An ICT based "*Turn on/off*" quinoline armed calix[4]arene fluoroionophore: its sensing efficiency of fluoride from waste water and Zn^{2+} from blood serum

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Materials and methods

All the reagents and chemicals like DCC (N,N'-Dicyclohexylcarbodiimide), DMAP (4-Dimethylaminopyridine) used were of analytical grade purchased from sigma aldrich. Silica gel (Merck, 0.040-0.063mm) was used for column chromatography. Metal salts used for the titrations were their perchlorate salts (Caution: Since perchlorate salts are known to explode under certain conditions, these are to be handled carefully!) with formula, $M(ClO_4)_2.xH_2O$.Melting points were taken on Veego (VMP-DS) using a Mel-Temp apparatus. The FT-IR spectra were recorded as KBr pellet on Bruker TENSOR-27 in the range of 4000-400 cm^{-1}. Discover BenchMate system-240 V (CEM Corporation) microwave synthesizer was used for synthesis. ^{1}H NMR spectra was scanned on 400 MHz FT-NMR Bruker Avance-400 in the range of 0.5 ppm -15 ppm and ^{13}C NMR spectra was recorded on a Bruker DPX-300 spectrometer using internal standard tetramethylsilane (TMS) and deuterated DMSO as a solvent in the range of 0.5 ppm to 250 ppm. ESI Mass spectra were taken on a Shimadzu GCMS-QP 2000A. Emission spectrum was recorded on Horiba Jobin, Fluorolog, and Edinburgh F900. UV–Vis absorption spectra were acquired on a Jasco V-570 UV–Vis. Spectrometer. Working standard solutions were prepared daily in deionized water.

Experimental

Synthesis of compound A Microwave assisted synthesis of p-tert-butylcalix[4]arene

A mixture of p-tert-butyl phenol (4.0 g, 0.33 mM), sodium hydroxide (NaOH) (1 g) and formaldehyde(1.8 ml,0.18 mM) solution was taken in an open vessel and was irradiated with 50 W power in a microwave synthesizer Discover(CEM)by stirring for 3 min. After cooling for 10 min, resulted yellow solid mass. Next, 4 ml of toluene and 30 ml of diphenyl ether was added in

this yellow solid, again irradiated with microwave power of 100 W for 5 min with stirring and obtained a dark brown solution. Further, this solution was added in to 75 ml of ethylacetoacetate and kept for 2 h. Finally, white precipitate was obtained which was filtered and washed with ethylacetoacetate and finally dried. Yield, 3.5 g (96%). Elemental analysis for $C_{44}H_{56}O_4$:Calcd.C;81.44%,H;8.70%,O;9.80%,Found:C;80.11%,H;8.261%,O;9.90%.^{1}HNMR: δ_H DMSO,400 MH_Z): 1.18(36H, t-butyl, s), 3. 81 (8H,$ArCH_2Ar$, s), 7.12 (8H,s,Ar-H), 9.71(4H, Ar-OH, s). ESI-MASS (m/z) 648 (M+1).

Synthesis of compound B and C were carried out according to previously reported method[1].

Synthesis of compound D:

A mixture of compound C (1 g, 0.001 mol) and 8-aminoquinoline (0.6 g, 0.004 mol) were dissolved into anhydrous dichloromethane (20-25 ml) and stirred this solution for 15 minutes. Then DCC (0.93 g, 0.004 mol) and catalytic amount of DMAP were added into reaction mixture. This reaction mixture was stirred at room temperature for 48 hours. The reaction progress was monitored by tlc using mixture of chloroform:methanol (7:3). After the completion of reaction, solvent was evaporated. The crude product then wash with 1N HCl followed by $NaHCO_3$ for the removal of unreacted 8-aminoquinoline and compound C. Then product was crystalized with dichloromethane. Yield 78%, mp >280^{0}C. Anal.calc: $C_{88}H_{88}N_8O_8$: C,76.28; H,6.40; N,8.09; O,9.24% Found: C,75.88; H,6.12; N,7.90; O.8.98% FT-IR (KBr)υ: 3180 cm^{-1}(-NH), 3240 cm^{-1}(-CH), 1680 cm^{-1}(-C=O). ^{1}H NMR(DMSO) 1.31 (s, $C(CH_3)_{12}$,36H), 3.82 (s, Ar-CH_2-Ar, 8H), 7.67 (s, Ar-H, 8H), 4.09 (s, -OCH_2, 8H), 8.22 (s, -NH, 4H), 8.10 (s, Ar-H, 4H), 8.06 (s, Ar-H, 4H), 7.88 (s, Ar-H, 4H), 7.38 (s, Ar-H, 4H), 7.32 (s, Ar-H, 4H), 7.40(s, Ar-H, 4H). ^{13}C NMR (DMSO) 31.3 (-CH_3), 67.2 (-CH_2), 168.2, 152.3, 148.6, 136.9, 132.3, 128.9 (Ar-C), 135.9, 128.2, 123.4, 123.1, 118.2 (Ar-CH), ESI-MASS : (m/z) 1386 (m+1).

Absorption and luminescence

Absorption spectra of compound lower rim calix[4]arene tetraamidoquinoline (TAQC) was recorded in acetonitrile and the data are given in experimental section. This compound show absorption band in the region between 290-390 nm, the band at 301 nm indicates π- π^* transition of aminoquinoline system. This compound shows a strong luminescence band at 475 nm in acetonitrile with excitation at the absorption maxima (λ_{max}) of the quinoline moiety , which is at 370-380 nm.

Ion-binding study

Stock solutions of the complex TAQC (1 x 10^{-8} M) and that of perchlorate salts (1 x 10^{-6}M) of various metal ions (Zn^{2+}, Cd^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Na^{+}, K^{+}, Cu^{2+}, Ni^{2+}, Mn^{2+}, Cr^{3+}, Pb^{2+} and Sr^{2+}) were prepared in freshly purified acetonitrile. Then 2 mL stock solution of the complex and 2 mL stock solution of each metal salts were taken in a 5 mL volumetric flask, so that the effective concentration of the complex is 1 x 10^{-8} M and that of the metal ions are 1 x 10^{-6}M (100 fold). The spectra of the cation added solutions were compared with that of the original solution to ascertain the interactions of the metal ions with the ionophore. For emission titration study, the same stock solutions of the complexes were used and the metal perchlorate solutions of desired concentration (1.0 – 100.0 equivalents) were prepared by proper dilution of the stock solution .The ion-binding property of fluoroionophore TAQC was investigated with a large number of cations as their perchchlorate salts (Zn^{2+}, Cd^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+}, Na^{+}, K^{+}, Cu^{2+}, Ni^{2+}, Mn^{2+}, Cr^{3+}, Pb^{2+} and Sr^{2+}) and anions (F^{-}, Cl^{-}, Br^{-}, I^{-}, CH_3COO^{-} and $H_2PO_4^{-}$) as their tetrabutyl ammonium salts in acetonitrile. Then solution for Zn^{+2} and F^{-} were prepared in the concentration range of (0-120 nM) and (0-160 nM) respectively with 1×10^{-8}M concentration of TAQC ligand.

The ion-recognition process was monitored by luminescence, UV-Vis and ESI-Mass spectral changes. The binding constants were calculated by fluorescence titration data. Here, we have shown representative spectra showing the changes observed in emission intensities upon the addition of increasing concentration of ions are shown in the figure. According to this procedure, the fluorescence intensity (F) scales with the metal ion concentration ([M]) through $(F_0\text{-}F)/(F\text{-}F_{\infty}) = ([M]/K_{diss})^n$. The binding constant ($K_s$) is obtained by plotting $Log[(F_0\text{-}F)/(F\text{-}F_{\infty})]$ vs.Log[M], where F_0 and F_{∞} are the relative fluorescence intensities without addition of guest metal ions and with maximum concentration of metal ions (when no further change in emission intensity takes place), respectively. The value of Log [M] at Log $[(F_0\text{-}F)/(F\text{-}F_{\infty})]= 0$ gives the value of $\log(K_{diss})$, the reciprocal of which is the binding constant (K_s).

Real sample preparation

For the analytical application of proposed fluorescence probe we have applied this probe for real sample analysis in blood serum for Zn^{2+} and industrial waste water for F^-. The blood sample was allowed to clot and serum was obtained by centrifugation at 3000 rpm for 30 minutes. We have used HEPES buffer for this experiment and blood serum sample was stored at -15^0 C. The blood sample was diluted upto 500 fold and analyzed by present sensor. This titration has been done by taking an *in situ* generated Zn^{2+} complex of TAQC with various blood serum concentrations ranging from 0-80 nM **(Fig. S12).**The waste water samples (100 ml) were collected from industrial water (vatava) where the amount of fluoride is much more than 2 ppm. The fluoride content water sample was applied for extraction procedure. Our compound was soluble in chloroform as well as in acetonitrile but as acetonitrile is soluble in water so we intentionally taken chloroform and dissolve our compound in it. Then in separating funnel, we took 60 ml of ligand solution and 40 ml of water sample and shake three-four times for half an hour. Then we

separated organic layer. This experiment was carried out three to four times. Then extracted portion was applied to AAS to find out the concentration of fluoride in organic layer. Then it was diluted upto 500 fold and analyzed by the presented method and results are shown in Table 2 with quantitative recovery up to 98%. The experiment was carried out in acetonitrile: water 7:3 (v/v) solutions buffered to pH = 2.5 with 0.1 M potassium hydrogen phthalate and HCl acid[2]. The concentration range during this experiment was 0-80 nM. This result confirms the use of calix[4]arene as fluroionophore have high sensitivity and specificity towards fluoride detection in industrial waste water **(Fig. S13).**

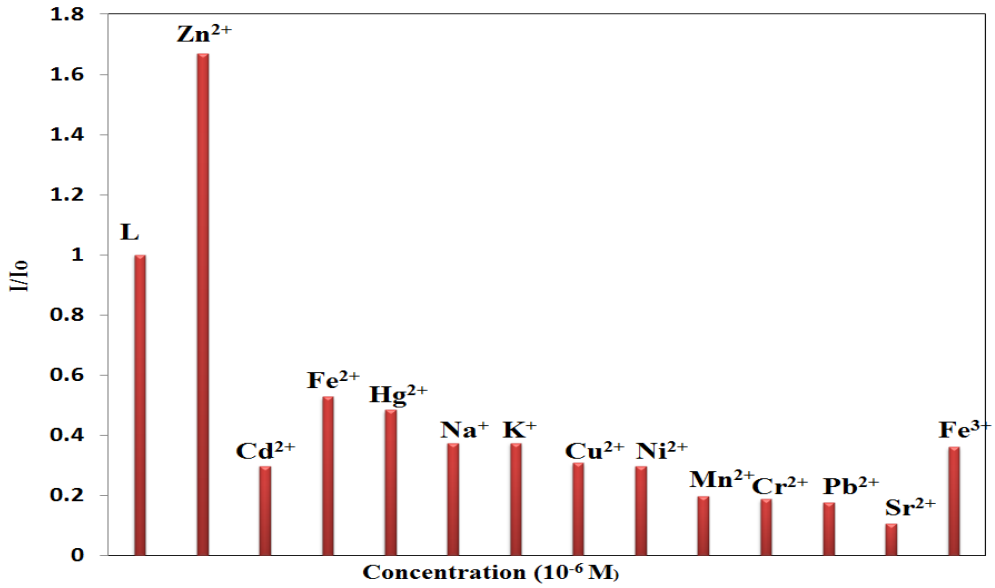

Fig.S1 Histogram showing fluorescence response of TAQC (1×10^{-6} M) with various cations (1×10^{-6} M).

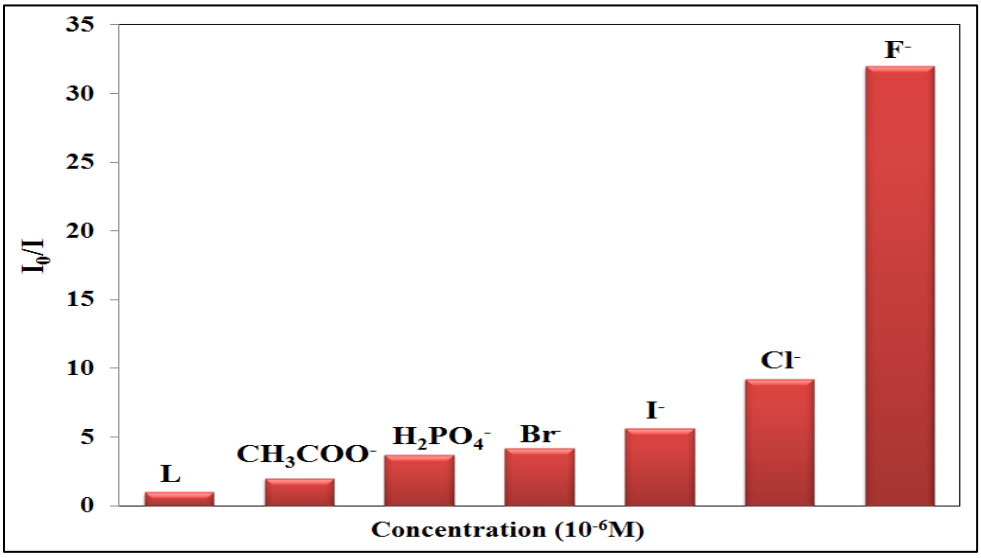

Fig.S2 Histogram showing fluorescence response of TAQC (1×10^{-6} M) with various anions (1×10^{-6} M).

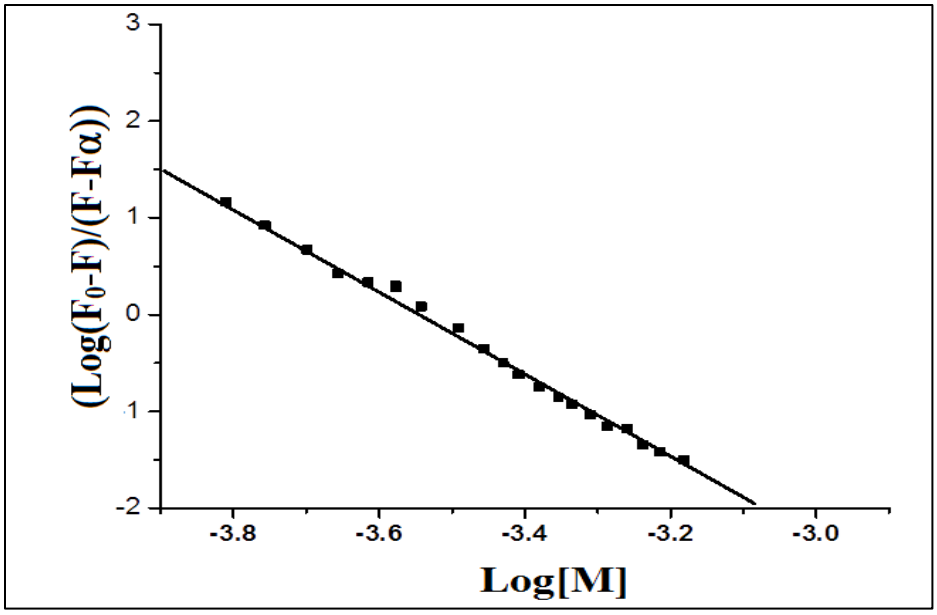

Fig.S3 Binding constant plot for Zn^{2+} with TAQC ligand from emission titration.

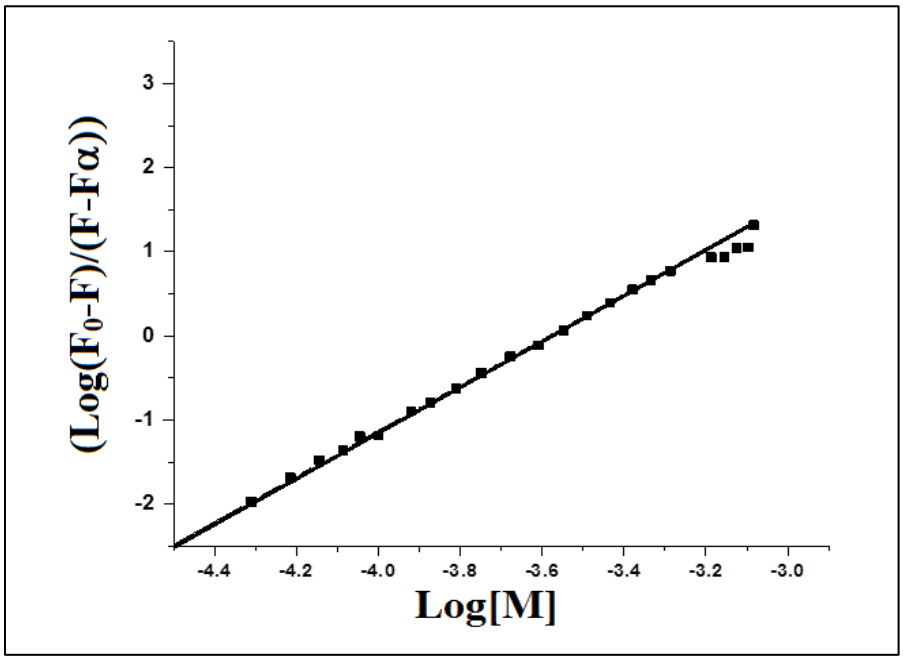

Fig.S4 Binding constant plot for F^- with TAQC ligand from emission titration.

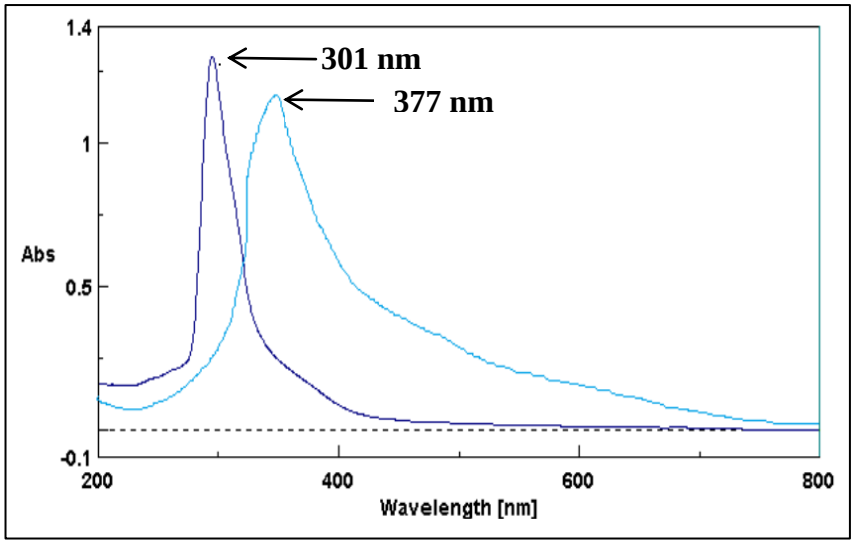

Fig. S5. Absorption spectral changes of TAQC (1×10^{-6}M) ligand in the presence of Zn^{2+} (1×10^{-6}M).

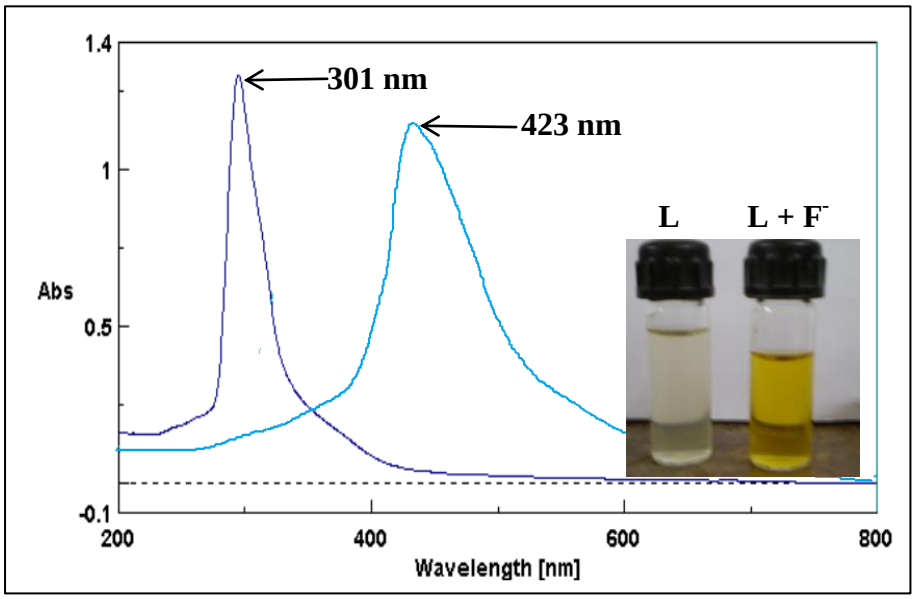

Fig. S6. Absorption spectral changes of TAQC (1×10^{-6}M) ligand in the presence of F^- (1×10^{-6}M).

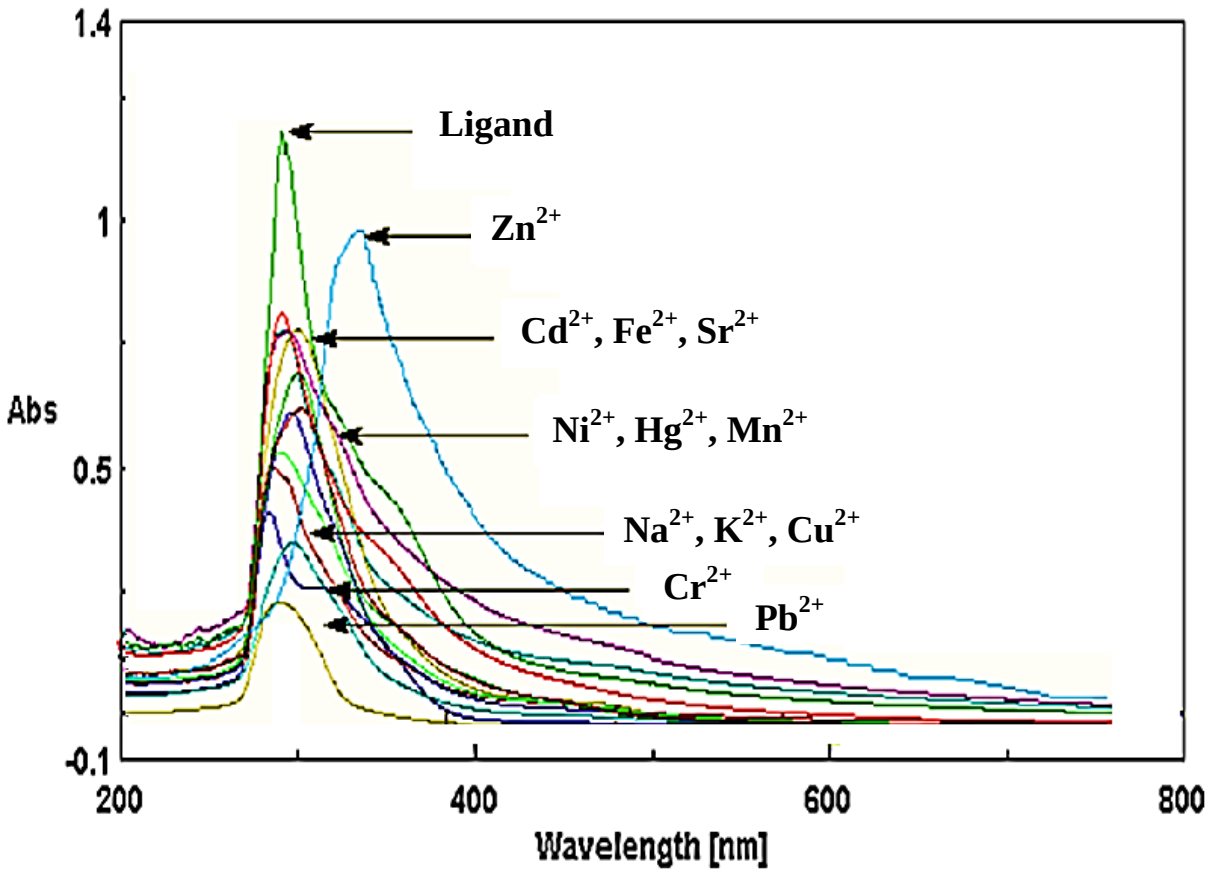

Fig.S7 Absorption spectral changes of TAQC (1×10^{-6} M) ligand in the presence of different metal cations(1×10^{-6} M).

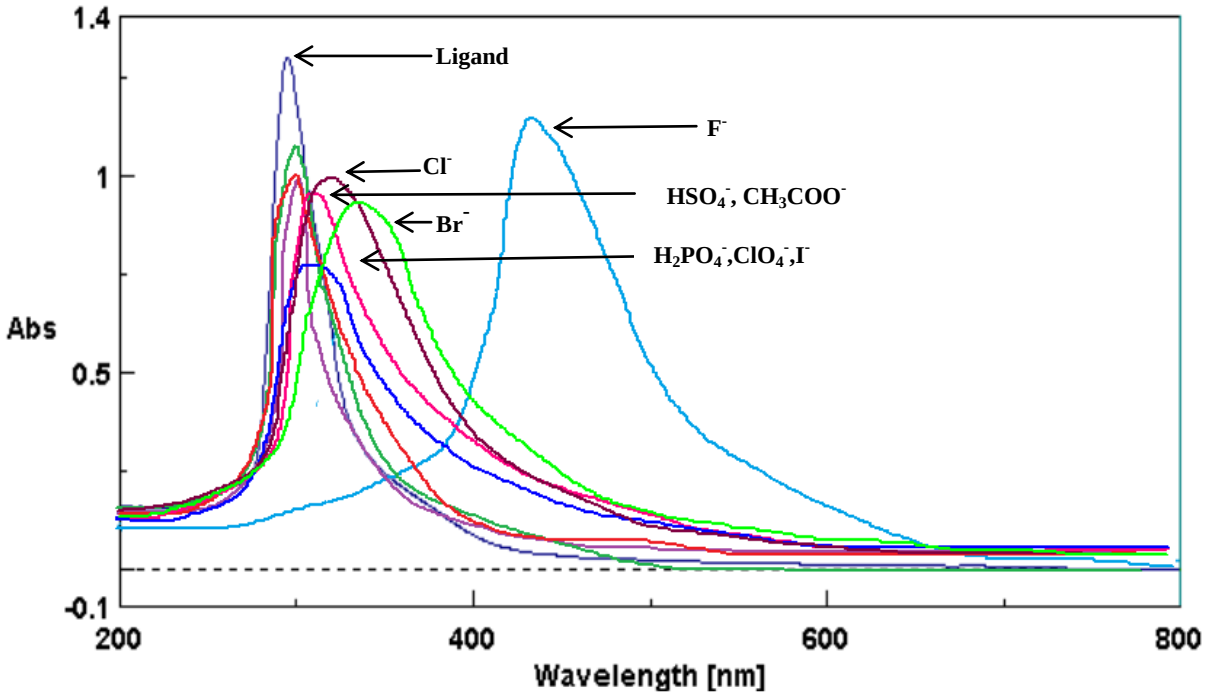

Fig.S8 Absorption spectral changes of TAQC (1×10^{-6} M) ligand in the presence of different metal anions (1×10^{-6} M).

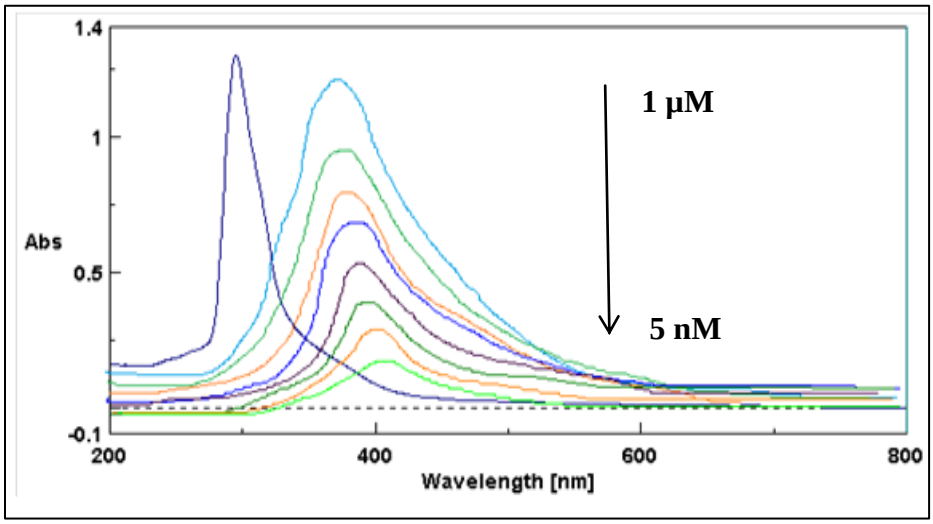

Fig. S9 The plot demonstrates the absorption spectral changes of TAQC in the presence of different concentrations of Zn^{2+} (1 µM, 500 nM, 250 nM, 100 nM, 50 nM, 20 nM, 10 nM and 5 nM)

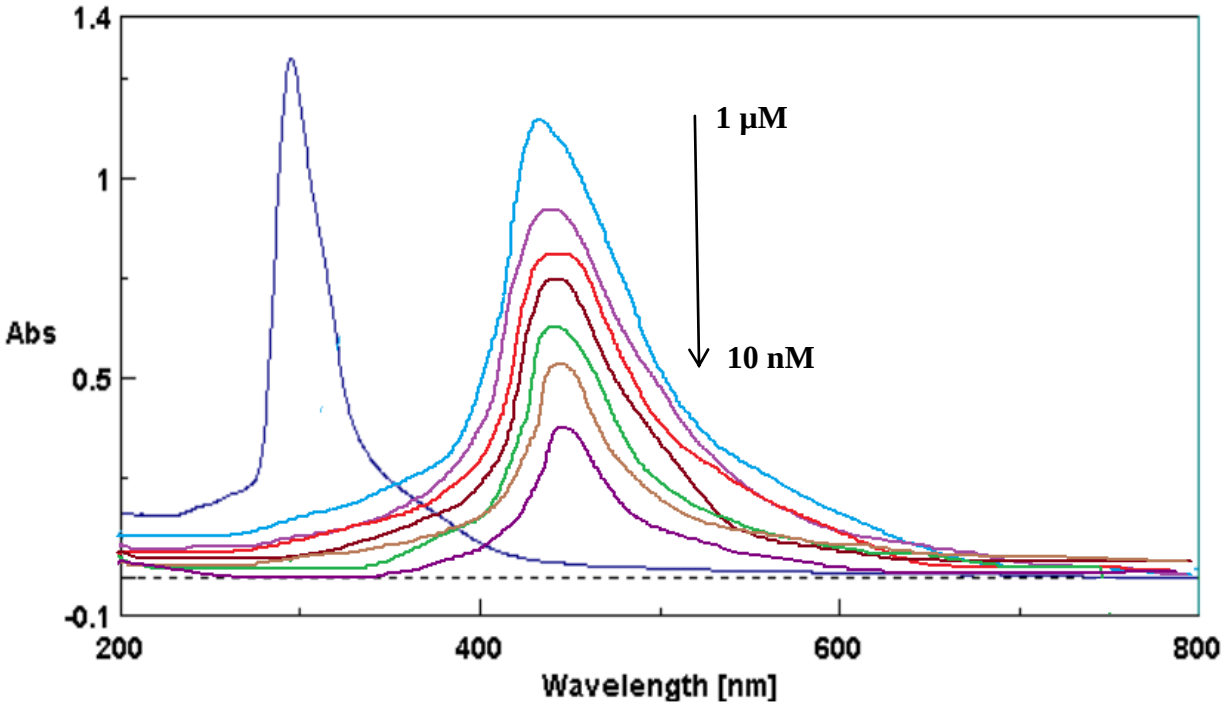

Fig. S10 The plot demonstrates the absorption spectral changes of TAQC in the presence of different concentrations of F^- (1 µM, 500 nM, 250 nM, 100 nM, 50 nM, 20 nM and 10 nM).

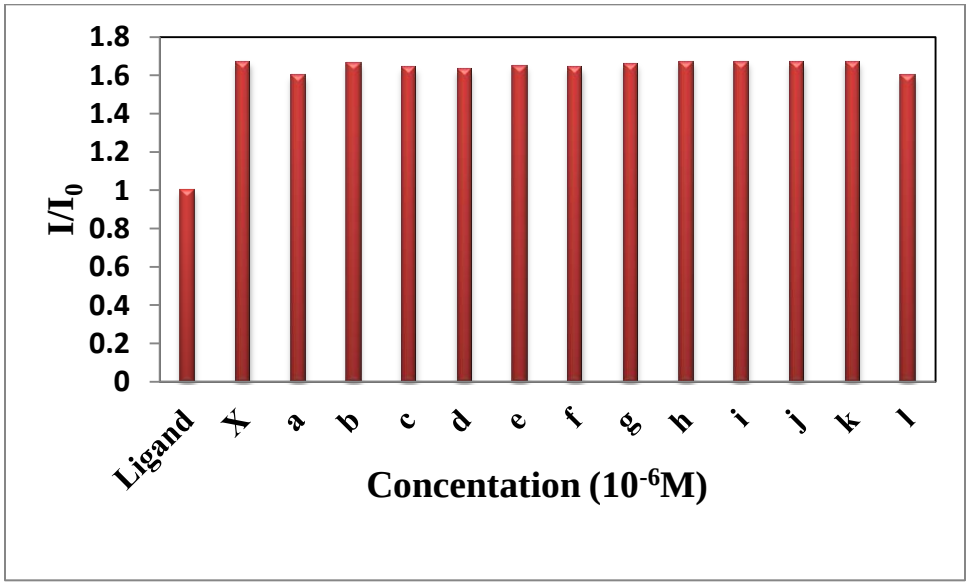

Fig. S11: Competitive emission spectra of TAQC (1×10^{-6} M) with Zn^{2+} in presence of other cations. (X= TAQC+Zn^{2+}, a = Cd^{2+}, b = Fe^{2+}, c = Hg^{2+}, d = Na^{+}, e = K^{+}, f = Cu^{2+}, g =Ni^{2+}, h = Mn^{2+}, i=Cr^{2+}, j= Pb^{2+}, k=Sr^{2+}, l= Fe^{3+}) (1×10^{-6} M) in acetonitrile.

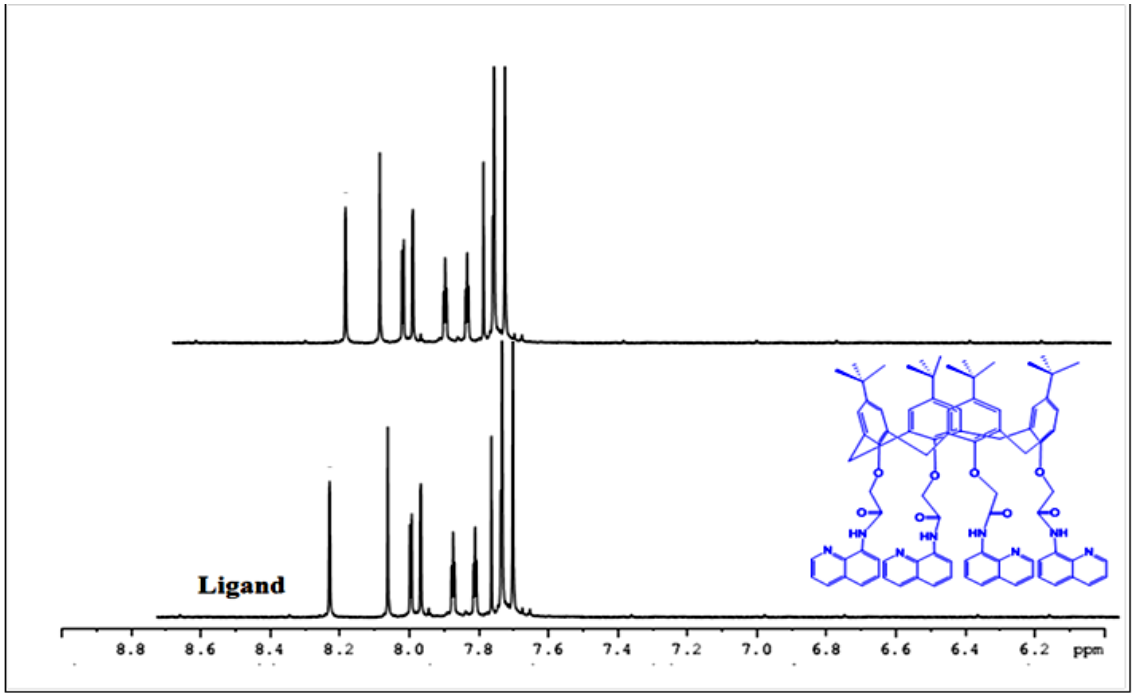

Fig. S12 ^{1}H NMR spectrum of TAQC ligand with Zn^{2+} recorded in $CDCl_3$.

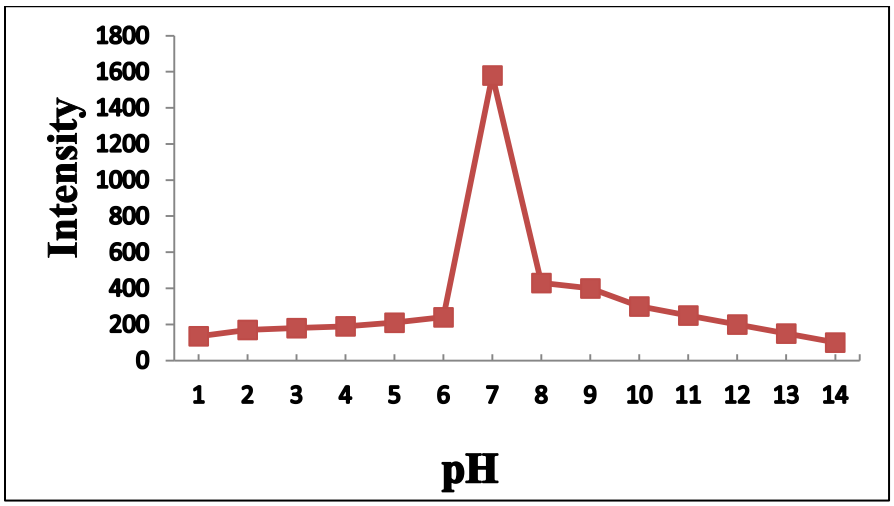

Fig. S13 Shows the effect of fluorescence intensities of TAQC with Zn^{2+} complex varying pH.

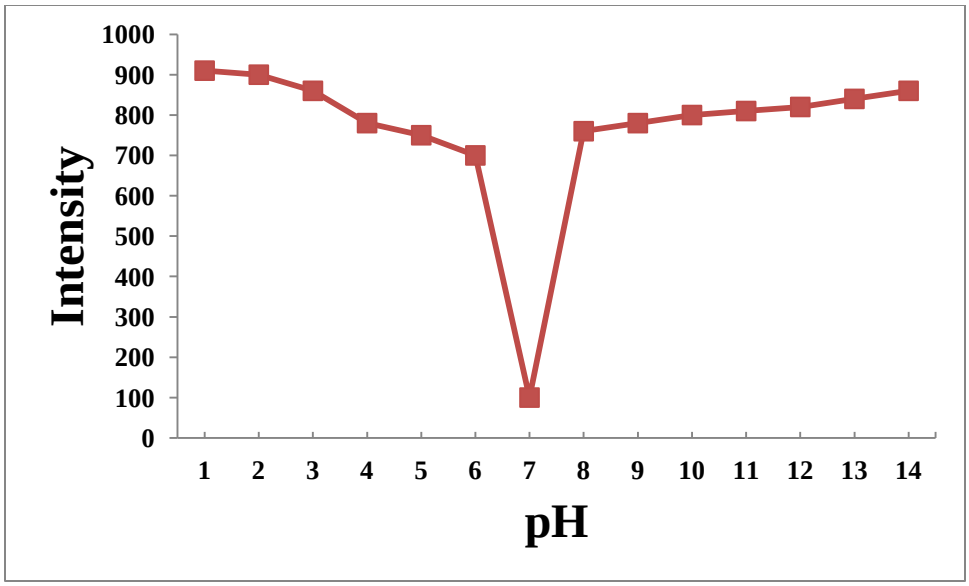

Fig. S14 Shows the effect of fluorescence intensities of TAQC with F^- complex varying pH

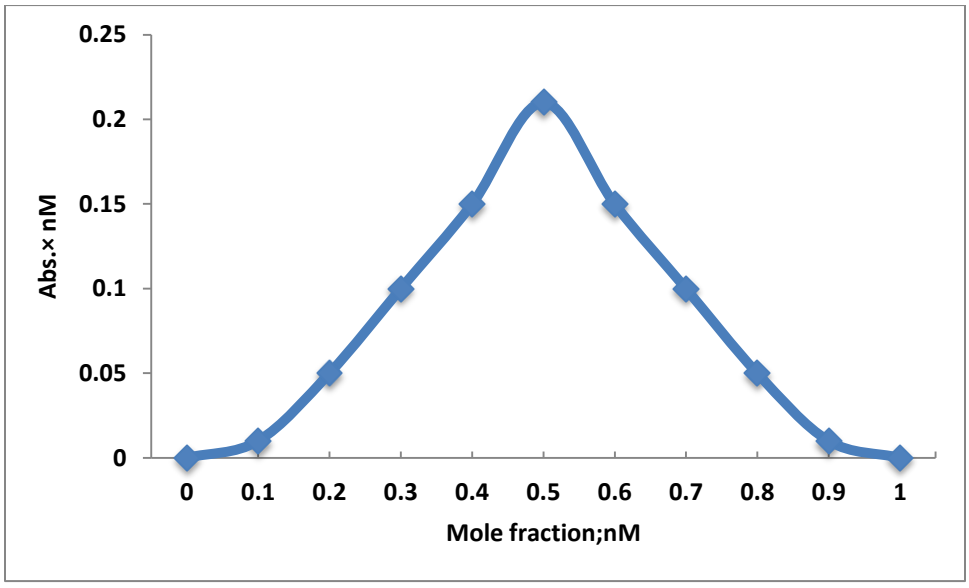

Fig. S15 Job's plot obtained from the absorption titration of TAQC with Zn^{2+}

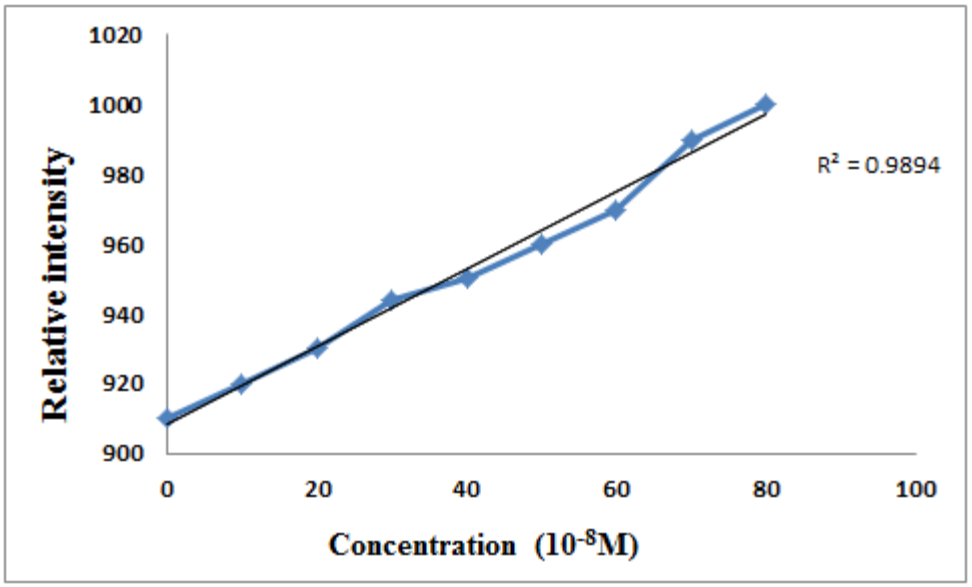

Fig. S16 The plot demonstrate a linear correlation exists over the range of 1 nM–80 nM, with R^2 = 0.9894 of TAQC with blood serum in acetonitrile.

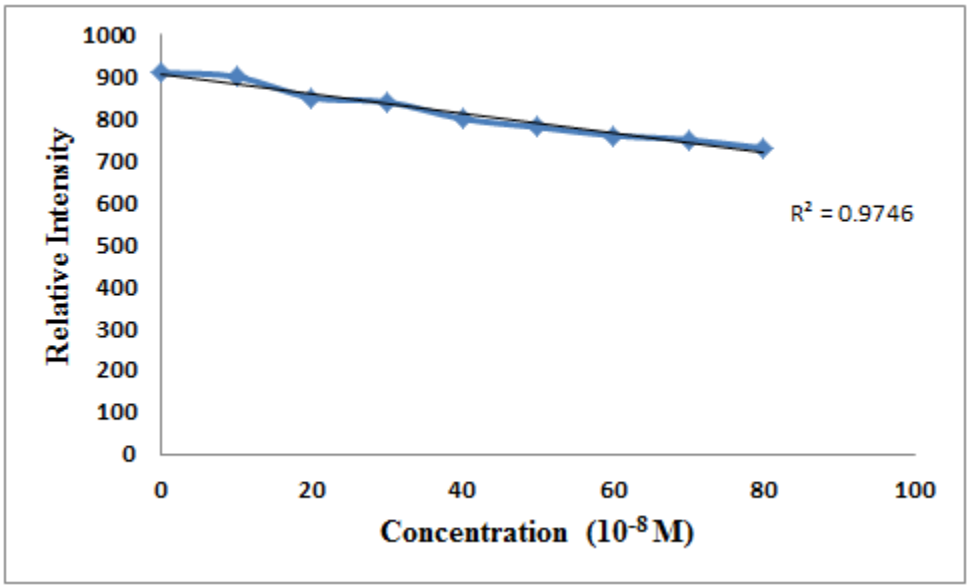

Fig. S17 The plot demonstrate a linear correlation exists over the range of 1 nM–80 nM, with R^2 = 0.9746 of TAQC with industrial waste water in acetonitrile.

Sample	Added (μgL^{-})	Found by AAS	Found by proposed sensor	%Recovery± SD (n=5)
Blood serum (Human)	0	18.1×10^{-8}	-	-
Blood serum (Human)	100×10^{-8}	117.7×10^{-8}	108.8×10^{-8}	98.2±1.3
Blood serum (Human)	200×10^{-8}	216.7×10^{-8}	215.1×10^{-8}	98.62±1.4
Blood serum (Human)	500×10^{-8}	527.1×10^{-8}	510.5×10^{-8}	98.53±1.6

Table S1: Results of the determination of Zinc in blood serum.

Sample	Added (μgL^{-})	Found by AAS	Found by proposed sensor	%Recovery±SD (n=5)
Industrial water (vatva)	0	2.0×10^{-8}	-	-
Industrial water (vatva)	100×10^{-8}	100.1×10^{-8}	100.5×10^{-8}	98.40±1.6
Industrial water (vatva)	200×10^{-8}	198.8×10^{-8}	199.1×10^{-8}	98.56±1.3
Industrial water (vatva)	500×10^{-8}	494.2×10^{-8}	496.1×10^{-8}	98.82±1.8

Table S2: Results of the determination of fluoride in waste water.

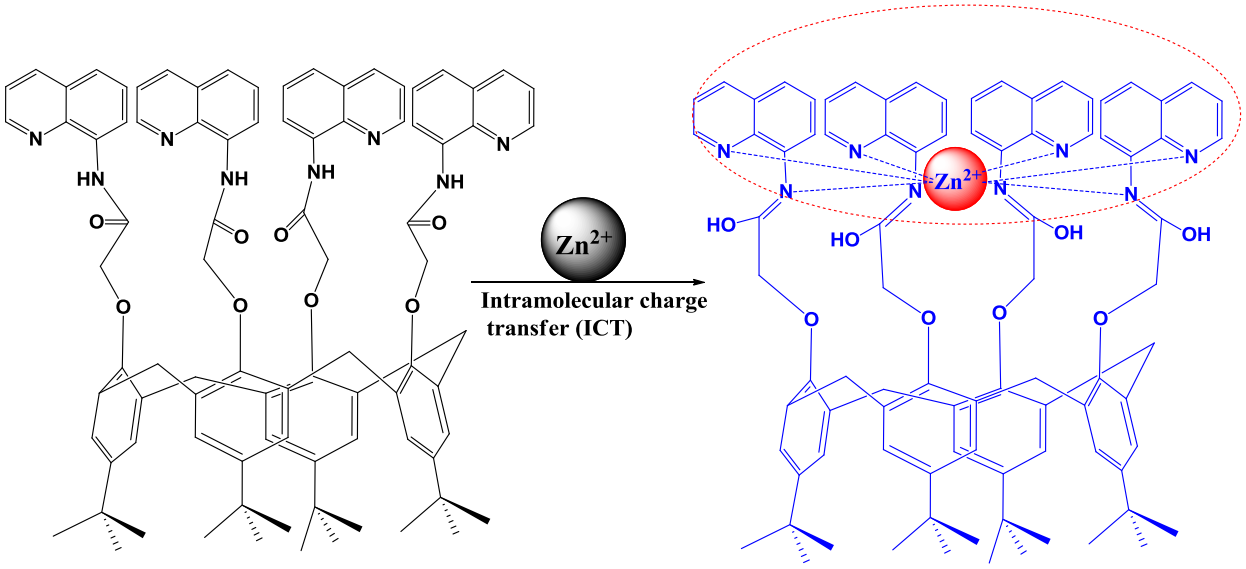

Fig. S18 Proposed mechanism of Zn^{2+} binding with TAQC via ICT process.

References:

(1) E. M. Collins, M. A. McKervey, E. Madigan, M. B. Moran, M. Owens, G. Ferguson and S. J. Harris, J. Chem. Soc., Perkin Trans.1991, **1**, 3137-3142.

(2) A. B. Descalzo,D. Jimenez,J. E. Haskouri,D. Beltran,P. Amoros, M.D.Marcos, R. M.Manez, J. Soto, chem. commun., 2002, 562–563.