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Selective Colorimetric Sensing of Anions in Aqueous Media through Reversible Covalent Bonding

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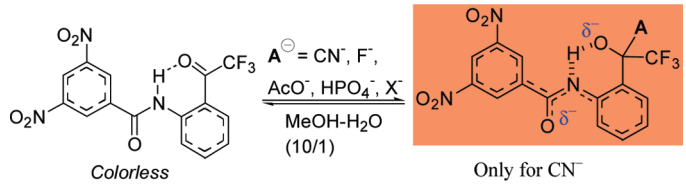


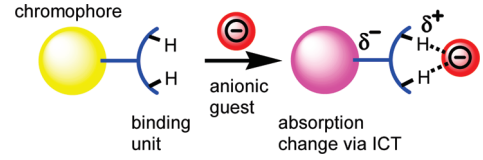
Selective colorimetric sensing of anions in aqueous media has been studied, which involves reversible covalent bonding as key binding interactions. By introducing a simple nitro chromophore into an *o*-(carboxamido)trifluoroacetophenone ionophore that recognizes anions through reversible covalent bonding, we have realized a complete selectivity in colorimetric sensing of cyanide among competing anions such as fluoride, acetate, and dihydrogen phosphate in aqueous media. Such selectivity is explained by dominant reversible covalent bonding over hydrogen bonding, which leads to indirect internal charge transfer. The sensing system is readily converted into a polymeric analogue, demonstrating its potential applicability to develop a naked eye detection material for highly toxic cyanide ions.

Introduction

The development of molecular probes for anions has been a subject of intense research interest as anions play important roles in biological systems and also constitute some pollutants in our environment. For example, phosphate anions not only play critical roles in biological processes but also are key pollutants, and cyanide anions are widely used in industrial processes of chemicals but are highly toxic. Therefore, easy and affordable detection methods are in great demand for various situations. In this regard, fluorescent or colorimetric probes are particularly attractive,[1] and especially colorimetric probes are useful for naked eye detection.

Typically, a colorimetric anion probe is constructed by combining a chromophore and an anion binding unit. In many cases, the anion binding unit is primarily composed of H-bond donors.[2] H-bonding interactions between an anion and the H-bond donors in a sensing system can induce internal charge transfer (ICT), which results in a change in the absorption of the chromophore, thus allowing the colorimetric detection (Scheme 1).[3]

SCHEME 1. Schematic Diagram of Anion Sensing by Hydrogen Bonding Interactions



Therefore, such chromogenic probes respond to anionic analytes depending on how much an anion induces ICT through the H-bonding interactions. The degree of ICT is dependent on the chemical nature of the binding unit that provides the H-bonding interactions toward anions. Also, the degree of ICT is influenced by the nature of analyte itself, that is, the anion's H-bonding ability and/or basicity. Therefore, the colorimetric probes that provide H-bonding interactions as the primary molecular interactions in general respond in preference to anions having strong H-bonding ability (F^-, AcO^-, $H_2PO_4^-$, etc.) or strong basicity (CN^-) but less efficiently toward weakly

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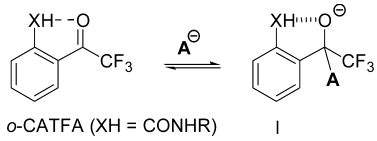
SCHEME 2. Schematic Diagram of Anion Binding with *o*-CATFA



H-bonding or weakly basic anions (Cl^-, Br^-, I^-, ClO_4^-, HSO_4^-, etc.).[3a,b] Since H-bonding interactions have been widely used as the primary molecular interactions in molecular recognition and sensing studies, it is not surprising to find that many anion probes reported so far show great selectivity for F^-, which has significant basicity as well as the strongest H-bonding ability.[4] Such a trend is inevitable with molecular probes based on H-bonding donors. Therefore, a new discipline in probe design through which we can alter such a general trend is in great demand.

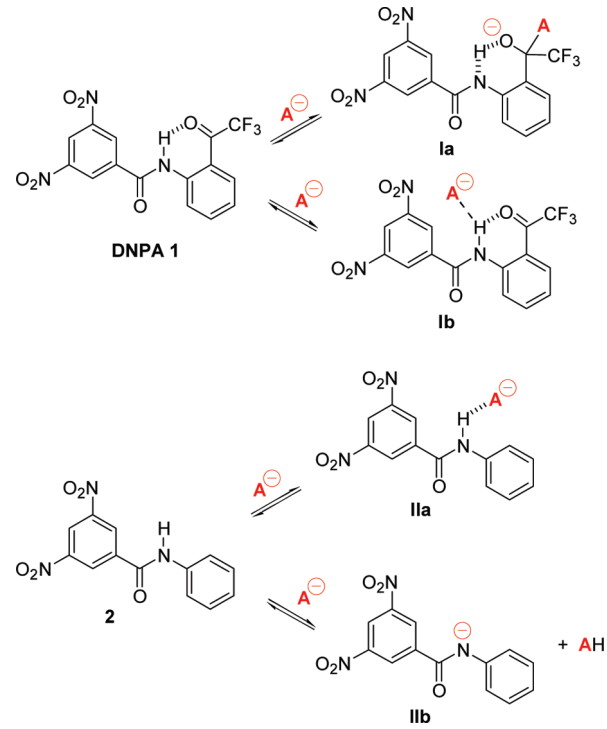
Herein, we disclose a new approach toward this goal. Our approach is to use organic molecular probes that interact with analytes through reversible covalent bonding, rather than H-bonding, as the primary molecular interaction. By this approach, the above-mentioned selectivity trend in chromogenic anion sensing is altered and thus selective sensing of a cyanide anion in aqueous media is demonstrated.

Results and Discussion

Recently we developed a novel anion recognition motif based on trifluoroacetophenone that recognizes anions through reversible covalent bonding rather than H-bonding.[5] The new anion recognition motif contains an H-bond donor (−XH) at the ortho position of trifluoroacetophenone ionophore, which stabilizes anion−ionophore adducts through intramolecular H-bonding (Scheme 2). When a carboxamide group (−NHCOR) was introduced as the H-bonding group, the association constant for an acetate anion increased more than 100 times compared to the case where such an H-bond donor was absent. The increase in association constant was explained by enhanced "charged" H-bonding in the anionic adduct. On the basis of this intramolecular H-bond stabilization approach, we have developed several anion receptors and fluorescent probes.[6]

As a further exploration of the novel binding motif for the development of colorimetric probes, we focused on several distinctive factors the *o*-(carboxamido)trifluoroacetophenone (*o*-CATFA) system provides: (1) the intramolecular H-bonding becomes stronger upon anionic adduct formation because of its charged nature; (2) the XH (−NHCOR′) proton is already involved in the intramolecular H-bonding and thus is less susceptible to "direct" H-bonding by anion analytes; and (3) certain anionic analytes would interact with the H-bond donor

SCHEME 3. Binding Interactions Plausible in the Cases of DNPA 1 and Reference 2



(XH) "indirectly" through adduct formation rather than direct H-bonding interaction. These factors seem to be valuable in altering the general trend of guest selectivity in colorimetric anion sensing through direct H-bonding.

A unique chromogenic probe is thus designed by introducing a simple chromophore such as 3,4-dinitrophenyl to the XH (−NHCOR) group in *o*-CATFA. This new CATFA analogue, DNPA **1** (Scheme 3), would interact with anions by reversible covalent bonding to form adduct **Ia** and less efficiently by direct H-bonding to form species **Ib**. Thus, the degree of ICT upon anion binding is expected to be dependent less on the anion's H-bonding ability but may be dependent on the anion's carbonyl carbon affinity; hence, the usual guest selectivity pattern dependent on the anion's H-bonding ability and/or basicity may be altered. An anion that is a weak H-bonding acceptor but has strong carbonyl carbon affinity is expected to be differentiated from other anions that are strong H-bonding acceptors, particularly in aqueous media, because weak solvation is expected in the former case. It is thus expected that DNPA **1** behaves differently from a simple model compound **2** that has no trifluoroacetyl group, which belongs to typical chromogenic probes that interact with anions mainly through H-bonding.[3a] Anions can interact with dinitrobenzamide **2** in two ways: H-bonding interactions or an acid−base equilibrium involving the amide NH. In both cases, different degrees of ICT dependent on anions would result, leading to absorption and thus color changes. Thus, among commonly tested anions such as F^-, Cl^-, Br^-, I^-, SO_4^{2-}, $H_2PO_4^-$, AcO^-, and CN^-, a strongly H-bonding F^- ($pK_a = 3.15$) or a relatively basic CN^- ($pK_a = 9.2-9.4$) can shift the equilibrium to the right side, forming species **IIa** or **IIb**, respectively, showing the most significant color change, as already observed in the literature.[3a] The color change may be reduced or negligible if the same experiment is carried out in aqueous media, due to the strong hydration.

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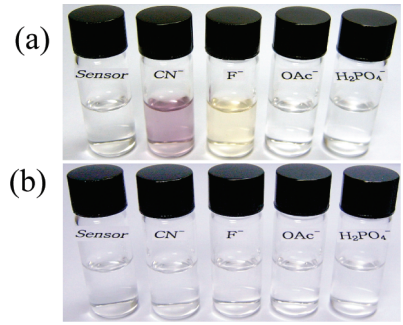


FIGURE 1. Color change of dinitrobenzamide **2** (5.0×10^{-5} M) upon addition of an equimolar amount of each anion (from the left: **2**, CN^-, F^-, AcO^-, and $H_2PO_4^{2-}$) (a) in CH_3CN and (b) in MeOH−water (10:1).

Indeed, when dinitrobenzamide **2** was treated with selected anions such as CN^-, F^-, AcO^-, and $H_2PO_4^{2-}$ in acetonitrile, both cyanide and fluoride anions exhibited color change from colorless to light purple (orchid color) and to light yellow, respectively (Figure 1a). In the cases of AcO^- and $H_2PO_4^-$, a color change resulted when 10 equiv of the anions was added (Figure S1, Supporting Information). However, there was no color change when the organic solvent was changed to aqueous media (Figure 1b), even with 250 equiv of anions (Figure S2, Supporting Information).

In contrast, DNPA **1** is expected to recognize anions mainly through the formation of adduct **Ia**. A direct H-bonding interaction such as in the **Ib** species is less feasible because the amide NH is already involved in the intramolecular H-bonding as discussed above. Therefore, ICT via direct H-bonding is minimal, whereas enhanced intramolecular H-bonding upon adduct formation may lead to indirect ICT and thus a color change. As a result, the anion's carbonyl carbon affinity can be a determining factor for the color change. In fact, when DNPA **1** was treated with CN^- in acetonitrile, two new peaks at λ_{max} = 433 and 533 nm appeared and increased dramatically with apparent color change, from colorless to orange (cinnamon color) (Figure 2). This result can be explained by the addition of cyanide to the trifluoroacetyl carbonyl carbon, because cyanide is a very weak H-bonding acceptor but has a strong affinity toward the carbonyl carbon.[6] Anions such as F^-, AcO^-, and $H_2PO_4^{2-}$ showed diminished absorption change compared to CN^- and showed light orange, and other anions such as HSO_4^-, SCN^-, Cl^-, and Br^- did not show any color change.

An even more striking feature results when the sensing experiment is carried out in aqueous media. Only CN^- shows a color change with DNPA **1** in a mixed solvent system of MeOH−water (10/1), whereas other competing anions such as F^-, AcO^-, and $H_2PO_4^{2-}$ are completely nonresponsive (Figure 3). The result indicates that, in aqueous media, anions with strong or significant H-bonding ability such as F^-, AcO^-, and $H_2PO_4^{2-}$ are stabilized by solvation through H-bonding and thus unable to form the corresponding adduct. Only CN^-, which is a poor H-bond acceptor, can add to DNPA **1** because it has strong affinity toward the carbonyl carbon, of which solution showed a dramatic change in the absorption spectrum and thus a color change from colorless to yellow (cinnamon color). Other anions did not show any color change even though an excess amount (50 equiv) was used (Figure S3, Supporting Information). We also checked whether OH^- species (K^+ salt) would respond to DNPA **1**. When DNPA **1** was treated with OH^- in acetonitrile (under the same conditions described in Figure 2), a color change similar to that of AcO^- was observed; however,

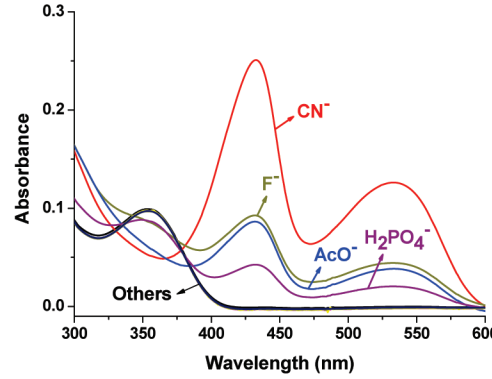
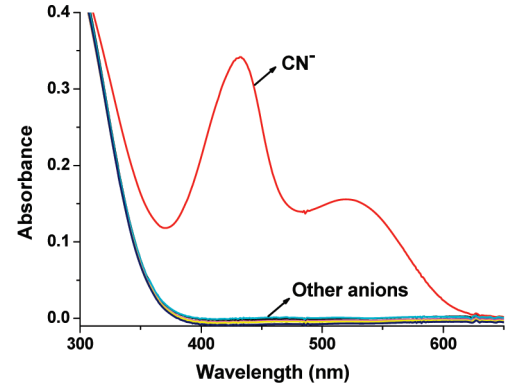


FIGURE 2. UV−vis absorption change of DNPA **1** (2.0×10^{-5} M in CH_3CN) upon addition of 1.0 equiv of the anions and color change of DNPA **1** (5.0×10^{-5} M) in CH_3CN upon addition of an equimolar amount of anions (from the left: **1**, CN^-, F^-, AcO^-, $H_2PO_4^{2-}$, HSO_4^-, SCN^-, Cl^-, Br^-).



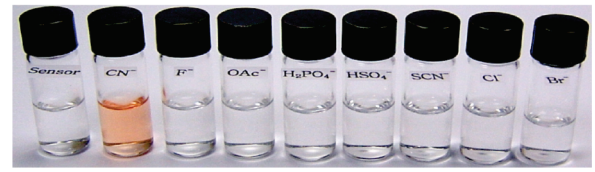


FIGURE 3. UV−vis absorption change of DNPA **1** (5.0×10^{-5} M) upon addition of 2.0 equiv of each anion in MeOH−H_2O (10/1) and color change of probe **1** (1.0×10^{-4} M) upon addition of 2.0 equiv of each anion in MeOH−H_2O (10/1) (from the left: **1**, CN^-, F^-, AcO^-, $H_2PO_4^{2-}$, HSO_4^-, SCN^-, Cl^-, and Br^-).

again there was no color change when the same experiment was carried out in MeOH−H_2O (10/1) (Figure S4, Supporting Information). Thus, a structurally very simple and easy-to-make DNPA **1** constitutes a specific probe for the naked eye detection of CN^- in aqueous media.[7]

The critical role of the intramolecular H-bond stabilization in DNPA **1** is evident from the sensing behavior observed with its para-analogue **3** (Figure 4). A solution of compound **3** in acetonitrile turned yellow (canaria color) upon addition of F^- and AcO^- as well as CN^-, because direct H-bond interactions at the amide NH and/or acid−base equilibria are possible, in addition to the trifluoroacetyl carbonyl addition. In the case of

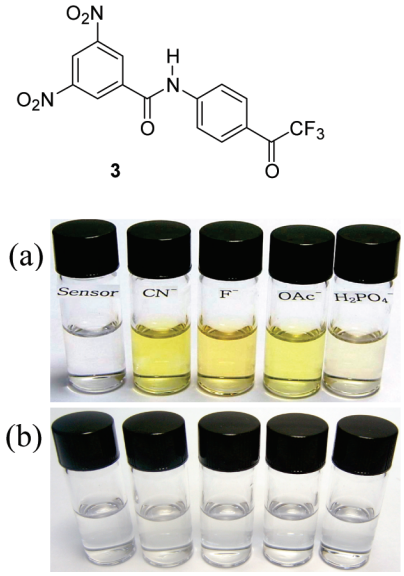


FIGURE 4. Color change of reference compound **3** (5.0×10^{-5} M) upon addition of 0.5 equiv of each anion (from the left: **3**, CN^-, F^-, AcO^-, and $H_2PO_4^{2-}$) (a) in CH_3CN and (b) in MeOH−water (10:1).

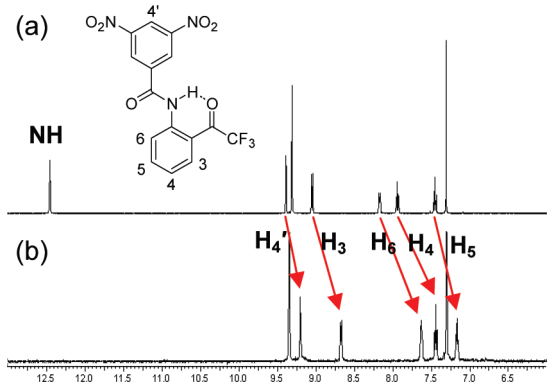


FIGURE 5. ^1H NMR spectra of (a) DNPA **1** and (b) an equimolar mixture of DNPA **1** and CN^- (as Bu_4N^+ salt) in $CDCl_3$ at −40 °C.

$H_2PO_4^-$, similar color change occurred when 10 equiv was added (Figure S5, Supporting Information). However, in aqueous media, compound **3** shows no color change even in the case of CN^-, even though an excess amount was added (250 equiv) (Figure S6, Supporting Information). The results clearly highlight the key feature of our indirect charge transfer approach.

The adduct formation between DNPA **1** and each of the anions can be followed by ^1H NMR spectroscopy. Upon addition of an equimolar amount of CN^- (as Bu_4N^+ salt) to DNPA **1** in CD_3Cl_3, all the aromatic protons of the trifluoroacetophenone moiety and even the aromatic proton between the two nitro groups shifted significantly to the upfield region (Figure 5). When a subequimolar amount of CN^- was added, both peaks from DNPA **1** and its adduct were observed, indicating that the equilibrium of adduct formation is slow compared to the NMR time scale. The upfield shifts can be explained by the diamagnetic shielding caused by increased electron density as the anionic adduct forms. The amide NH peak disappeared as adduct formed, probably buried in the solvent peak.

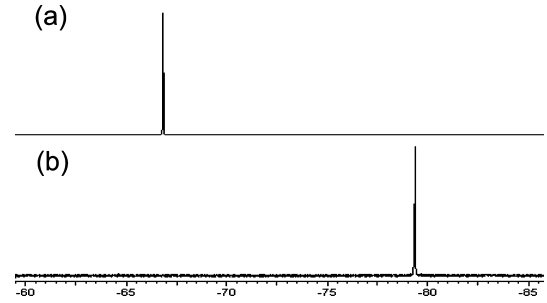


FIGURE 6. ^{19}F NMR spectra of (a) DNPA **1** and (b) an equimolar mixture of DNPA **1** and CN^- (as Bu_4N^+ salt) in $CDCl_3$.

TABLE 1. Thermodynamic Data for the Complexation between DNPA 1 and Selected Anions, Determined by ITC[a]

entry	guest[b]	$\Delta H^{o\,c}$	$-T\Delta S^{o\,c}$	$\Delta G^{o\,c}$	$K_{ass}{}^d$	n^e
1	CN^-	−9.7	1.9	−7.8	3.7×10^5	1.02
2	AcO^-	−15.2	7.4	−7.8	1.5×10^5	1.00
3	$H_2PO_4^-$	−5.7	0.3	−5.4	7.0×10^3	1.27
4	F^-	−3.3	−2.9	−6.2	2.8×10^4	—[f]
		1.3	−6.9	−6.1	1.2×10^4	
		51	−54	−2.9	1.2×10^2	
		−38	381	−3.6	3.5×10^2	

[a] Determined in CH_3CN at 303 K. [b] As Bu_4N^+ salts. [c] In kcal/mol. [d] In M^{-1}. [e] Binding stoichiometry. [f] Sequential binding.

The adduct formation was also clearly observed in the ^{19}F NMR spectra taken in the same solvent for both DNPA **1** and its equimolar mixture with CN^-: The trifluoromethyl peak, appearing as a singlet in both cases, showed a large upfield shift, from −67.2 to −79.8 ppm, as the adduct formed (Figure 6). As expected, the adduct peak intensity decreased in the order of $CN^- > F^- > AcO^- > H_2PO_4^{2-}$, which is in agreement with the data of absorption spectral change depending on the anions.

The formation of the alkoxide adduct was also supported by IR spectroscopy. The NH stretching band in DNPA **1** appearing at 3271 cm^{-1} as a sharp peak changed into a strong and broad peak at 3447 cm^{-1} when 1 equiv of cyanide was added, supporting the enhanced charged H-bonding character as the alkoxide adduct forms.

To obtain thermodynamic parameters for the binding process between DNPA **1** and selected anions, we carried out isothermal titration calorimetry (ITC),[8] the results of which are summarized in Table 1. To a calorimetry cell containing DNPA **1** (0.2 mM, 1.5 mL) at 303 K was injected a solution of each anion (3−10 mM, depending on anions, 5 μL × 40 times) and the resulting heat transfer was measured (Figure 7). The binding isotherms were analyzed by nonlinear least-squares fit to give the thermodynamic data. The data suggest that all the binding processes are governed by major favorable enthalpy change accompanied by minor unfavorable entropy change, conforming to the formation of covalent adducts under the conditions. The association constants of DNPA **1** toward the anions ($H_2PO_4^-$, AcO^-, and CN^-) increased 2−5 times compared with the original (*N*-propionyl)trifluoroacetophenone,[5] which can be attributed to the increased electrophilicity owing to the electron-withdrawing dinitrobenzoyl group. The data clearly show that

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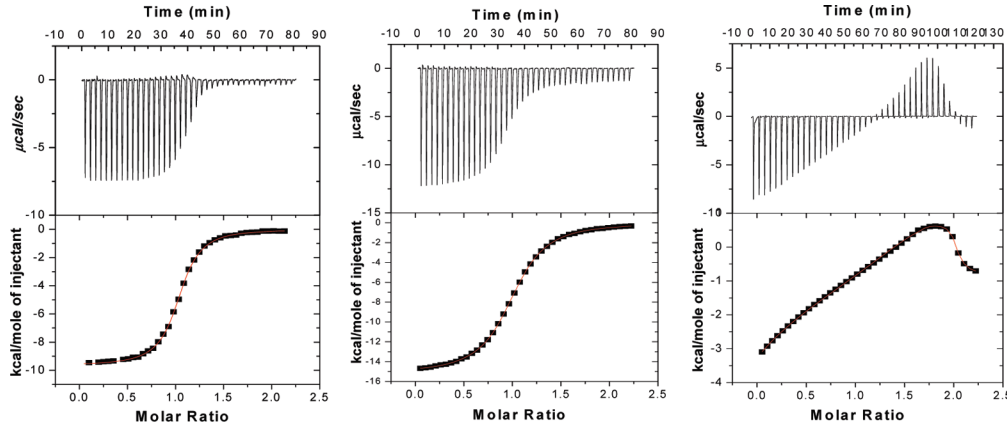

FIGURE 7. Binding isotherms and their integration plots obtained from the ITC titrations of DNPA **1** (0.2 mM, 1.5 mL) in CH_3CN at 303 K: from the left, with (a) CN^-, (b) AcO^-, and (c) F^- (as Bu_4N^+ salts, 3.0 mM, 0.2 mL).

DNPA **1** binds CN^- or AcO^- with a 1:1 stoichiometry, as their *n* values, the binding stoichiometry, are close to unity. This 1:1 binding stoichiometry is also indicative of a predominant binding mode, the carbonyl addition mode in these cases. However, in the case of $H_2PO_4^{2-}$, the *n* value is a little deviated from unity ($n = 1.3$), suggesting that another binding mode, plausibly direct H-bonding, is competing with the adduct formation. Interestingly, in the case of F^-, more complex binding modes are inferred from the titration isotherms: A sequential binding mode best fit the titration isotherms, of which two dominant processes at early stages are similar in their association constants (entry 4, Table 1). The complex binding mode may be explained by evoking the facts that both the direct H-bonding at the amide NH and the carbonyl addition by F^- are possible, and also once initially formed these binary complexes may further interact with additional fluoride to give the corresponding ternary complexes, respectively.

Cyanides are widely used in industrial processes of organic chemicals and polymers such as nitriles, nylon, and acrylic plastics, as well as in the gold-extraction process. However, cyanides are highly toxic and thus should be strictly regulated.[9] The detection of cyanide ions in drinking water by colorimetric, ion-selective electrode, and ion-exchange chromatography methods has been established.[10] However, still there is a need to develop versatile molecular sensing systems for cyanide detection in a variety of settings. To evaluate DNPA **1** as colorimetric probe for CN^-, we carried out UV−vis titrations in MeOH−H_2O (10/1). Upon addition of CN^-, the absorption peaks of DNPA **1** ($\lambda_{max} = 432$ and 520 nm) linearly increased up to the equivalent point (Figure 8). From a plot for the linear region, a detection limit of cyanide by DNPA **1** was estimated to be ~3 μM, a value close to the maximum permissible level for drinking water (0.07 mg/L or 2.7 μM in water) set by the WHO (Figure S7, Supporting Information).[10]

A similar color change was observed when CN^- was added to a solution containing all the other anions such as F^-, AcO^-, $H_2PO_4^-$, HSO_4^-, SCN^-, Cl^-, and Br^- (Figure S8, Supporting Information). Because DNPA **1** was not soluble in sole water even at the low concentration level, we used the mixed solvent system. Furthermore, the colorimetric sensing of CN^- can be carried out for a sample of NaCN in water (~10^{-3} M) if we use a solution of DNPA **1** in CH_2Cl_2 (10^{-4} M) in the presence of a phase transfer catalyst such as $Bu_4N^+Br^-$ (Figure S9, Supporting Information). Thus, DNPA **1** can be used for colorimetric sensing of CN^- present in aqueous samples.

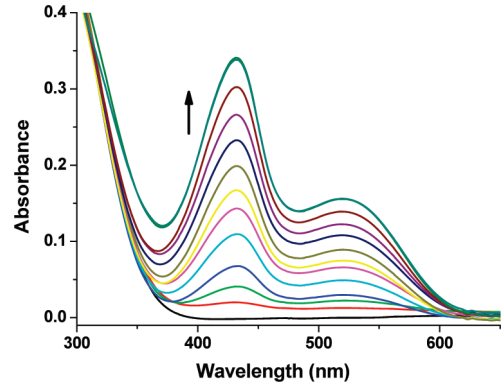

FIGURE 8. UV−vis titration of DNPA **1** (5.0×10^{-5} M) with CN^- (0−3.0 equiv) in MeOH−H_2O (10/1) at 25 °C.

Finally, a water-soluble analogue of DNPA **1** was synthesized and its sensing behavior was evaluated. We introduced a poly(ethyleneglycol) unit to DNPA **1** to give *peg*-DNPA **4**, which is soluble both in usual organic solvents and also in sole water. *peg*-DNPA **4** also showed a significant change in the UV−vis absorption spectra only toward CN^- and very little change toward other anions in a buffered aqueous solution (pH 8.2, Tris buffer) (Figure 9). Accordingly, a solution of *peg*-DNPA **4** (1.0×10^{-4} M) became yellow (egg color) when 30 equiv of CN^- was added, and there was no change for the other anions.

The results demonstrate that the molecular interactions involved in DNPA **1** can also be realized in its polymeric analogue. A further elaboration of DNPA **1** into a heterogeneous sensing material may lead to a useful cyanide probe for specific purposes.

Conclusions

We have disclosed a selective colorimetric sensing of anions in aqueous media through reversible covalent bonding between an ionophore and an anion. By combining a trifluoroacetophenone ionophore and a simple nitro chromophore, we have realized a complete selectivity in colorimetric sensing of cyanide among competing anions such as fluoride, acetate, and dihydrogen phosphate in aqueous media. Such selectivity results

(9) ATSDR 2006. Toxicological Profile for Cyanide: Atlanta, GA; U.S. Department of Health and Human Services.
(10) *Guidelines for Drinking-Water Quality*; The World Health Organization: Geneva, Switzerland, 1996.

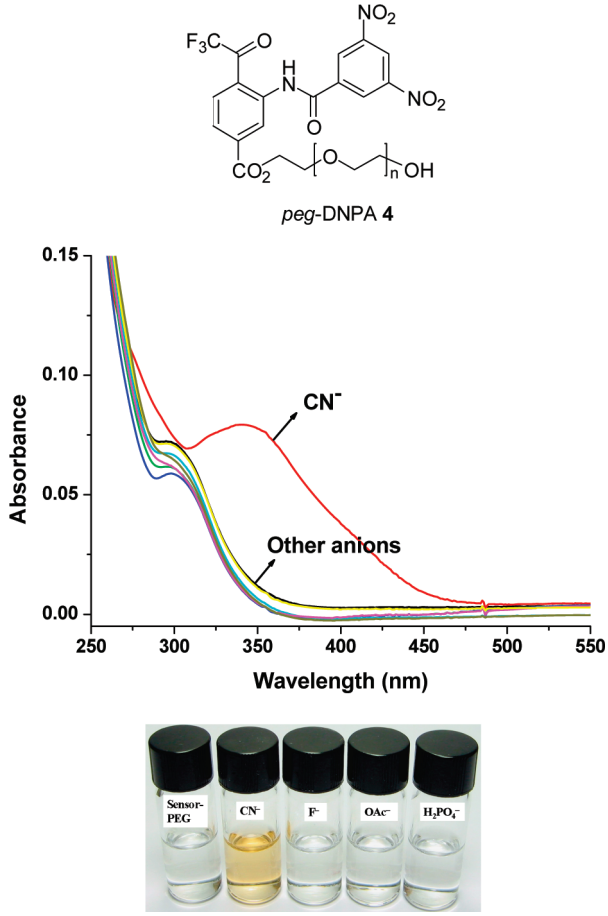

FIGURE 9. Change in the absorption spectra of *peg*-DNPA **4** (1.0×10^{-5} M) upon addition of anions (CN^-, F^-, AcO^-, $H_2PO_4^{2-}$, HSO_4^-, SCN^-, Cl^-, Br^-: 30 equiv) in a buffered solution (pH 8.2, Tris buffer) and color change under the same conditions (*peg*-DNPA **4**, CN^-, F^-, AcO^-, and $H_2PO_4^{2-}$, from the left).

from the unique binding mode of the *o*-(trifluoroacetyl)carboxanilde group toward the anions, which leads to indirect internal charge transfer. The sensing system is converted into a polymeric analogue, demonstrating its potential applicability to develop a naked eye detection material for highly toxic cyanide ions.

Experimental Section

Characterization data for the compounds **1**−**4** are given below. For detailed experimental procedures, see the Supporting Information.

***N*-[2-(2,2,2-Trifluoroacetyl)phenyl]-3,5-dinitrobenzamide (1):** R_f 0.23 (EtOAc/hexane = 1/4); mp 153.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.20 (s, 1H), 9.25 (t, J = 3 Hz, 1H), 9.20 (d, J = 2 Hz, 2H), 8.97 (d, J = 8.5 Hz, 1H), 8.14−8.11 (m, 1H), 7.86 (dt, J = 7.9 and 1.3 Hz, 1H), 7.39 (dt, J = 7.9 and 0.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.48, 185.00, 184.55, 184.07 (q, J = 34.7 Hz, $-COCF_3$), 162.0, 149.7, 143.2, 139.0, 138.5, 133.25, 133.20, 133.14, 133.07 [q, J = 4.79 Hz (coupled with F), an aromatic carbon], 133.1 128.1, 125.0, 122.5, 122.2, 116.6, 122.5, 119.0 115.2, 111.3 [q, J = 292.03 Hz (coupled with F), $-CF_3$]; ^{19}F NMR (300 MHz, $CDCl_3$) δ 7.24; HRMS (FAB) m/z for $C_{15}H_9F_3N_3O_6$ ($M + H^+$) calcd 384.0443, found 384.0443.

3,5-Dinitro(*N*-phenyl)benzamide (2): mp 235.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.23 (t, J = 1.8 Hz, 1H), 9.07 (d, J = 2.1 Hz, 2H), 7.65 (s, 1H), 7.67 (d, J = 8.1 Hz, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.29 (s, 1H); ^{19}F NMR (300 MHz, $CDCl_3$) δ 4.55; HRMS (FAB) m/z for $C_{13}H_{10}N_3O_5$ ($M + H^+$) calcd 288.0620, found 288.0623.

***N*-[4-(2,2,2-Trifluoroacetyl)phenyl]-3,5-dinitrobenzamide (3):** R_f 0.5 (hexane/EtOAc = 7/3); mp 168.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.26 (t, J = 2.0 Hz, 1H), 9.12 (d, J = 2.0 Hz, 2H), 8.56 (s, 1H), 8.17 (d, J = 8.2 Hz, 2H), 7.95−7.92 (m, 2H); ^{19}F NMR (300 MHz, $CDCl_3$) δ 4.55; HRMS (FAB) m/z for $C_{15}H_9F_3N_3O_6$ ($M + H^+$) calcd 384.0443, found 384.0443.

***peg*-DNPA 4.** Poly(ethyleneglycol) of molecular weight of about 1100 was used to couple with the 4-carboxy derivative of *o*-CATFA to give *peg*-DNPA **4** in 20% yield after purification by flash column chromatography (DMF/EtOAc = 6 mL/100 mL). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.30 (d, J = 2.0 Hz, 2H), 9.24 (t, J = 2.0 Hz, 1H), 8.26 (d, J = 1.4 Hz, 1H), 8.20 (dd, J = 8.3, 1.6 Hz, 1H), 87.78 (d, J = 8.0 Hz, 1H), 4.6 (t, J = 4.8 Hz, 2H), 3.88 (t, J = 5.4 Hz, 9H), 3.65 (br s, ~120H).

ITC Experiments: A Typical Procedure. To a solution of DNPA **1** (0.2 mM, 1.5 mL) in CH_3CN taken in the calorimetry cell was added 5 μL of guest solution (3.0 mM in CH_3CN, except for $Bu_4N^+H_2PO_4^-$ in which case 10 mM solution was used) a total of 40 times at 303 K. In all the titrations, dilution effects were corrected, which were done by carrying out separate titration experiments. Thus, the titration result obtained by adding the same guest solution into the cell in the absence of the probe was subtracted from the raw titration data to obtain the final binding curve. The titration data were analyzed by curve-fitting software, which gave thermodynamic values such as the apparent binding affinity K and the standard enthalpy change $\Delta H°$ as well as the binding stoichiometry n.

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Supporting Information Available: Experimental procedures for the synthesis of all the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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