilic attack to the carbon atom of an electron-deficient carbonyl group can achieve naked eye detection of the cyanide anion in protic solvents. With these considerations in mind, we introduce an effective colorimetric sensor **1**, which utilizes a nitrophenyl group as a chromophore and a thiourea group as an electrophile.

Preparation of receptor **1** is depicted in Scheme 1. Reaction of 4-nitrophenyl isothiocyanate with bis(2-pyridylmethyl)amine in dichloromethane afforded **1** in 85% yields. **1** was characterized by ^{1}H NMR, elemental analysis, and LRMS. The structure of **1** was further confirmed by single crystal X-ray diffraction and is shown in Figure 1.

The chromogenic sensing ability of **1** was studied first in ethanol in the presence of seven different anions such as CN^-, F^-, Cl^-, Br^-, I^-, CH_3COO^-, $H_2PO_4^-$. Figure 2a shows that only the addition of CN^- induced distinct spectral changes while other anions such as F^-, Cl^-, Br^-, I^-, CH_3COO^-, $H_2PO_4^-$ did not induce any spectral changes. In addition, the solution color changed from colorless to yellow only with cyanide (Fig. 2b). Cyanide has a strong thiocarbonyl carbon affinity, which results in the addition reaction of CN^- to the thiocarbonyl carbon. Subsequent proton transfer of thiourea hydrogen to the developing alkylsulfide anion of **1** produces an anionic state of **1**, which enhances the charge-transfer interactions between the electron-rich and electron-deficient moieties resulting in a visible color change (Scheme 2).

Titration of receptor **1** with cyanide in ethanol was performed for the quantitative study. In pure ethanol, receptor **1** displayed a

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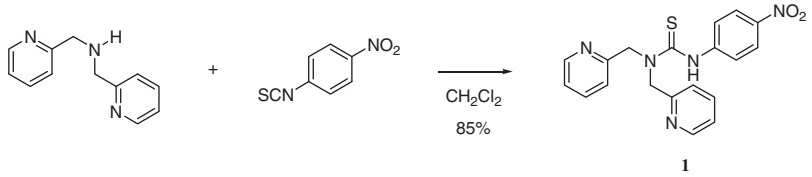


Scheme 1. The synthetic procedure for receptor **1**.

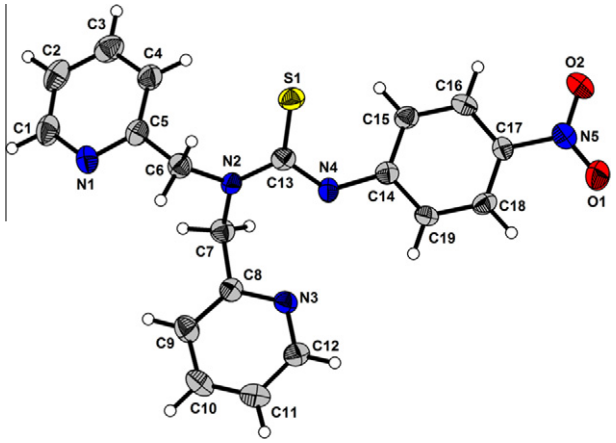


Figure 1. Crystal structure of **1** along with the atom labeling. Displacement ellipsoids are shown at the 50% probability level.

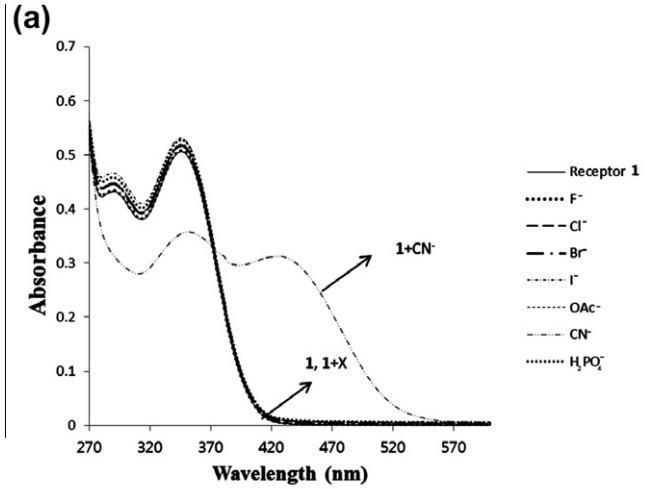


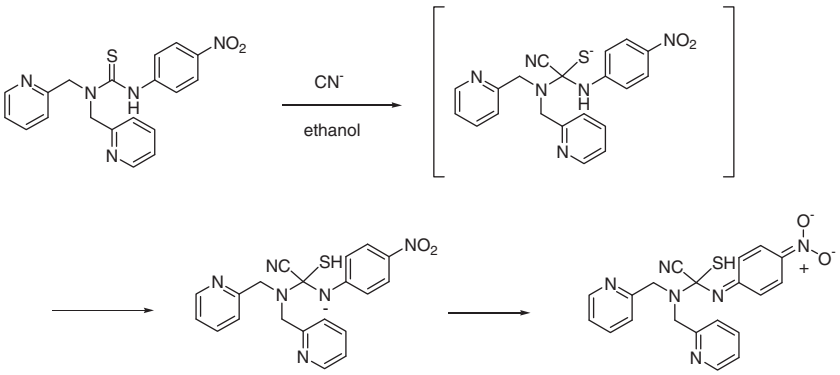
Figure 2. UV–vis spectra of **1** (40 μM) upon the addition of various anions (5 equiv) in ethanol (a) and color changes of solution of **1** in the presence of various anions (50 equiv) in ethanol (b).

strong absorption band at 337 nm, which is caused by the combination of a nitrophenyl group and a thiourea group. Figure 3 shows the family of spectra obtained over the course of the titration of solution **1** with tetraethylammonium cyanide in ethanol. As cyanide ions were added to the 40 μM solution of **1**, the intensity of the absorption peak at 337 nm gradually decreased, while the intensity of the peak at 424 nm began to increase until it reached a limiting value. The presence of the sharp isosbestic point at 376 nm indicates that only two species were present at equilibrium over the course of the titration experiment. By plotting the changes of **1** in the absorbance at 424 nm as a function of CN^- concentration, a sigmoidal curve was obtained and is shown in the inset of Figure 3. To corroborate the 1:1 ratio between **1** and CN^-, Job's plot analysis was executed. The measured absorbance variation at 424 nm ($A = A_{abs} - A_i$) reaches to a maximum when the molar fraction of ($[\mathbf{1}]/[CN^-] + [\mathbf{1}]$) is 0.5, confirming the 1:1 stoichiometry (Fig. 4). A Benesi–Hildebrand plot by the use of change at 424 nm in UV–vis spectrum gave the association constant of 2.5 (±0.2) × 10^3 M^{-1}.

Colorimetric and absorption detection limits of **1** for CN^- ion were tested. A plot of ($A - A_0$) versus the cyanide concentration in ethanol solution gave a linear relationship (Fig. 5). The detection limit calculated on the basis of $3\sigma/K$[8] is 0.19 μM. This value is far below the WHO guidelines of drinking water (1.9 μM),[9] which makes receptor **1** a powerful tool for the detection of the cyanide ion.

We also investigated the interaction mechanism between the receptor **1** and cyanide in aprotic solvents to compare with interaction mechanism in protic solvents. Figure 6 shows the family of spectra obtained over the course of the titration of solution **1** with tetraethylammonium cyanide in acetonitrile. As cyanide ions were added to the 40 μM solution of **1**, λ_{max} of **1** moved from 343 to 434 nm and the spectra showed the clear isosbestic point at 370 nm. The presence of the sharp isosbestic point also indicates that only two species were present at equilibrium over the course of the titration experiment. Other basic anions such as F^-, AcO^-, and $H_2PO_4^-$ showed almost the same phenomena. These results indicate that only direct deprotonation occurs with basic anions in acetonitrile. Therefore, in acetonitrile, the selectivity for CN^- is rather poor as basic anions such as F^-, AcO^-, and $H_2PO_4^-$ were detected by a simple deprotonation mechanism (Fig. 7a). All of these basic anions showed color change in acetonitrile while only CN^- showed color change in protic solvents such as ethanol (Fig. 7b).

The interaction between **1** and cyanide was further studied through ^1H NMR in CD_3OD. Upon the addition of the CN^- to the receptor **1**, most of the aromatic peaks were shifted upfield except H_5 and H_6 (Fig. 8). Especially, pronounced upfield shifts were observed for H_1 and H_2. These large upfield shifts could be explained from the proposed sensing mechanism shown in Scheme 2. After the addition reaction of CN^- to thiocarbonyl carbon and subsequent proton transfer of thiourea hydrogen, alkylsulfide anion formed. Then, delocalization of the electron to the nitroaromatic ring increased the electron density in the aromatic ring, which results in large upfield shifts of H_1 and H_2. The formation of a cyanide adduct was further confirmed by mass spectroscopy. The electrospray ionization mass spectrum of the cyanide adduct showed a



Scheme 2. The proposed sensing mechanism of **1** for cyanide in ethanol.

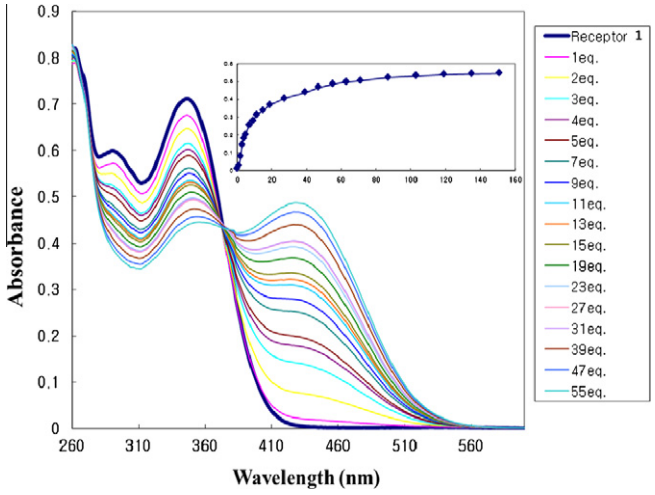


Figure 3. Family of UV–vis spectra recorded over the course of titration of 40 μM ethanol solution of the receptor **1** with tetraethylammonium cyanide.

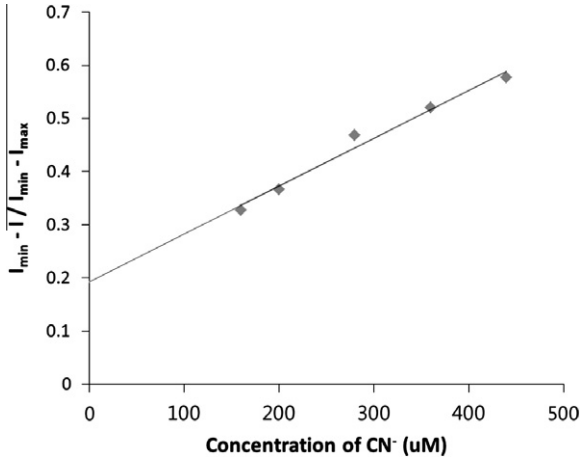


Figure 5. Absorption intensity of **1** versus CN^- concentrations [1] = 40 μM.

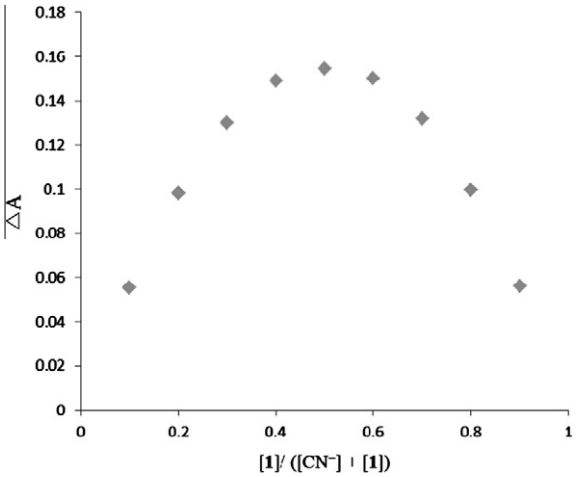


Figure 4. Job plots of receptor **1** and cyanide in ethanol.

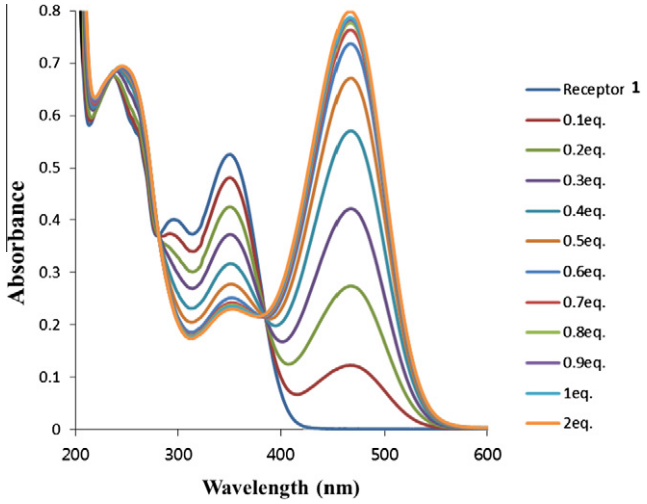


Figure 6. Family of UV–vis spectra recorded over the course of titration of 40 μM acetonitrile solution of the receptor **1** with tetraethylammonium cyanide.

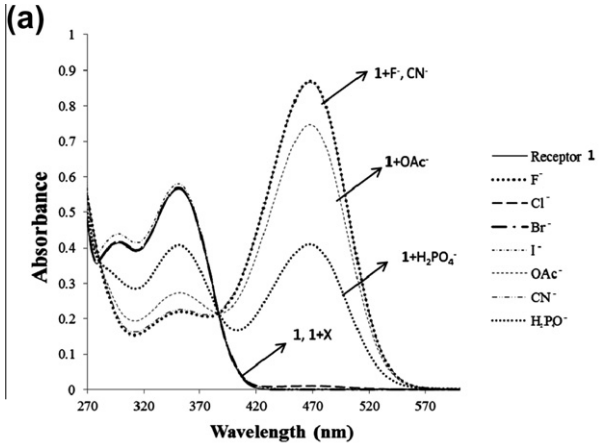


Figure 7. UV–vis spectra of **1** (40 μM) upon the addition of various anions (5 equiv) in acetonitrile (a) and color changes of solution of **1** in the presence of various anions (50 equiv) in acetonitrile (b).

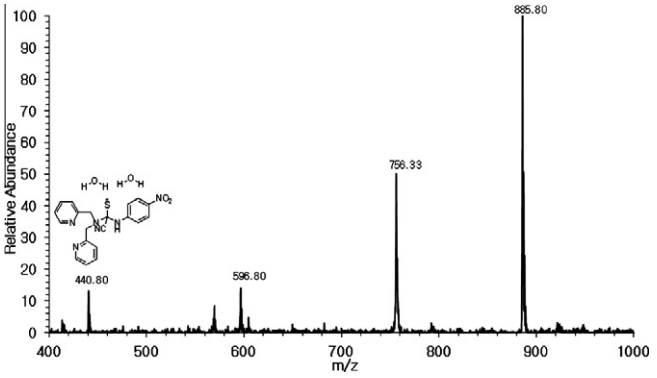


Figure 9. ESI-mass spectrum of **1** (0.1 mM) upon the addition of tetraethylammonium cyanide (0.1 mM) in ethanol.

molecular mass of 440.80, which corresponds to the formula of [**1** + CN + $2H_2O$] (Fig. 9). However, ^{1}H NMR titration experiments carried out in CD_3CN showed different interaction mechanisms. Upon the addition of 0.5 equiv of the CN^- to the receptor **1**, the N–H peak appearing at 12.36 ppm disappeared completely, which indicates immediate deprotonation of the NH in the aprotic solvent. In addition, pronounced upfield shifts of the aromatic protons H_1 and H_2 were observed again as in the case of CD_3OD (Fig. 10). These upfield shifts also resulted from the delocalization of electrons to the nitroaromatic ring. However, the interaction mechanism in CD_3CN is somewhat different from the interaction mechanism in CD_3OD. The delocalized electron comes from the direct deprotonation from urea N–H (Scheme 3). These different interaction mechanisms depending on the type of solvent were in accord with results of UV–vis titration and colorimetric experiments.

In conclusion, we have synthesized a new receptor **1**, which showed high selectivity toward the CN^- ion over other competitive anions in protic solvents such as ethanol. In addition, it distinguished CN^- from other anions by color changes. Furthermore, its detection limit is far below the WHO guidelines of drinking water. However, in aprotic solvents such as acetonitrile, poor selectivity for cyanide was observed due to unselective deprotonation by strongly basic anions. These results suggest that receptor **1** interacts with cyanide with different mechanisms depending on the solvents. While direct deprotonation occurred in acetonitrile, the nucleophilic attack of CN^- to the thioncarbonyl group occurred first in protic solvents such as ethanol and methanol. It is known that the nucleophilicity of the chemical species is solvent-dependent. The protic solvents decrease the anion's nucleophilicity by hydrogen bonding to the nucleophile. Anions such as F^-, AcO^-, and $H_2PO_4^-$ interact with protic solvents through hydrogen-bonding leading to a large decrease in their nucleophilicity. However, CN^- has weaker hydrogen-bonding ability and stronger nucleophilicity toward the carbonyl group. Therefore, the colorimetric sensor **1** allows a selective detection of very low CN^- concentration by the naked eye in protic solvents.

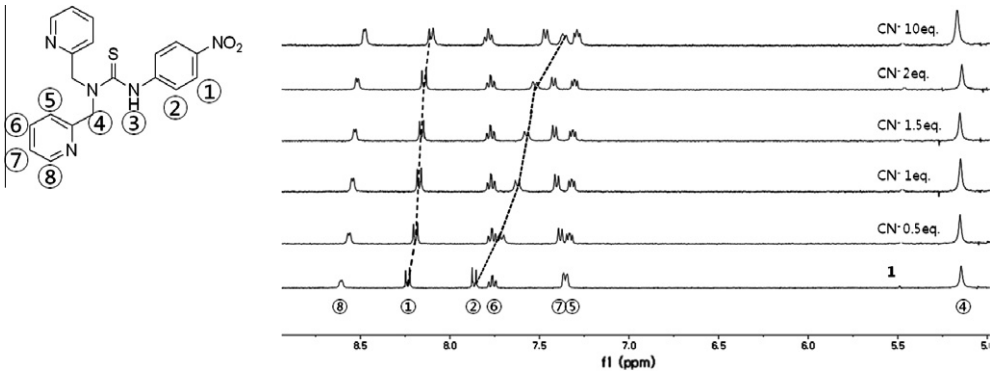


Figure 8. ^{1}H NMR spectra of 2 mM of **1** upon successive addition of tetraethylammonium cyanide in CD_3OD. The shifts of H_1 and H_2 peaks are designated by dotted lines.

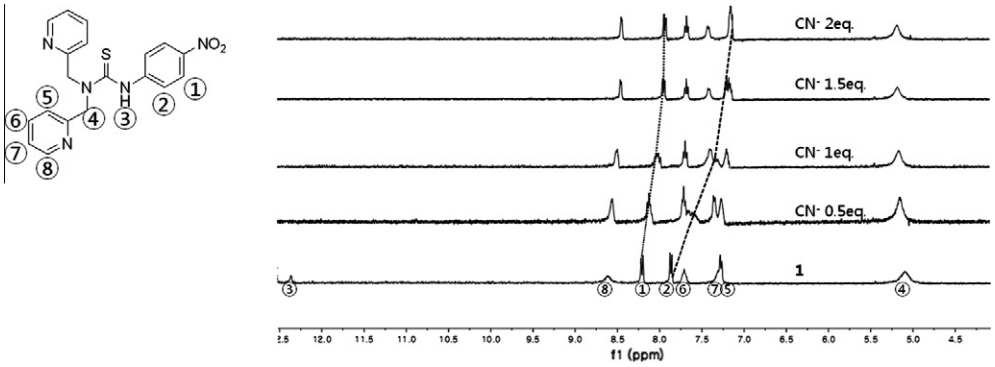
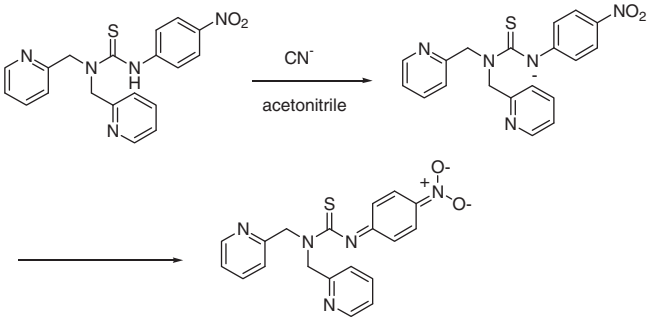


Figure 10. ^{1}H NMR spectra of 2 mM of **1** upon successive addition of tetraethylammonium cyanide in CD_3CN. The shifts of H_1 and H_2 peaks are designated by dotted lines.



Scheme 3. The proposed sensing mechanism of **1** for cyanide in acetonitrile.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.12.053.

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