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

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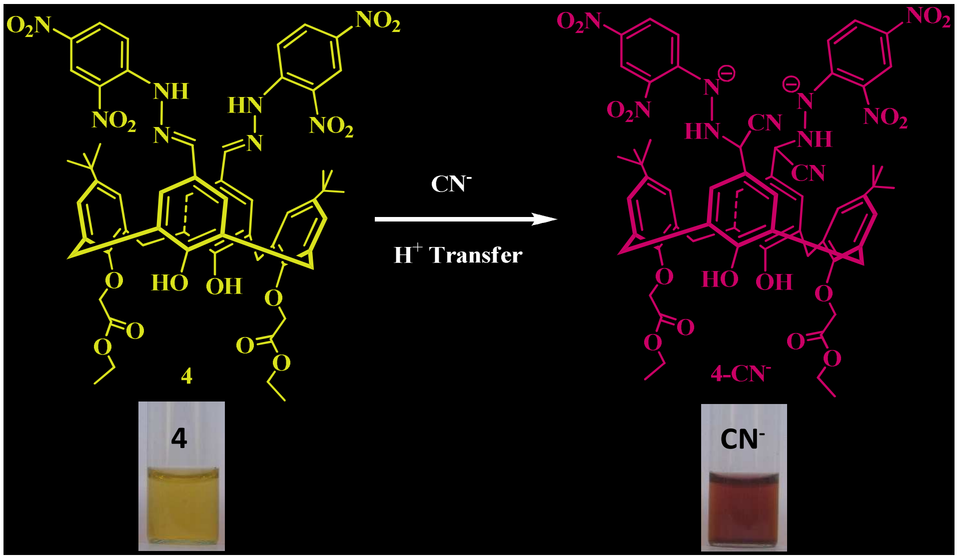

A molecular diagnostic for CN^- ions in aqueous media promises development of disposable filter paper strips for field applications

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Letter

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

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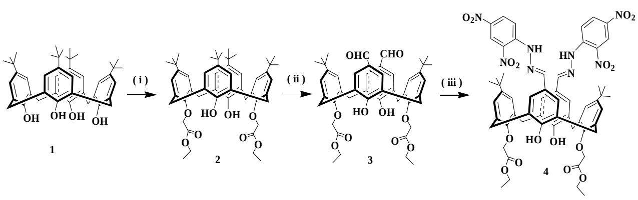
Calix[4]arene based molecular probe,4 has beenproposed as a diagnostic forCN⁻ions in aqueous media.The investigation promises development of disposable filter paperstripsfor field applications.

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 ofa disposablediagnostic strip for cyanide ions.

Cyanide playsa significant role in chemical, biochemical, environmental and industrial operations.[1,2,3]There is an urgent need for development of methods for detection and estimation of cyanide in aqueous solutions through change of color or adisposable filter paper strip. Published methods for cyanide analysisuseCu-complexes,[4]nucleophilic addition reactions,quantum dots,[5a]mesoporous silica,[5b] BODIPY,[5c] trifluoro-acetophenone,[5d] amino carboxylate,[5e] and imidazole[5g] derivatives withthe detection limit in the range of 0.03 to 260 ppb.[5,6] Effective ratiometric color change probes for CN^- are rare.[6e]



Scheme 1 (i) Ethylbromoacetate/K_2CO_3/MeCN/reflux, (ii) HMTA/TFA/reflux, (iii) 2,4-Dinitrophenylhydrazine/ethanol/reflux.

Calix[4]arene **1** was acylated with ethylbromoacetate in the presence of K_2CO_3 to get**2** in 76% yield. Compound **2** when refluxed with hexamethylenetetramine (HMTA) in trifluoroacetic acid (TFA) gavecalix[4]arene diesterdialdehyde (**3**) in 85% yield. **3**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).^{13}C NMR spectral analysis (ArCH_2Ar appear at 31.5 and 34.4 ppm)indicating **4** to be in non symmetric cone or partial cone conformation. Gross structure **4**has been examinedearlier 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^-, $H_2PO_4^-$, HSO_4^- and AcO^-,as their tetrabutylammonium salts) to a solution of **4**,led to the disappearence of characteristic intramolecular charge transfer (ICT) band at 407 nm with appearence of a new transition band at ~473nm on interation with CN^- ions only.

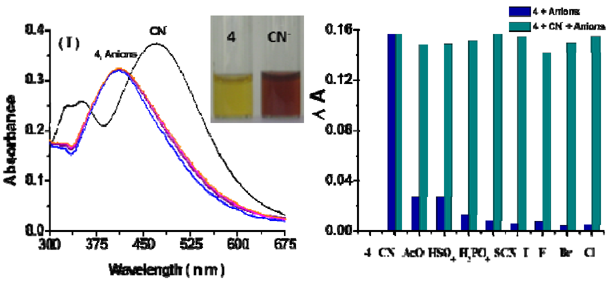


Fig. 1 (I) Change in absorption spectra of **4** (10 μM) upon addition of various anions (10 equiv) in aqueous-MeCN (50%, v/v) and (II) Interference studies of **4**.

A significant change in color from light orange to red-wine was observed (Figure1, S9). The other tested anions failed to exhibit any change in the absorption spectraor the color. The high selectivity of **4**for CN^- in semi-aqueous medium could be ascribed to low solvation energy for CN^- (ΔHhyd = -67 kJ/mol).

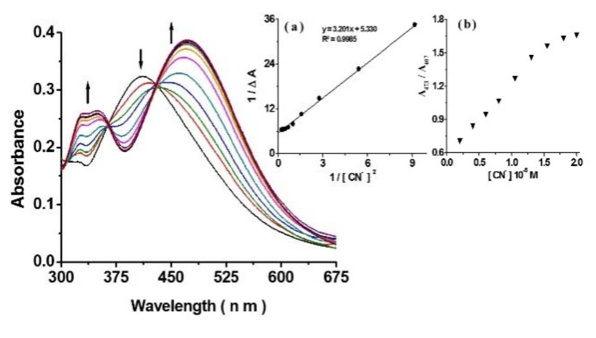
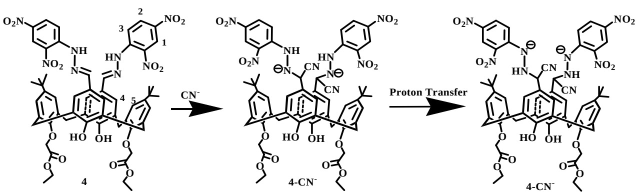


Fig. 2 Absorption titration spectra of **4** (10 μM) upon addition of CN^- ions (0 – 2 equiv) in aqueous-MeCN (50%, v/v). Inset: (a) B-H plot of **4** for CN^- and (b) ratiometric calibration curve, A_{473} / A_{407} as a function of CN^- ion concentration (0–20 μM).

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

363 and 429 nm (Figure 2)were observed. Thisindicated 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 detction limit of 2.6 ppb (0.1 µM) (Figure S10). This was found to be comparable to the recommendation of World Health Organization[8] (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 comparativelyhigher solvation energy of fluoride[6d,f]andpartial cone conformation of utilizedcalix[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 ^{1}H NMR titration experiments. ^{1}H NMR spectrum of **4** (1.1 x 10^{-2} M) in DMSO-d_6 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 enhancementof nucleophilic additionof CN^- to the aldimine group (*CH=N*) to form a new **4**-CN^- Michael type adduct (Scheme 2). The trasfer of *NH* proton leads to the development of a new doublet for the *NH'* signalwithultimate formation of a new anionic species in the medium.These observations are in consonance with those given in the scientific literature.[1b]

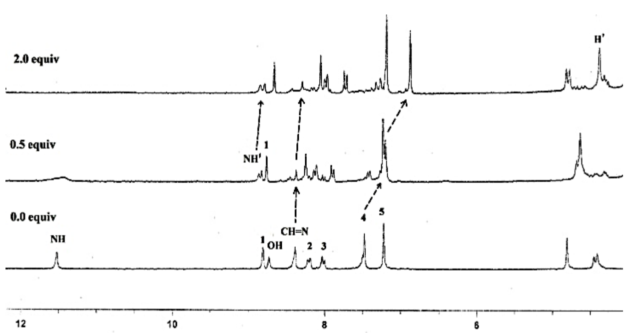


Fig. 3 Stacked ^{1}H NMR spectra of **4** (1.1 x 10^{-2} M) upon addition of CN^- ions (0.0, 0.5, 2.0 equiv) in DMSO-d_6.

The practical utility of **4** was investigated by developingadisposablefilter 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) folllowed by its drying in air.[7b] The sodium cyanide solution of two different concentrations, 2 µMand 20 µM were prepared in water and examined by the prepared test paper strips when significant color changes were observed(Figure4). The response time of sensing of **4** with CN^- is found to be 20 sec (Figure S16).[7c]In addition to fast response, the applicable pH range is also important for practical appplication. It was observed that **4** can detect cyanide best between pH 5-8 (Figure S17).

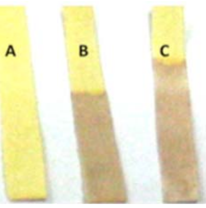


Fig.4 Changes in the color of test paper strip for detection of CN^- ion.(A) **4** without CN^- ion; (B) **4** + CN^- (2µM) and (C)**4** + CN^-(20 µM) in aqueous solution.

In conclusion, anew calix[4]arene based efficient ratiometric and colorimetricprobeforCN^-in aqueous media**4**has been achieved.The observations promise possible realization of disposable sensor strips for the target anion. The observations also sugggest the importance of template geometry fordifferential sensing of anionsthrough calix[4]arene hydrazone conformers. The key findingsentail 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 obtained light orange colored solid in 88% yield. M.p. 198-200 °C; R_f= 0.52 (EtOAc:Hexane, 2:8, v/v); ^{1}H NMR (DMSO-d_6) 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); ^{13}C NMR (DMSO-d_6) δ (ppm): 170.6, 159.6, 159.3, 155.3, 146.5, 136.0, 136.5, 128.5, 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 (υ 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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