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Bisindole anchored mesoporous silica nanoparticles for cyanide sensing in aqueous media†

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For CN^- recognition, a series of bisindolyl compounds 1–3 were prepared, and their chromodosimetric color changes toward anions were investigated. Nucleophilic addition of the cyanide ion to the *meso* position of the bisindolyl group gave rise to breaking of the double bond conjugation, thereby inducing spectroscopic changes in the compound. Mesoporous silica nanoparticles 3 also gave color changes from deep orange to yellow in response to the cyanide ion.

Anion and cation sensing have received considerable attention because of their important roles in biological, industrial, and environmental processes.[1] Cyanide, known especially for being a detrimental anion, can cause biological and environmental poisoning.[2] The sources of cyanides in water are discharged from metal mining processes, organic chemical industries, iron and steel plants or manufacturers, and wastewater treatment facilities.[3] Other cyanide sources include vehicle exhaust, release from certain chemical industries, burning of municipal waste, and use of cyanide-containing pesticides. When humans are exposed to cyanide, the cyanide anion rapidly binds to enzymes and to other proteins that contain ferric iron, resulting in inactivation and loss of proper function. In particular, cyanide has been also used as a chemical warfare agent, and even as a terror material.[4–6]

In this regard, sensing the cyanide anion through coordination[7] or covalent bonding[8] has received particular interest by chemists. However, most of cyanide anion receptors reported to date have mostly relied on hydrogen-bonding motifs and, as a consequence, have generally displayed moderate selectivity over other anions.[9] To overcome this limitation, reaction based receptors (chemodosimeters) have been developed recently; these include oxazines,[10] cationic borane derivatives,[11] and acridinium salts.[12]

Silica-based nanoparticles are of great interest for biomedical and environmental research applications such as bio-separation, drug targeting, cell isolation, enzyme immobilization, and stability against degradation.[13] It is clear that the receptor-immobilized nanoparticles have some important advantages as solid chemosensors. First, immobilized receptors on inorganic supports can liberate the organic guest molecules (metal ions or anions) from the pollutant solution. Second, the functionalized nanomaterials, combined with a chemodosimeter such as a chromophore, display extremely high selectivity and sensitivity to absorption changes compared to spherical structures because of their larger surface areas and well-defined pores. The homogeneous porosity and large surface area of mesoporous silica make it a promising inorganic support.[14]

Motivated by this approach for a cyanide sensor, we herein report a new Michael type reaction based chromogenic bisindole derivative **1** and its mesoporous silica-immobilized **3** for the purpose of cyanide detection. Numerous bisindolyl derivates have been isolated from various terrestrial and marine natural sources exhibiting important biological activities, which lead chemists to synthesize the bisindole derivatives.[15,16] H atom in the *meso* position of the bisindolyl group was known to be unstable and easily oxidized to give a corresponding conjugated product. We therefore hypothesized that the *meso* position of the bisindolyl group would immediately react with CN^-, which may cause distinct color changes. The dosimeter **1** and its mesoporous silica-immobilized **3** selectively displays drastic changes in UV-vis absorption wavelength for CN^- in H_2O/CH_3CN (7 : 1, v/v).

Scheme 1 indicates a synthetic route to compounds **1–3**. The bisindolyl group at the *para*-position of toluene (**4**) was introduced by the coupling reaction of indole with *p*-tolualdehyde in CH_3OH. Compound **1** was then prepared by treating **4** with DDQ in CH_3CN. Chromogenic **2** was also synthesized by the pathway shown in Scheme 1. In consideration of extending its usefulness, **3** was fabricated by a sol–gel reaction of **2** with mesoporous silica possessing the isocyanate group (**6**). Immobilization of receptor **2** was conducted under reflux conditions for 24 h in toluene to give **3**. In this process, the hydroxyl group of **2** undergoes hydrolysis and is covalently immobilized to the isocyanate group attached onto the surface of mesoporous silica. After cooling to room temperature, the red solid product was filtered, washed with THF, and then dried

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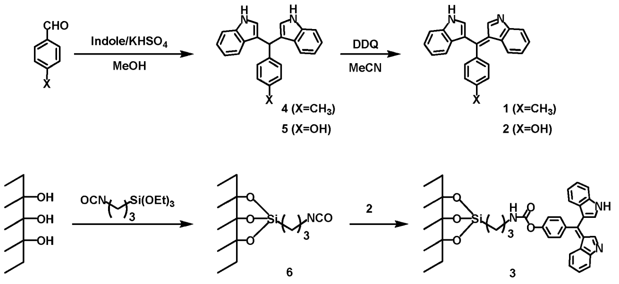


Scheme 1 Synthetic pathways of **1–3**.

overnight. The solid product **3** was characterized by transmission electron microscopy (TEM), FT-IR, BET isotherms, and TOF-SIMS.

Spectral changes of the CH_3CN solution of **1** (2.0×10^{-5} M) in the presence of various anions are shown in Fig. S1 (ESI†). In the presence of 30 equiv. of F^-, CN^-, AcO^- and $H_2PO_4^-$, the absorption band at 422 nm diminished, while a new red-shifted absorption band appeared at 518 nm with concomitant color change from yellow to red. This effect is probably due to the H-bonding between the tested anion and the hydrogen atom of the bisindole. We found that the selectivity of **1** towards specific anions varies with the solvent system. Upon addition of a considerable amount of water, *e.g.* H_2O/CH_3CN (7 : 1, v/v), the absorption band of **1** at 492 nm decreased, but a new band at 450 nm concomitantly appeared upon the addition of CN^- as seen in Fig. 1A. Other anions (F^-, Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$, and HSO_4^- as their tetrabutylammonium salts) did not cause significant absorption changes of **1** under the identical condition (Fig. 1B). Selectivity changes of **1** towards the CN^- reaction can be explained by the hydration energy of the corresponding anions in an aqueous environment. In H_2O/CH_3CN (7 : 1, v/v) solution, a very high solvation energy of F^- ($\Delta H_{hyd} = -505$ kJ mol^{-1}), Cl^- ($\Delta H_{hyd} = -363$ kJ mol^{-1}), Br^- ($\Delta H_{hyd} = -336$ kJ mol^{-1}), I^- ($\Delta H_{hyd} = -295$ kJ mol^{-1}), HSO_4^- ($\Delta H_{hyd} = -1103$ kJ mol^{-1}), CH_3COO^- ($\Delta H_{hyd} = -375$ kJ mol^{-1}), and $H_2PO_4^-$ ($\Delta H_{hyd} = -260$ kJ mol^{-1}) could account for the very weak/negligible reaction to receptor **1**.[17] On the other hand, the much lower hydration energy of CN^- ($\Delta H_{hyd} = -67$ kJ mol^{-1}) primarily contributed to the product formation (**1**–CN) with high selectivity.

Fig. S2 (ESI†) shows the absorption spectral changes of **1** on the gradual addition of CN^-. The solution displayed a distinct color change from deep orange to yellow simultaneously. The isosbestic points at 414 and 457 nm suggest that the reaction of **1** with CN^- produces a single component. The 1 : 1 reaction is confirmed by FAB-MS (Fig. S3, ESI†); a solution of **1** with CN^- showed a peak at m/z 361.4, assigned to the [**1** + CN^-] ion. The reaction mechanism is depicted in Scheme 2.

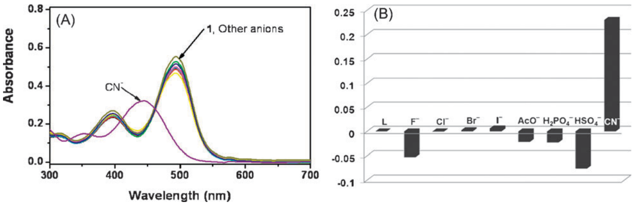


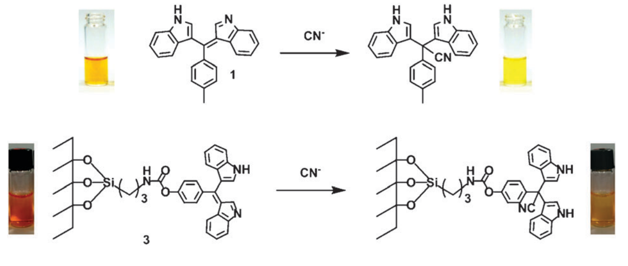
Fig. 1 (A) UV/vis spectra of **1** (20.0 μM) upon addition of various anions (30 equiv.) in H_2O/CH_3CN (7 : 1, v/v). (B) Absorption changes ($A_0 - A$) of **1** upon addition of 30 equiv. of various anions. A_0: absorbance of free **1**. *A:* absorbance of **1**–anion complexes.

We then investigated ^1H NMR and ^{13}C NMR spectra of **1** in the presence of cyanide anions and compared them with that of reactant **1** (Fig. S4, ESI†). When 3 equiv. of cyanide anions were added to a solution of **1**, a new marked carbon peak of the chemodosimetric product of **1** was clearly observed at 44.6 ppm (Fig. S4c, ESI†). We newly found that the C=C bond conjugated to the bisindolyl system is labile to a good nucleophile such as CN^-, similar to a Michael type reaction, to form a C–C single bond. To the best of our knowledge, the bisindolyl group we report has never been previously exploited for this Michael reaction-based anion sensing.[18,19] ^1H NMR, ^{13}C NMR, and FAB-MS analysis upon addition of the cyanide anion clearly indicates that the cyanide reacts with the *meso*-position of the bisindole compound.

Various thiols including cystein have been added to a solution of **1** to see any sensing event for thiols which are known as a good nucleophile for Michael reaction. We then noticed that addition of thiols to a solution of **1** gives rise to similar spectroscopic changes to that of the cyanide ion, but the reaction time is much slower than the case of CN^-.

Among various sensing systems for cyanide, ensemble based demetallization of copper ion by cyanide anion has been utilized, because the cyanide reacts with copper ions to produce stable $[Cu(CN)_x]^{n-}$ species.[20] To address any possibility of the Cu^{2+} interference toward CN^- detection in our chemodosimetric system, we added Cu^{2+} to a solution of **1**–CN^-, and tested their absorption and emission spectral changes. The resulting blue-shifted absorption bands of **1** occurred by addition of CN^- and showed no absorption changes upon addition of Cu^{2+} ions, demonstrating that unlike other chemosensors, **1** undergoes an irreversible chemical reaction with CN^- (Fig. 2A).

The TEM image of **3** revealed the mesopores with a narrow size distribution (*ca.* 4–5 nm) (Fig. 2B). For further proof of the new bond formation, we acquired FT-IR and TOF-SIMS spectra of **3**. From the FT-IR spectrum of **3**, in addition to the bands attributed to the mesoporous silica nanoparticles themselves, new strong bands at 3420, 2900, 2670, 2100, 1700, 1651, 1510, 1480, 1010, 998, 751 and 502 cm^{-1} appeared, which originate from receptor **2**, in accordance with **2** residing on the mesoporous silica nanoparticles (Fig. S6, ESI†). The TOF-SIMS spectrum of the fragment obtained from **3** displayed the characteristic fragment of the bisindole moiety (m/z = 337), also giving us a firm evidence that the bisindole moiety was anchored onto the surface of the mesoporous silica nanoparticles (Fig. S7, ESI†).



Scheme 2 Reaction mechanism of CN^- for **1** and **3**.

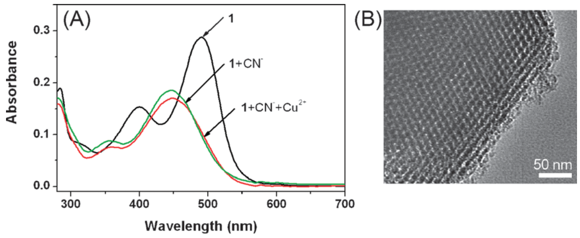


Fig. 2 (A) Absorption spectra of **1** (black), **1** + 3.0 equiv. of CN^- (green) and **1** + 10.0 equiv. of Cu^{2+} + 3.0 equiv. of CN^- (red) in H_2O/CH_3CN (7 : 1, v/v), (B) TEM image of the solid product **3**.

Solid **3** shows some advantages over the parent **2**. Whereas **2** is insoluble in water, solid **3** can be used in aqueous media. The sensing ability of solid **3** was studied in water through assays involving the addition of 30 equivalents (with respect to receptor **2** anchored to solid **3**) of the corresponding guest to water suspensions of the assayed solid. The suspension color of **3** was red in the absence of specific analytes. However, in the presence of CN^-, the suspension of **3** showed a remarkable color change from red to yellow (Fig. 3). In these colorimetric changes, we noticed that the solid **3** reveals a high selectivity for CN^- ions over other anions, showing a similar spectroscopic response to that of **1** obtained in the solution system. The results imply that the solid **3** is considerably applicable to the environmental field as a new organic–inorganic hybrid sensor for the detection of CN^- ions.

As studied in the solution system, we also observed interface effects of the Cu^{2+} ion toward CN^- detection in the solid chemosensor **3**. We added Cu^{2+} to the suspension of the solid **3**–CN^-, and observed their absorption spectral change. The resulting blue-shifted absorption bands of the solid **3** caused by CN^- showed no absorption changes upon addition of Cu^{2+} ions, implicating that solid chemodosimeter **3** proceeds in an irreversible chemical reaction upon addition of CN^-, same as that observed in **1** (Fig. S8, ESI†).

For biological and environmental applications as a colorimetric sensor, the sensing should be effective over a wide pH range. The effect of pH on the solid **3** in the absence of CN^- was examined (Fig. S9a, ESI†). At pH < 5, the absorption intensity is largely decreased, presumably due to protonation of the nitrogen atoms of the bisindoyl group. However, minimal or no significant absorption changes were observed even between pH 6–9. This result clearly demonstrates that the solid **3** can be used in physiological environments where a pH > 5 occurs. Moreover, upon addition of CN^- ions, a blue-shift occurred over the full range of pH 6–9 with the same absorption intensity (Fig. S9b, ESI†), signifying that the solid **3** can be useful as a chemosensor for CN^- at pH > 5.

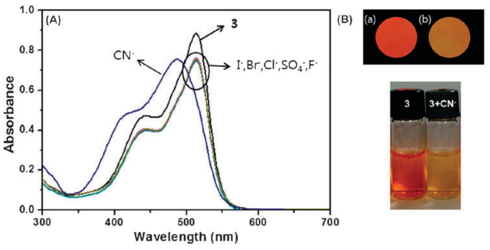


Fig. 3 (A) UV/vis spectra and (B) photograph of the pellet prepared from **3** in the (a) absence and (b) presence of CN^-. (C) Suspension of **3** in the absence and presence of CN^-.

In order to extend the above performance to a portable chemosensor kit, a disk-type pellet has been prepared from the solid **3** (Fig. 3B). The orange color of the disk-type pellet produced from solid **3** was changed to yellow when dipped in CN^- (0.01 M) aqueous solution. On the other hand, no significant changes in absorption were observed in the parallel experiments in the case of F^-, Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$ and HSO_4^- solutions (0.01 M). In addition, the solid absorption spectrum of the disk-type pellet of **3** with CN^- was the same as that obtained from **3** dispersed in aqueous solution. It is notable that the disk-type pellet prepared from solid **3** is applicable as a portable chemosensor for the detection of CN^- in biological and environmental fields. In addition, from the plot of absorbance at 515 nm *versus* increasing quantities of CN^- added to **3** suspension at pH 7, a detection limit of *ca.* 3 μM was determined (Fig. S11, ESI†).

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