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A new calix[4]arene based molecular probe for selective and sensitive detection of CN\(^-\) ion in aqueous medium

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A molecular diagnostic for CN\(^-\) ions in aqueous media promises development of disposable filter paper strips for field applications
A new calix[4]arene based molecular probe for selective and sensitive detection of CN⁻ ion in aqueous medium

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Calix[4]arene based molecular probe,4 has been proposed as a diagnostic for CN⁻ ions in aqueous media. The investigation promises development of disposable filter paper strips for field applications.

In this communication, we report an efficient calix[4]arene based ratiometric and colorimetric probe 4 for CN⁻ in aqueous-acetonitrile (50%, v/v). The investigation promises development of disposable diagnostic strip for cyanide ions. Cyanide plays a significant role in chemical, biochemical, environmental and industrial operations.1,2,3 There is an urgent need for the development of methods for detection and estimation of cyanide in aqueous solutions through change of color or disposable filter paper strip. Published methods for cyanide analysis use Cu-complexes,4 nucleophilic addition reactions, quantum dots,5mesoporous silica,5b BODIPY,5c trifluoro-acetophenone,5d amino carboxylate,5e and imidazole6 derivatives with the detection limit in the range of 0.03 to 260 ppb.5,6 Effective ratiometric color change probes for CN⁻ are rare.5e

Scheme 1 (i) Ethylbromoacetate/K₂CO₃/MeCN/reflux, (ii) HMTA/TFA/reflux, (iii) 2,4-Dinitrophenylhydrazine/ethanol/reflux.

Calix[4]arene 1 was acylated with ethylbromoacetate in the presence of K₂CO₃ to get 2 in 76% yield. Compound 2, when refluxed with hexamethylenetetramine (HMTA) in trifluoroacetic acid (TFA) gave calix[4]arene diesterdialdehyde (3) in 85% yield. On subsequent reaction with 2,4-dinitrophenylhydrazine gave 4 as a light orange colored solid in 88% yield. The characterization of 4 was done by spectral and analytical data (Fig. S1-7).13C NMR spectral analysis (ΔCH₂Ar appear at 31.5 and 34.4 ppm) indicating 4 to be in a non-symmetric cone or partial cone conformation. Gross structure of 4 has been examined earlier for metal ion extraction with poor performance.7a

The ability of 4 to interact with various anions was explored in aqueous-MeCN (50%, v/v) through absorption spectroscopy. Addition of different anions (2μL = 10 equiv, F⁻, Cl⁻, Br⁻, I⁻, SCN⁻, CN⁻, H₂PO₄⁻, HSO₄⁻ and AcO⁻ as their tetrabutylammonium salts) to a solution of 4 led to the disappearance of characteristic intramolecular charge transfer (ICT) band at 407 nm with appearance of a new transition band at ~473 nm on interaction with CN⁻ ions only.

A significant change in color from light orange to red-wine was observed (Figure 1, S9). The other tested anions failed to exhibit any change in the absorption spectra or the color. The high selectivity of 4 for CN⁻ in semi-aqueous medium could be ascribed to low solvation energy for CN⁻ (ΔHlyd = -67 kJ/mol).

Fig. 1 (I) Change in absorption spectra of 4 (10 μM) upon addition of various anions (10 equiv) in aqueous-MeCN (50%, v/v) and (II) Interference studies of 4.

Studies on specific selectivity for CN⁻ over other anions in aqueous-MeCN (50%, v/v) is depicted in Figure 1. The extent of binding efficiency could be evaluated by titration experiments in the UV-Vis region, when isosbestic points at

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363 and 429 nm (Figure 2) were observed. This indicated the presence of more than one species in solution. Association constant was calculated for 1:2 stoichiometry of 4 and CN− which showed a high $K_{assoc}$ of 1.66 x 10^{10} M^{-2} with detection limit of 2.6 ppb (0.1 μM) (Figure S10). This was found to be comparable to the recommended of World Health Organization5 (WHO) on permissible concentration of cyanide in drinking water (1.9 μM, Figure S11). 4 was determined to be insensitive to fluoride and other related basic anions in aqueous-MeCN (50%, v/v) plausibly due to comparatively higher solvation energy of fluoride64, and partial cone conformation of utilized calix[4]arene scaffold. The use of the calix[4]arene framework in 4 increased both the affinity and efficiency as compared to the simple phenolic hydrazone model system (see ESI and Figure S12,13 for details).

Scheme 2 Plausible mechanism of sensing of 4 with CN− ion.

Further insights into the nature of molecule–anion interactions was investigated by 1H NMR titration experiments. 1H NMR spectrum of 4 (1.1 x 10^{-2} M) in DMSO-d6 showed singlets for NH, OH, CH=N at δ 11.59, 8.81, 8.47 ppm which upon addition of CN− (0.5 equiv) led to the broadening of NH resonance. Reduction in the spectrum of -CH=N- resonances (at δ 8.47 ppm) with appearance of a new doublet at δ 8.92 ppm (Figure 3) confirmed the change in structure. On further increase in concentration of CN− (2 equiv), CH=N resonance disappeared and a new signal attributable to $H'$ appeared at δ 4.40 ppm. The resonance signal at δ 8.92 ppm became more prominent. Other aromatic phenyl ring protons shifted upfield as expected. This clearly suggested the enhancement of nucleophilic addition of CN− to the aldimine group (CH=N) to form a new 4-CN− Michael type adduct (Scheme 2). The transfer of $H'$ proton leads to the development of a new doublet for the $NH'$ signal with ultimate formation of a new anionic species in the medium. These observations are in consonance with those given in the scientific literature.1b

Fig. 3 Stacked 1H NMR spectra of 4 (1.1 x 10^{-2} M) upon addition of CN− ions (0.0, 0.5, 2.0 equiv) in DMSO-d6.

The practical utility of 4 was investigated by developing disposable filter paper strip for cyanide detection. Filter paper strips (Whatman filter paper Grade 1) were prepared (0.4 x 2.5 cm^2) by treatment with 4 in chloroform (2 mg/ml) followed by its drying in air.7b The sodium cyanide solution of two different concentrations, 2 μM and 20 μM were prepared in water and examined by the prepared test paper strips when significant color changes were observed (Figure 4). The response time of sensing of 4 with CN− is found to be 20 sec (Figure S16). In addition to fast response, the applicable pH range is also important for practical application. It was observed that 4 can detect cyanide best between pH 5-8 (Figure S17).

In conclusion, a new calix[4]arene based efficient ratiometric and colorimetric probe for CN− in aqueous media has been achieved. The observations promise possible realization of disposable probe for the target anion. The observations also suggest the importance of template geometry for differential sensing of anion through calix[4]arene hydrazone conformers. The key findings entail further investigations.

Experimental

Synthesis of 4
To a solution of 3 (0.07 g, 0.1 mmol) in ethanol (10 ml) containing catalytic amount of acetic acid, 2,4-dinitrophenyl hydrazine (0.04 g, 0.2 mmol) was added and the reaction mixture was refluxed for 3 h. After completion of the reaction (as monitored on TLC), the reaction mixture was allowed to cool to room temperature and filtered, washed with ethanol to obtain light orange colored solid in 88% yield. M.p. 198-200 °C; $R_f$ = 0.52 (EtOAc:Hexane, 2:8, v/v); 1H NMR (DMSO-d6) δ (ppm): 11.59 (s, 2H, NH), 8.90 (s, 2H, DNP), 8.81 (s, 2H, OH), 8.47 (s, 2H, CH=N), 8.31 (d, 2H, J = 9.6 Hz, DNP), 8.12 (s, 2H, J = 9.6 Hz, DNP), 7.58 (s, 4H), 7.19 (s, 4H), 4.89 (s, 4H), 4.53 (d, 4H, J = 12.6 Hz), 3.46 (merge with solvent band), 1.22 (s, 18H), 1.16 (t, 6H, J = 6.9, 6.9 Hz), 13C NMR (DMSO-d6) δ (ppm): 170.6, 159.6, 159.3, 155.3, 146.5, 156.0, 136.5, 128.3, 128.1, 127.9, 127.6, 122.9, 122.1, 119.5, 118.4, 73.4, 65.2, 34.4, 31.5, 27.3, 14.0, FT-IR (κ cm⁻¹) 3278, 2957, 1735, 1618, 1518, 1479, 1422, 1333, 1308, 1271, 1218, 1140, 1080, 832, 742; HR-MS (m/z) band at 1147.3986 for [4+Na]+.

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