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An Indolium Ion Functionalized Naphthalimide Chemodosimeter for Detection of Cyanide in Aqueous Medium

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Abstract

A naphthalimide platform based indolium ion functionalized colorimetric as well as fluorometric chemodosimeter (**L**) has been synthesized and characterized. This can selectively sense cyanide (CN⁻) in aqueous medium with a low limit of detection (approximately 0.5 μ M), which is around four times lower than the value of 1.9 μ M set by WHO. The UV-vis and PL studies have been carried out in 40% aqueous-acetonitrile medium which shows a significant change in the visible region allowing naked eye colorimetric detection of CN⁻. The mass spectrometry and ¹H-NMR spectroscopy are used to characterize the corresponding cyanide adduct which has also been corroborated by time-dependent density functional theory (TD-DFT) during the establishment of the sensing mechanism.

Keywords: Chemodosimeter, Cyanide sensor, Aqueous media, Colorimetric, Fluorometric, NMR titration, DFT.

1. Introduction

Cyanide is one of the most toxic species to the living systems. It occurs naturally in some of the common foods such as peach, cassava, almond and apricot [1]. It is also released artificially from several industrial sources such as plastic industries, gold mining, etc. [2]. The adverse physiological effect [3] of cyanide is based upon its strong and irreversible binding with metal ions originating from its strong π -acidity [4]. When cyanide enters in biological systems, it binds with mitochondrial cytochrome c oxidase and inhibits the respiratory chain resulting in rapid suffocation death [5]. Cyanide contamination also affects the central nervous system [6]. Hence detection of cyanide in an aqueous environment is of prime importance. Although various analytical techniques are being practically utilized to detect and quantify cyanide [7] however, simple organic molecule-based [8-16] chemosensors are found to be the most convenient and popular method to detect such ion presently. Metal ions, mainly Cu²⁺ based sensors have been utilized for the detection of cyanide due to the strong binding affinity of Cu⁺/Cu²⁺ with cyanide [17-18]. Imidazole complexed with Cu^{2+} appended from polyacetylene backbones can trigger fluorescence response on interaction with cyanide [19]. Again, mimicking vitamin B12 as a reliable platform for sensing cyanide in millimolar as well as micromolar concentrations in water can be achieved through the binding of cyanide with Co^{3+} [20]. Sensing of cyanide over the gold surface is also known [21]. The more environmental friendly metal zinc based ditopic receptors where Zn^{2+} -porphyrin complex is coupled with a crown or aza-crown ethers are used for binding with NaCN or KCN [22]. So far we have a glimpse of metal-based chemosensors for cyanide where co-ordination of cyanide with metal ions attributes the sensing process. There are examples in the literature where a chemical reaction forming a covalent bond between the chemosensors and cyanide is the key phenomenon which triggers the sensing mechanism [23].

Boronic acid [24], borane [25, 26], coumarin [27-29], BODIPY [30, 31], naphthalimide [25, 32], calix[4]pyrrole [33] platform based sensors have been used more conveniently for sensing cyanide considering the very good nucleophilicity of cyanide [34]. Based on the well-established fact that cyanide forms cyanohydrins on reaction with carbonyl functional groups (>C=O), several chemodosimeters are known [35, 36]. Few polymeric sensors for cyanide have also been reported, mainly containing pyrylium cation, fluorene and borane functionalities [33, 37-41]. Further, indolium ion functionalized chemodosimeters have also been explored earlier where cyanide adds to the activated [>C=N<]⁺ bond [31, 42, 43]. Detection of cyanide produced from various cyanogenic glycosides [44] due to enzymatic hydrolysis has also been accomplished by indolium moiety [42]. Herein, we report a new chemodosimeter L (Scheme 1) based on long chain incorporated naphthalimide platform functionalized with an indolium ion to detect CN⁻ over other anions such as F', Cl⁻, Br⁻, Γ, NO₂⁻, NO₃⁻, ClO₄⁻, H₂PO₄⁻, HSO₄⁻ and OAc⁻ in the aqueous medium.



Scheme 1. Synthetic route for L: (a) Br_2 , KOH; (b) 3-Amino-1-propanol, ethanol, 70°C, 2h; (c) 4-Formylphenylboronic acid, $Pd(PPh_3)_2Cl_2$, Cs_2CO_3 , 80°C, 6h; (d) 1,2,3,3-tetramethyl-3H-indolium iodide, piperidine, ethanol, 70°C, 4h.

2. Experimental

1.1. Materials and instrumentation

Most of the chemicals were bought from Sigma-Aldrich Co. and were used without further purification. Other chemicals were supplied by Spectrochem, India. HPLC grade acetonitrile and double distilled water were used for absorption and emission studies. Whereas, acetonitrile- d_3 , CDCl₃, and D₂O were used as were available in Sigma-Aldrich Co.

HRMS analyses were performed with a QToF-Micro YA 263 mass spectrometer where ESI (+ve) as well as (-ve) modes were used. ¹H and ¹³C-NMR experiments were carried out using an FT-NMR Bruker DPX 300 MHz NMR spectrometer. Chemical shifts for ¹H and ¹³C-NMR were reported in parts per million (ppm), calibrated to the residual solvent peak set. The absorption and emission studies were performed with a PerkinElmer Lambda 900 UV–vis–NIR spectrometer (NIR = near-infrared) (with a quartz cuvette of path length 1 cm) and a FluoroMax-3 spectrophotometer from Horiba Jobin Yvon, respectively. Solution electronic spectra (single/time-dependent) were measured on an Agilent 8454 diode array spectrophotometer.

The following equation was used to analyze the time-resolved emission decays:

$$P(t) = B + \sum_{i} \alpha_i e^{-t/\tau_i}$$

P(t) is decay, i is the number of discrete emissive species, B is the baseline correction, α_i is the pre-exponential factor, and τ_i is the excited state lifetime associated with the ith component. In the case of multi-exponential decays the following equation was used to calculate an average lifetime:

$$\langle au
angle = \sum_i lpha_i au_i$$

where ai is the contribution of the ith decay component, and $a_i = \alpha_i / \Sigma \alpha_i$.

A diffractive size crystal was collected from the mother liquor, dipped in paratone oil and using epoxy resin it was cemented on the tip of a glass fiber. The intensity data of the crystals were collected using Mo K α ($\lambda = 0.7107$ Å) radiation on a Bruker SMART APEX diffractometer, equipped with a CCD area detector at 100 K. CCDC 1863558 contains the supplementary crystallographic data for this paper.

1.2. Synthesis

Synthesis of 3. Compound 1 and 2 were synthesized following previously reported procedure [45, 46]. For synthesis of 3 compound 2 (388 mg, 1 mmol) was taken in a 100 ml two neck round-bottomed flask along with 4-formylphenylboronic acid (180 mg, 1.2 mmol), caesium carbonate (1.3 g, 4 mmol) in degassed DMF/Water (2:1, v/v) mixture. Bis(triphenylphosphine)palladium(II) dichloride (30 mg, 0.04 mmol) was added to the heterogeneous mixture under inert condition. The whole system was allowed to be heated at 80°C for 6 hours. After the completion of the reaction the crude product was extracted with ethyl acetate, the organic layer was dried over anhydrous Na₂SO₄ and concentrated in rotary evaporator. Pure compound was isolated through column chromatography (using 230-400 mesh silica) using 2.2% EtOAc-Hexane as eluent. Yield: 250 mg (60%). ESI-MS: m/z calculated for [M]⁺ 413.1991, found 413.9969 (Fig. S3); ¹H-NMR (300 MHz, $\overline{CDCl_3}$): δ (ppm) = 0.84 (t, 3H, J=6 Hz), 1.24-1.40 (m, 10H), 1.66-1.76 (m, 2H), 4.12 (t, 2H, J=7.5 Hz), 7.66–7.72 (m, 4H, Ar-H), 8.05 (d, 2H, J=9 Hz, Ar-H), 8.14 (d, 1H, J=9 Hz, Ar-H), 8.58–8.63 (m, 2H, Ar-H), 10.12 (s, 1H) (Fig. S1). ¹³C-NMR (75 MHz, $CDCl_3$): δ (ppm) = 14.1, 22.6, 27.2, 28.1, 29.2, 29.3, 31.8, 40.6, 122.6, 123.1, 127.3,

127.8, 128.6, 129.7, 130.0, 130.6, 130.6, 131.3, 131.9, 136.1, 144.9, 145.1, 163.8, 164.0, 191.6 (Fig. S2).

Synthesis of L. Compound 3 (250 mg, 0.6 mmol), 1,2,3,3-tetramethyl-3H-indolium iodide (192 mg, 0.63 mmol) were taken in a 100 ml round-bottomed flask. 10 ml of dry ethanol was added to the mixture under N_2 atmosphere. Then 10 μ L of piperidine was added to it. The whole suspension was heated at 70°C for 4 hours. The suspension became solubilised under heating condition. Upon slow cooling L got precipitated from the solution. The solid was filtered, washed with cold ethanol and dried in vacuum to get the pure compound. Yield: 230 mg (55%). ESI-MS: m/z calculated for $[L-I]^+$ 569.3163 found 569.4860 (Fig. S6); Elemental analysis for C39H41IN2O2: found: C, 67.24; H, 5.93; N, 4.02. Calculated: C, 67.37; H, 5.98; N, 4.15; ¹H-NMR (300 MHz, ACN-*d*₃): δ (ppm) = 0.88 (t, 3H, J=7.5 Hz), 1.30-1.39 (m, 10H), 1.72 (m, 2H), 1.85 (s, 6H), 4.11-4.15 (m, 5H), 7.58 (d, 1H, J=15 Hz), 7.65–7.84 (m, 8H, Ar-H), 8.21 (d, 2H, J=9 Hz, Ar-H), 8.29 (d, 1H J=9 Hz, Ar-H), 8.38 (d, 1H, J=15 Hz), 8.59-8.63 (m, 2H, Ar-H) (Fig. S4); ¹³C-NMR (75 MHz, ACN- d_3): δ (ppm) = 13.3, 22.3, 24.9, 26.8, 27.7, 28.9, 29.0, 31.5, 34.8, 40.1, 52.8, 113.5, 115.1, 122.6, 122.8, 123.2, 127.5, 128.1, 128.5, 129.3, 129.5, 130.1, 130.1, 130.3, 130.8, 131.0, 131.9, 134.2, 141.8, 143.6, 144.9, 152.6, 163.7, 163.9, 182.6 (Fig. S5).

3. Results and discussion

Designing aspect: Our basic idea is to exploit the facile nucleophilic addition of cyanide into an activated double bond of indolium moiety which can reduce the extent of conjugation in the chemodosimeter **L**. Thus the produced output signal can be monitored spectroscopically, as well as, through visual color change. A long chain alkyl (octyl)

group has been strategically incorporated to make the molecule more lipophilic, so that the molecule might be suitable for interaction/sensing studies, even in biological systems/membrane. On the other hand, the polarity of the indolium ion functionality can be utilized to enhance its aqueous solubility.

The synthetic approach for **L** is outlined in **Scheme 1.** Thus **L** can be synthesized through some steps in reasonably good yield (55%). **L** has been well characterized by spectroscopic as well as spectrometric methods (Fig. S4-S7). When **L** was subjected to ESI-MS (+ve) in acetonitrile (ACN) a peak at m/z = 569.4860 appeared corresponding to the monocationic species, $[\mathbf{L}-\mathbf{I}]^+$ of the ligand (Fig. S6). The experimental isotopic distribution pattern of the mass of the ligand matches quite well with the simulated pattern and indicates the presence of the mono charged species of **L** (Fig. S7). Various spectroscopic and colorimetric studies with different anions as their tetrabutylammonium salts have been performed to establish the selectivity and sensitivity of **L** in acetonitrile/aqueous-acetonitrile binary solution.

Detection of Cyanide via Colorimetric, UV-vis, and PhotoLuminescence (PL) methods:

The anion sensing ability of **L** was tested by Colorimetric, UV–vis and PL spectroscopy acetonitrile or 40% aqueous-acetonitrile at room temperature. Firstly, the chemodosimetric property of **L** towards cyanide over other anions was examined colorimetrically through visual colour change by adding 1.0 eqv. of each of the anion solutions (F^{-} , Cl^{-} , Br^{-} , Γ , CN^{-} , NO_{2}^{-} , NO_{3}^{-} , ClO_{4}^{-} , $H_{2}PO_{4}^{-}$, HSO_{4}^{-} and OAc^{-} as their tetrabutylammonium salts) into a solution of **L** in acetonitrile or 40% aqueous-acetonitrile (Fig. 1). Addition of cyanide (TBACN) solution triggers the visual color change of **L**

from yellow to colorless, whereas, in the presence of other anions no appreciable visual change is observed. Such color change can be employed to distinguish cyanide from other anions by the naked eye.



Fig. 1. Naked eye color changes upon addition of 1.0 eqv. of all anions as their TBA salts to **L** (40 μ M) in 40% H₂O/ACN binary solvent mixture; The numbers in the inset indicate different anions; color code: 1: F⁻, 2: Cl⁻, 3: Br⁻, 4: I⁻, 5: CN⁻, 6: NO₂⁻, 7: NO₃⁻, 8: ClO₄⁻, 9: H₂PO₄⁻, 10: HSO₄⁻, 11: OAc⁻.

Spectroscopic proof for cyanide sensing property of **L** was studied by absorption spectroscopic measurements. In the UV-vis channel, the absorption spectrum of **L** in ACN exhibits maximum at about 400 nm which undergoes significant absorption changes, i.e., the blue shift of λ_{max} ($\Delta\lambda = 30$ nm) with CN⁻ which can be correlated with the naked eye color changes from yellow to color less. Interestingly, no significant changes of λ_{max} was observed in the presence of other anions, such as F⁻, Cl⁻, Br⁻, I⁻, NO₂⁻, NO₃⁻, AcO⁻, HCO₃⁻, H₂PO₄⁻, and HSO₄⁻ (Fig 2a), indicating a selective reaction of CN⁻ with the conjugated indolium double bond of **L**. This selective reaction of cyanide is further monitored by UV-vis titration. Addition of increasing amounts of CN⁻ (0–1.5 equiv) to the ACN solution of **L** (40 µM) at room temperature reveals a gradual decrease of the absorbance at 400 nm with concomitant appearance of band at 370 nm and no

further change is observed after addition of more than 1.0 equiv of CN^{-} ions (Fig. 2b). During the



Fig. 2. (a) Qualitative UV-vis studies upon addition of 1.0 eqv. of other anions and cyanide (as their TBA salts) to **L** (40 μ M) in 40% H₂O/ACN binary solvent mixture; (b) UV-vis titration of **L** (40 μ M) with TBACN (1mM) in 40% H₂O/ACN solvent mixture.

course of the UV-vis titration one isosbestic point was clearly observed at ~380 nm during the addition of 0–1 equiv of CN^- (Figure 2b) indicating the existence of one equilibrium between the probe **L** and CN^- . A plot of the absorbance at 400 nm as a function of the amount of cyanide clearly shows that it decreases linearly up to 1.0 equiv of CN^- and then saturation takes place which clearly indicates 1:1 reaction stoichiometry between the probe **L** and CN^- (Fig. 3b) which is further verified by Job's plot analysis(Fig. 3a). The observed relationship should allow for a quantitative determination of cyanide in the UV-vis channel. The CN^- sensing property of L is further studied in ACN (100%) solvent system. Upon addition of 1.0 equiv TBACN solution to the 40 μ M



Fig. 3. (a) Job's plot of absorbance changes with the different ratio of L (40 μ M) and TBACN (40 μ M) in 40% H₂O/ACN binary solvent mixture; (b) Changes in absorbance of L (40 μ M) with increasing amount of TBACN(1mM) added during UV-vis titration) in 40% H₂O/ACN solvent mixture.

solution of L, ~30 nm blue shift of the absorption maximum is observed (Fig. S7, Supporting Information). Hence L can detect cyanide both in aqueous as well as non-aqueous media, indicating that similar mechanistic phenomena might be operative in both the solvent systems.

Probe L shows emission at ~550 nm in acetonitrile at room temperature. Upon treatment of L with various anions show a notable behavior only with CN^- resulting in a ~100 nm blue shift of the emission maximum (Fig. 4a), whereas other anions remain silent, indicating the selective sensing of CN^- through PL channel. The CN^- detection ability of L was thoroughly investigated via PL titration experiment. During titration of L with CN^- intensity of the PL band at ~550 nm gradually decreases with the concomitant increase of band ~470 nm with a clear isosbestic point at ~500 nm, indicating the existence of one equilibrium between L and CN^- as obtained from UV-vis titration experiment.



Fig. 4. (a) Qualitative PL studies upon addition of 1.0 eqv. of other anions and cyanide (as their TBA salts) to **L** (8 μ M) in 40% H₂O/ACN binary solvent mixture; (b) PL titration of **L** (8 μ M) with TBACN (1mM) in 40% H₂O/ACN solvent mixture.

This PL spectroscopic change continues till the addition of the one equiv CN^- at which the saturation occurs. From the PL titration profile the host: guest stoichiometry is calculated as 1:1 (Fig. 4b inset). The blue shift of the PL spectra must be due to the conjugate addition of the cyanide to the indolium double bond and its truncation in the conjugation after that. From the PL titration, it is thus reasonable to assume that one step reaction is taking place between L and CN^- to form the 1:1 adduct. When the PL intensity of L at 550 nm is plotted against the amount of added CN^- , the graph shows a good linear relationship, as in the case of UV–vis titration during the course of 0 to 1.0 equiv of $CN^$ addition. No more intensity change is observed after more than 1.0 equiv of CN^- has been added, confirming the formation of 1:1 adduct (Fig. 4b inset).



Fig. 5. (a) Competetive Fluorescence graph of L with TBACN in the presence of other anions; (b) Linear fitting of Fluorescence intensity vs. Cyanide concentration calibration curve.

To confirm the high selectivity of L toward cyanide a competition study was performed as done in UV-vis experiment. The selectivity plot is displayed in Figure 5a, which shows that no remarkable PL intensity change of L was observed upon addition of excess (> 10 equiv) of other possibly competing anions to the solution of L in the absence of cyanide. However, upon addition of CN the PL spectra change drastically. Therefore, L may be considered as a highly selective probe for CN⁻. This PL intensity change of L when plotted against the increasing concentration of CN⁻ a good linear relationship is obtained and the corresponding detection limit is calculated as 0.476 μ M (Fig. 5b) which is lower than 1.9 μ M set By WHO [47]. This selectivity and sensitivity plots are well reproducible, and error limits are within 10%. The plot of the PL intensity change (I₀-I) at 550 nm for L as a function of the cyanide concentration shows a good linear relationship in the range of 0–1 equiv of cyanide, indicating L could be used to quantitatively detect the CN⁻ concentration in an unknown sample (Fig. 5b).

Reaction kinetics of CN^- with **L** was performed through UV-vis spectroscopy in 40% H₂O/ACN medium by adding 1.0 equiv. of CN^- (1.0 mM) solution to **L** (40 μ M), and the

absorption maximum (λ_{max}) at 400 nm was monitored (Fig. 6a). From this kinetics, it is observed that with time the absorbance at 400 nm decreases and the reaction between **L** and CN⁻ is found to follow a pseudo first-order rate equation possessing the first order rate constant of $4.78 \times 10^{-3} \text{ s}^{-1}$. The plot of absorption spectral changes with time shows



Fig. 6. Time course of response of L with the addition of 1 equiv CN⁻ in (a) UV-vis and (b) PL channel.

that the reaction takes 20 min to complete (Fig. 6a). This same reaction kinetics is monitored via the PL channel also. The time course of the PL response of L upon addition of 1.0 equiv of cyanide at room temperature was monitored (Fig. 6b), showing that the reaction is saturated ~30 min. The little slow PL response compared to the UV-vis one can be realized from the point that PL experiment was done with lower host-guest concentration (10 μ M) as compared to that taken in UV-vis experiment (20 μ M).

Apart from this steady state PL experiment, the CN⁻ sensing behavior of the probe **L** was also established *via* time-correlated single photon counting (TCSPC) measurements (Figure 7). The decay profile as well as the lifetime of the probe **L** is changed significantly upon addition of the CN⁻. Interestingly the probe shows lifetime of 1.574 ns whereas upon addition of CN⁻ the life time of the probe monitored at 550 nm is decreased

to 0.083 ns (Table S1), indicating that the probe has changed its structure/ property upon addition of the CN⁻. Moreover, when these lifetime measurements are monitored at 460 nm, it is observed that the lifetime of the probe **L** at 460 nm was 0.22 ns which increase upon addition of CN⁻ to 0.54 ns (Table S1). Thus the lifetime data also supports the ratiometric behavior of probe **L** towards cyanide sensing as that is established *via* UV-vis and PL titration experiments. Thus PL and TCSPC data suggest a selective reaction based sensing of CN⁻ through the conjugate addition of the analyte in the ligand structure. Further the sensing study via PL experiment in semi-aqueous (40% aqueous acetonitrile) environment leading to same results as obtained in 100% ACN medium.



Fig. 7. Decay profile of L (20 μ M) in the presence of TBACN (0.2 mM) in 40% H₂O/ACN monitored at 550 nm; Color code: red: L, green: L+CN[.]

Thus probe L can be utilized as a selective and sensitive reaction based stoichiometric probe for CN^- in aqueous and semi-aqueous medium even in the presence of large excess of other competitive anions.

Mechanistic Investigation of Cyanide Sensing by NMR, Mass and TD-DFT Study:

The reaction based cyanide sensing property of **L** was finally confirmed by the ¹H NMR experiments in D₂O/ACN- d_3 binary solvent mixture, and similar observations were found in both the media (Fig. 8 and Fig. S8). We were able to increase the percentage of D₂O up to 15%. The selectivity of **L** towards CN⁻ as obtained from spectroscopic studies (UV-vis and PL) was also confirmed by the ¹H-NMR experiments whereas no noticeable change was observed with other competitive anions of same concentration (Fig. S9). In the presence of CN⁻, some signals in the ¹H-NMR spectrum get vanished, and some new signals are generated in the aromatic region as well as in the aliphatic region, indicating the formation of a new species in solution. But other anions do not show any change in spectra which confirms the chemodosimetric selectivity of **L** towards CN⁻ (Fig. S9). The stoichiometry of this reaction based cyanide sensing property of **L** was monitored *via* ¹H-NMR titration studies in D₂O/ACN- d_3 (15% D₂O, v/v).



Fig. 8. ¹H-NMR titration of **L** (8.25 mM) with TBACN (38.17 mM) in 15% $D_2O/ACN-d_3$ solvent mixture exhibiting that saturation attains on the addition of 1.0 equiv. of TBACN (enlarged figure).

Upon gradual addition of 38.17 mM solution of cyanide to 8.25 mM solution of **L**, the peaks corresponding to **L** is diminished with the concomitant appearance of new peaks related to [**L-CN**] adduct. This phenomenon gets saturated upon addition of 1.0 equiv. of TBACN solution (Fig. 8). The same observation is found in case of ACN- d_3 alone where 50.49 mM solution of cyanide in ACN- d_3 was gradually added to 8.97 mM solution of **L** in ACN- d_3 (Fig. S8).

To have an insight into the mechanistic pathway of CN^{-} sensing by L, both the NMR spectra of L and L in the presence of excess CN⁻ are compared. It is observed that the peaks corresponding to both the vinylic protons H_a and H_b, which appear as a doublet due to trans-coupling with J = 15 Hz, show upfield shift from 8.38 and 7.58 ppm to 7.22 and 6.51 ppm respectively, in the presence of excess CN⁻ (Fig. 9). On the other hand, the signal corresponding to N-CH₃, *i.e.*, H_c protons also exhibits an upfield shift from 4.11 to 2.81 ppm. Again, from ¹H-NMR titration studies of L with TBACN, it is observed that the reaction gets saturated after the addition of 1.0 equiv. of CN⁻ (Fig. 8). From these findings, a plausible mechanism of the reaction can be drawn as depicted in Fig. 9, as reported earlier by another group [48]. Since CN⁻ is a good nucleophile compared to all other considered anions, it can add to the electrophilic $[>C=N<]^+$ bond of the indolumring in L forming 1:1 addition product rendering the positively charged nitrogen atom neutral. This phenomenon is further supported by the ESI-MS experiment. When L and TBACN are mixed in 1:1 ratio in acetonitrile and subjected to ESI-MS (-ve), a peak at m/z = 721.1680 corresponding to $[(L-CN)-H]^{-1}$ species appears (Fig. S10) indicating the formation of a new [L-CN] compound whose isotropic distribution pattern of mass exactly matches with the simulated pattern (Inset of Fig. S10).



Fig. 9. ¹H-NMR spectrum of **L** in 15% $D_2O/ACN-d_3$ (bottom) and ¹H-NMR spectrum of **L** with CN⁻ (1.2 equiv.) in 15% $D_2O/ACN-d_3$ (top) showing the upfield shift of H_a, H_b and H_c on addition of TBACN solution and the plausible mechanism for binding of CN⁻ with **L**.

Here it is to be noticed that since CN⁻ is a good nucleophile compared to all other considered anions when a solution of TBACN is added to a solution of L, it adds to the electrophilic $[>C=N<]^+$ group, forming a covalent bond. In L, the activated as well as an electrophilic double bond is conjugated with the naphthalimide bound benzene moiety. Hence the whole molecule has a π - π * absorption band near 390-400 nm. When all other anions except cyanide are added to L, due to their less nucleophilic character they do not add to the activated double bond as a result of which absorption band near 390-400 nm does not show any kind of shift. But whenever cyanide is added to L, due to its greater nucleophilic character, it adds to the electrophilic double bond rendering the positively charged nitrogen atom neutral. Thus the extent of conjugation in the molecule is decreased, resulting in the shift of the absorption band towards the shorter wavelength that means the cyanide adduct of L absorbs at shorter wavelength, and a blue shifted spectrum is observed in UV-vis experiment. To account for the decrease in the emission intensity of L on the addition of cyanide, excited state electron transfer phenomenon can be considered. When cyanide adds to L indolium nitrogen atom becomes neutral leaving the molecule neutral as a whole. Now there is a possibility of excited state photoinduced

electron transfer (PET) from the neutral nitrogen atom of the indolium moiety to the electron deficient naphthalimide ring. Due to this phenomenon, the emission intensity of L gets quenched by the addition of cyanide.

To support the mechanistic pathway further and explain the experimental findings obtained from UV-vis, fluorescence and ¹H-NMR studies, DFT calculations have been performed both on **L** and the ligand-cyanide adduct (**L-CN**) with B3LYP functional [49] using 6-311G(d) [50] basis set for all the atoms with conductor-like polarizable continuum model (CPCM) [51] for acetonitrile solvent in Gaussian 09 package [52].

The Hartree–Fock-type exchange was mixed with Becke's exchange functional [53] and that proposed by Lee-Yang-Parr for the correlation contribution [54]. The optimized energy structure of L shows that the indolium moiety and the benzene ring attached to the naphthalimide moiety lie in the same plane (Figure S11). But in the energy optimized structure of the L-CN adduct, they come out of planarity hampering the conjugated π framework (Fig. S11). This observation supports the occurrence of a blue shift in the UVvis studies on the addition of TBACN. For the probe L, it is expected that the lower energy band at ~ 400 nm is due to intraligand charge transfer. The electron with drawing character of the indolium unit and its π conjugation should efficiently decrease the LUMO energy. A significant enhancement of the LUMO energy level is observed after cyanide addition to the indolium double bond due to the much less electron-withdrawing character of the corresponding neutral analogue and concomitant loss of extended π conjugation. Time-dependent DFT calculated UV-vis spectra of the cyanide adduct of L matches very well with the one obtained experimentally which also supports the formation of the adduct (Figure S12).

We can also get some idea about the quenching phenomenon in the PL studies from TD-DFT calculations. In **L**, the HOMO is distributed both on the naphthalimide moiety, the adjacent benzene ring and the indolium unit (Fig. 10). Whereas, in the **L-CN** adduct the HOMO is mostly concentrated on the indolium moiety and the LUMO is concentrated on the naphthalimide unit. Hence HOMO to LUMO charge transfer in the excited state may cause the quenching process.



Fig. 10. Frontier Molecular Orbitals (MOs) of (a) L and (b) L-CN complex generated from DFT calculations (isovalence = 0.02).

Single Crystal X-ray Structural Evidence:

The cyanide binding mechanism as established by NMR, ESI-Ms and TD-DFT studies is finally corroborated by the single crystal X-ray structure of the cyanide adduct of the probe L. Slow layer diffusion of stoichiometric (1:1) mixture of probe L and CN^- in acetonitrile into benzene results in colorless crystals of the [L-CN] adduct. The crystal structure of the L-CN adduct is demonstrated in Fig. 11, which shows that the cyanide



Fig. 11. Single crystal X-ray structure of the cyanide adduct of L (L-CN). Thermal ellipsoids are drawn at 30% probability level; Color code: Carbon-grey, hydrogen-white, nitrogen-blue, oxygen-red.

adduct is formed through the attack of the cyanide anion into the indolium ring as discussed in the UV-vis, PL and NMR experimental section. The crystal structure of the cyanide adduct clearly evidences in favor of the fact that the conjugation in the probe L is truncated upon addition of the cyanide which is reflected in the spectroscopic properties of the probe L.

Conclusion

In conclusion, we report a new naphthalimide-indolium ion conjugate molecule which can selectively sense cyanide in the presence of other anions in an aqueous medium. The facile nucleophilic attack of CN^{-} to the $[>C=N<]^{+}$ group makes it an effective chemodosimeter to sense CN⁻ with a low limit of detection. The ease of synthesis of the molecule and its ability to detect CN⁻ through a visual color change in aqueous medium, make it imperative. Currently, we are interested to explore the possibility of interactions the having alkyl functionality with synthetic of sensor long chain membranes/biomembranes, as this molecule has both polar and non-polar ends which exist together just like a surfactant molecule. Moreover, functionalization of the molecule with appropriate side chain in the imide part instead of long chain alkyl can lead to its

immobilization onto polymeric backbone, on which we are working on presently in our laboratory extensively.

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An Indolium Ion Functionalized Naphthalimide Chemodosimeter

for Detection of Cyanide in Aqueous Medium

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Graphical Abstract

A new naphthalimide platform based indolium ion functionalized colorimetric as well as fluorometric chemodosimeter (L) has been synthesized which selectively sense CN^- ion in aqueous media through nucleophilic addition of CN^- in L with low detection limit.



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Highlights

Rock

- Novel colorimetric chemodosimeter **L** is synthesised and characterised
- Visual detection of CN⁻ ion is observed in aqueous media
- Nucleophilic addition of CN⁻ ion in **L** makes the sensing process irreversible
- L exhibits high sensitivity and selectivity towards CN⁻ion.