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ORIGINAL ARTICLE

Mannich Base Based (*β*-Amino Carbonyl Compound) Receptor for Efficient and Selective Sensing of Fluoride Ions

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Abstract

Mannich Base (MB) based (β-Amino carbonyl compound) (**4**) was synthesized by adopting one pot Mannich reaction by taking 3,4-dihydroxybenzaldehyde, aniline and acetophenone as starting materials and the product was characterized using analytical techniques such as FT-IR, NMR, mass spectrometry, UV-Visible spectroscopy. The compound **4** utilized as colorimetric sensor for selective sensing of F^- ions. The particular sensing of F^- is obviously noticeable to the naked eye with a dissimilar colour variation. The F^- detection mechanism has been examined by UV-visible and ^{1}H NMR titration experimentations. The ^{1}H NMR titration data describes the deprotonation of OH and N-H protons by F^- as a noticeable stage in the detection. Furthermore, the studies was also carried out for reproduction of deprotonated **4** using trifluoroacetic acid as protonating agent. In addition, Boolean logic gates were fabricated for demonstrating the fluoride sensing mechanism and compound **4** in methyl cellulose biofilm was also been made and effectively used for film based detection of fluoride ion.

Keywords *β*-Amino carbonyl compound · Fluoride sensing · UV-visible spectroscopy · Biological investigation

Introduction

Anion detecting from aqueous solution is one of the ongoing enthusiasm because of the anions are playing the noteworthy role in natural and wellbeing related perspectives. Among these the detection of F^- have turned to be more imperative as their being in the environment is very dangerous and causes numerous hazards [1]. As of United States Environmental Protection Agency (USEPA) and World Health Organization (WHO), satisfactory boundary of F^- in water is 1.5 mg/L (79 μM) [2]. The F^- ion is standout amongst the utmost noteworthy anions since it is a fundamental job in dental consideration and treatment of osteoporosis. Fluoride also existing in numerous pharmaceutical compounds such as anaesthetic, hypnotic and in mental medication drugs. Concentration of F^- in drinking water in abundance can causes several fluorosis, thyroid activity unhappiness etc. Fluoride ion sensors ought to likewise be valuable in the recognition of U(VI) enrichment via hydrolysis of UF_6. Thus, it is essential to sense F^- in water. There is an immense interest for the recognition of F^-ion in numerous waste streams [3].

Chemosensor have attention to detect the fluoride ions as a result of naked eye detection. Several chemosensors have been reported in the literature such as pyrrole [4, 5], diketopyrrole [6], pyrazole [7], naphthalene diimide [8], maleimide [9], salicylaldehyde [10], acylhydrazone [11], terphenylurea [12], urea and thiourea [13], benzoxazole [14], thiazole [15] and Lewis acid [16], have been exploited for the fluoride detection. Many researchers are reported that the sensing of F^- ion mainly due to the removal of proton in organic compounds as well as the hydrogen bonding [17–20].

Mannich reactions are mostly, *β*-amino carbonyl compounds and its spin-offs are utilized in the preparation of peptides, lactams, and precursors to optically active amino acids. The products of Mannich reactions are most suitable intermediates in medicinal applications and natural materials synthesis; these intermediates are used in drug delivery for antimalarial, antitumor and antihypertensive disease [21–25]. Based on the literature survey there was no reports for fluoride ion sensing using 3-(3,4-dihydroxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (**4**) as colorimetric chemosensor. Hence, we have tempted to taken up the

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research for using β-amino carbonyl compound as a simple and cost effective calorimetric chemosensor for fluoride ion sensing. The present study, one pot three component synthesis of 3-(3,4-dihydroxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (**4)** by taking 3,4-dihydroxy benzaldehyde, acetophenone and aniline triazole based ionic liquid act as catalyst. The compound **4** were characterized using the spectroscopic techniques such as FT-IR, NMR, and mass spectrometry. The synthesized compound **4** was used as calorimetric chemosensor for selective sensing of F^- ions. In addition, UV-visible titration, proton NMR titration and Boolean logic gates were also carried out for understanding the fluoride ion sensing mechanism of **4** interacted with TBAF. In addition, compound **4** methyl cellulose bio film was also been prepared and used for sensing studies.

Experimental

Materials

1-Hexy-1,2,4-triazolium methane Sulfonate (ILs), Trifluoroacetic acid, All anions (F^-, Cl^-, Br^-, I^-) in the form of tetrabutylammonium salts, 3,4-dihydroxy benzaldehyde, acetophenone, aniline, ethanol, hexane, were purchased from Loba chemicals. All solvents used for spectroscopic studies were of Loba grade.

Instruments

FT-IR spectrum was recorded in a Bruker Vector 22 FT-IR spectrophotometer in the region of 4000–400 cm^{-1} using a KBr pellet technique. ^1H NMR and ^{13}C NMR spectrum of 3-(3,4-dihydroxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one were logged on to Bruker AVANCE 300 FT-NMR in DMSO d_6 as NMR solvent. Electrospray Ionization mass spectrophotometry (ESI-MS) was logged on the water Q-TOF Premier mass spectrophotometer. UV-visible spectra were logged in Jasco V 370 spectrophotometer using tetrahydrofuran (THF) as solvent.

Synthesis of Mannich Base 3-(3,4-Dihydroxyphenyl) -1-Phenyl-3-(Phenylamino)Propan-1-One (4)

To the stirring of 1-hexyl-1, 2, 4-triazolium mehtanesulfonate (0.5 mmol) and 0.25 mL of ethanol in a dry 10 mL round bottom flask. 3,4-dihydroxy benzaldehyde (1 mmol) and aniline (1 mmol) was added into the reaction flask and stirring was continued for a few minutes followed by the addition of acetophenone (1.25 mmol) in drop wise at ambient temperature. The stirring was continued till the completion of the reaction. The starting materials and product formation were monitored by a TLC ethyl acetate: petroleum ether (30:70%) as eluent; the product was seen as a single compound by TLC. After completion of the reaction 3 mL of water was added into the reaction flask and the solid product (**4**) was filtered followed by the washing of hexane at least thrice and the product was dried using a high vacuum pump for 2–3 h [26] (Scheme 1).

Characterization of 3-(3,4-dihydroxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (4):

Yield: 87%; m.p.: 149–151; FT-IR (KBr, cm^{-1}) 3623, 3452, 3152, 2822, 1648, 1602, 1515, 1462, 1213, 1175, 790, 821. ^1H NMR (300 MHz, DMSO-d_6) δ ppm 9.68 (s, 2H), 8 (s,1H), 7.981 (d, $J = 1.2$ Hz, 2H), 7.564 (t, $J = 8.1$ Hz, 1H), 7.498 (t, $J = 7.2$ Hz, 4H), 7.128 (d, $J = 14.7$ Hz, 1H), 6.988 (d, $J = 8.1$ Hz, 1H), 6.892 (d, $J = 2.1$ Hz, 1H), 6.865 (d, $J = 2.4$ Hz, 1H), 6.587 (s, 1H), 6.240 (t, $J = 7.2$ Hz, 1H), 2.515 (d, $J = 6.5$ Hz, 2H). ^{13}C NMR (100 MHz, MeOD) δ ppm 191.2, 148.7, 146, 145.5, 138.3, 132.5, 129.8, 128.3, 128, 126.8, 122.3, 122.2, 118.2, 115.2, 114.3, 48.2, 38. ESI-MS, Calcd: 333; Found [M + Na]: 356.

UV – vis Absorption Spectral Studies

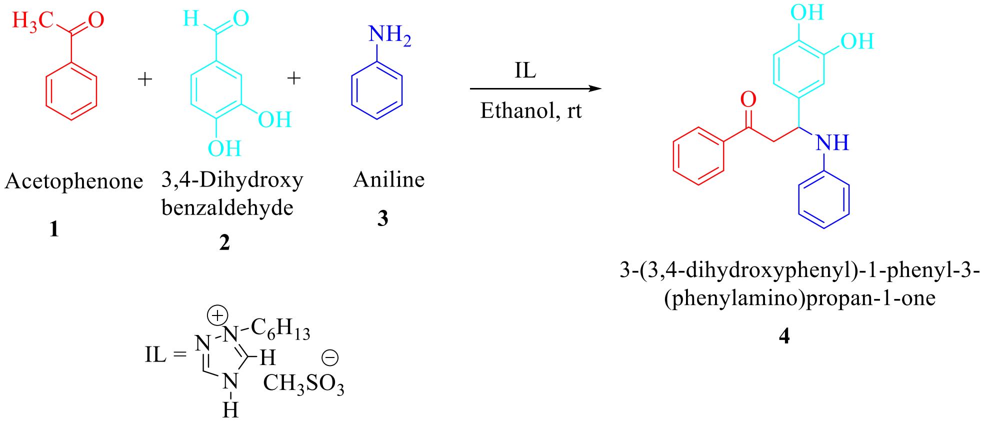
A standard solution of 3-(3,4-dihydroxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (1×10^{-3} M) was prepared in a tetrahydrofuran as solvent and 50 μl of compound 4 were taken from the stock solution and mixed with the same solvent in a quartz cuvette, which is used in the UV-visible titration experiments. The 0.01 M of all anions I, Br, Cl and F in the form of tetrabutylammonium salts were prepared in tetrahydrofuran solvent. Primarily, selectivity of anions were carried out by taking 50 μl of **4** stock solution in 2.95 mL of THF in cuvette and 50 μl of the above anions added in the same cuvette to recorded the UV-visible absorption spectrum individually. Afterwards, the gradual addition of fluoride anion was added in the cuvette containing **4** in THF for the UV-visible titration experiments. The spectrum was recorded at 30 s after adding the anions. To examine the meddling from other anions in the recognition of F^- ion, competitive binding investigations were also been done. The **4** stock solution and 50 μl of fluoride anion were taken in the cuvette recorded the spectrum followed by 50 μl stock solutions of each anion were consecutively added and absorption spectral variations were recorded. The limit of detection and limit of quantification was envisioned utilizing the subsequent eqs. (1 and 2),

$$\text{Limit of detection (LOD)} = 3\sigma/k \tag{1}$$

$$\text{Limit of quantification (LOQ)} = 10\sigma/k \tag{2}$$

Where, σ is the standard deviation of the blank dimension, and k is the slope between the ratio of the UV-Vis absorbance versus concentration of F^- ion. To get a slope, the UV-Vis absorbance at 484 nm was plotted as a role the relating concentration of F^- ion.

Scheme 1 Synthesis of 3-(3,4-dihydroxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (4) utilizing 1-hexyl-1, 2, 4-triazolium mehtanesulfonate ionic liquid as catalyst



Methyl Cellulose Film Preparation

To a stirred solution of methyl cellulose (280 mg) and compound **4** (3 mg) in the beaker containing 10 mL of ethanol and 4 mL of water at room temperature. After dissolving the starting materials 4 drops of ethylene glycol was added in the reaction mixture and sustained the stirring for further 1 h. The reaction mixture was poured in petridis and kept for 12 h in oven at 65 °C. The obtained compound **4** incorporated bio film was taken for the fluoride ion sensing.

Results and Discussions

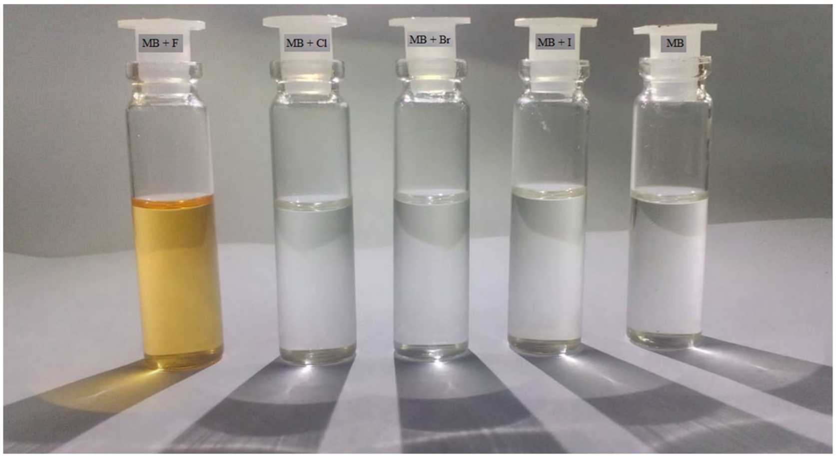
Anions Selectivity

The anion selectivity of synthesized chemosensor 3-(3,4-dihydroxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one were tested by subjecting to several anions namely, TBAF, TBABr, TBACl and TBAI. Figure 1 showed that compound **4** displayed a protuberant and immediate colour variation from colourless to orange with F^- ion, while no significant visual change was observed with other anions like chloride, bromide and iodide under identical conditions. In addition, the compound **4** and **4** with anions UV-visible spectrum were recorded. The Fig. 2 shows that new peak appeared at 484 nm by adding fluoride ion, while adding other anions there was no noteworthy change in the UV-visible spectrum, which confirms compound **4** is selective for fluoride ion sensing.

UV-Visible Absorption Titration Studies

UV-visible titration experimentations were carried out to know the nature of compound **4**-anions interactions. Figure 3 displays the absorption spectra of compound **4** with changing the concentration of tetrabutylammonium fluoride. The absorbance of compound **4** was moved step by step with a landing of new peak at 484 nm. Nonetheless, there was no peak when added with Cl, Br, I anions to compound **4** (Fig. 3a). Thus, the development of new peak 484 nm as a result of compound **4** interacted with TBAF, which is inferable from the creation of hydrogen bonding with fluoride and compound **4** as a results of its high electronegativity than that of other anions. The mechanism of F^- recognition is the deprotonation of compound **4** N-H and OH proton (Scheme 2) and the observed experimental changes are ratio metric (Fig. 3b). The recognition limit of **4** for F^- anion is calculated and bring into being 1×10^{-4} M. The saturation concentration of

Fig. 1 Colorimetric changes of compound 4 with various anions (TBAF, TBACl, TBABr and TBAI)



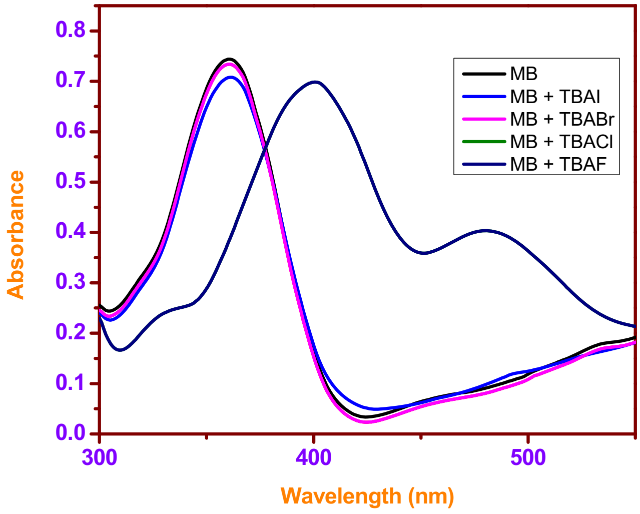


Fig. 2 UV-Visible absorption studies of compound 4 with various anions (TBAF, TBACl, TBABr and TBAI)

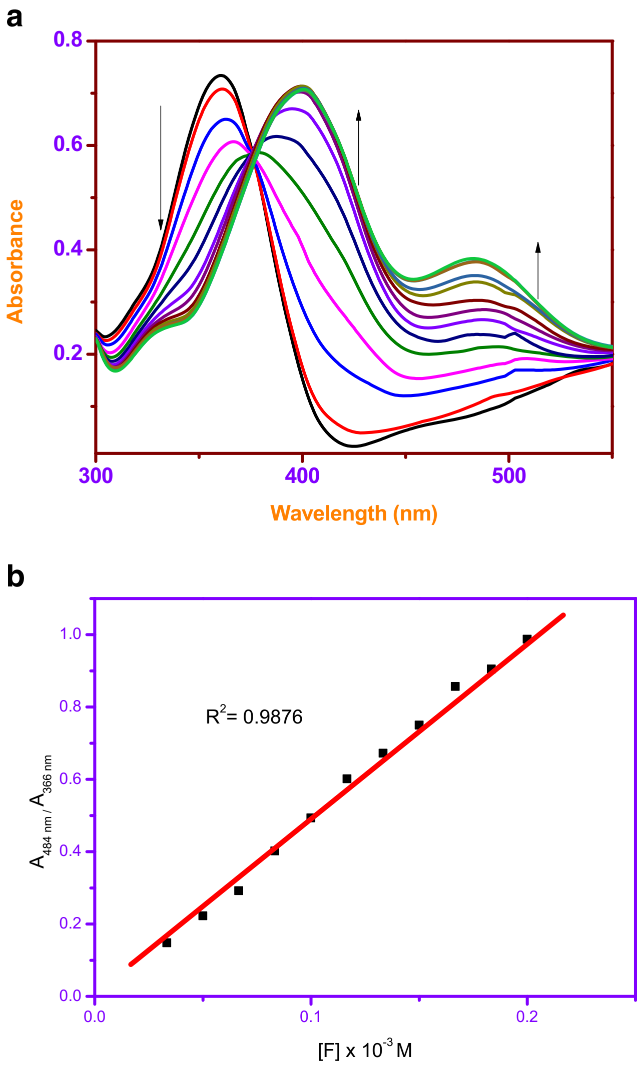
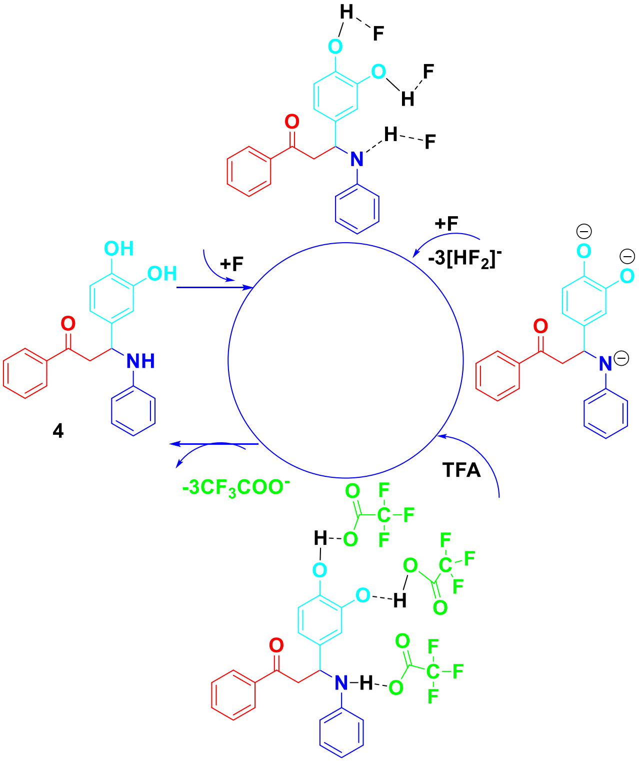


Fig. 3 **a** UV-Visible absorption studies of compound 4 with increasing concentration of TBAF addition. **b** Ratio metric plot A $_{484\ nm}$/A $_{366\ nm}$



Scheme 2 The possible fluoride ion sensing mechanism

fluoride anion with **4** was additionally done and observed to be 0.20 mm beyond that concentration did not produce any noteworthy changes at 484 nm, which could be the saturation of the hydrogen bonding sites in the **4** chemosensor.

Trifluoroacetic Acid Titration

After the sensing of fluoride ion the deprotonated **4** was present in the cuvette, which was subjected to the addition of trifluoroacetic acid (TFA) (0.001 M, 50 μl) for protonation to reproduce **4** (Fig. 4). For this purpose, 0.001 M of TFA

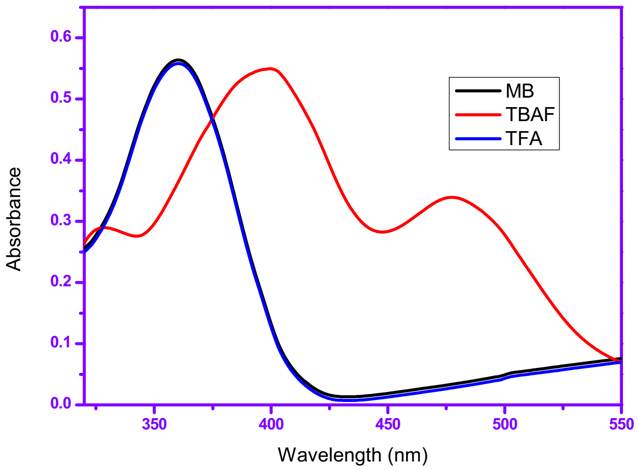


Fig. 4 UV-Visible absorption studies for protonation of deprotonated 4 with 50 μl of TFA (0.001 M)

was prepared in tetrahydrofuran (THF) as solvent. The systematic addition of TFA (5 μl for each addition) in THF solution in to deprotonated **4** solution in the cuvette and recorded the UV-visible spectrum. The Fig. 5. confirms that while snowballing the concentration of TFA, the recovery of **4** was observed with the disappearance of newly formed peak at 484 nm and reproducing original peak confirmed the protonation.

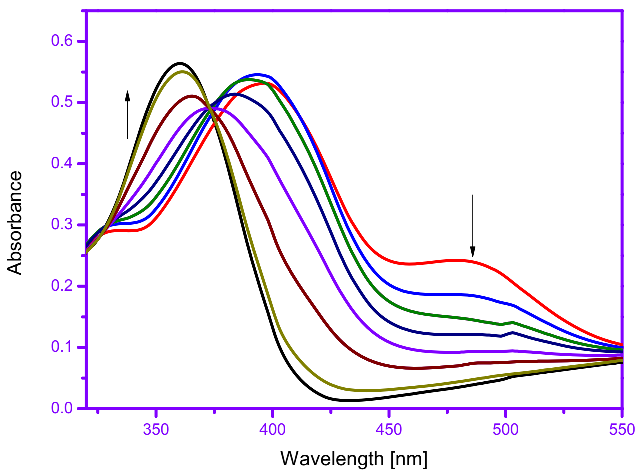


Fig. 5 UV-visible absorption studies for protonation of deprotonated 4 with increasing concentration of TFA addition

NMR Titration Studies

The binding ability of **4** with fluoride anion was evident from ^{1}H NMR titration experimentations in DMSO-d_6 as solvent. Before adding fluoride anion the ^{1}H NMR spectrum of **4** displayed a singlet at 9.76 ppm and 8.08 ppm for OH proton and N-H proton, respectively, Kumar et al also reported similar kind of NMR titration mechanism [27]. To examine the selectivity of tetrabutylammonium fluoride was treated with **4** in DMSO-d_6 (Fig. 6). After the addition of 1 equivalent of TBAF, the resonances were shifted upfield to 9.23 for OH and 8 ppm for NH. This might be as a result of the creation of hydrogen bonds between the F^- ions and OH, NH protons. If 2 equivalent of F^- was added, OH and N-H proton was completely disappeared, which is clear evidence for **4** interacted with fluoride anion. The obtained results confirmed that **4** act as chemosensor for fluoride ion sensing.

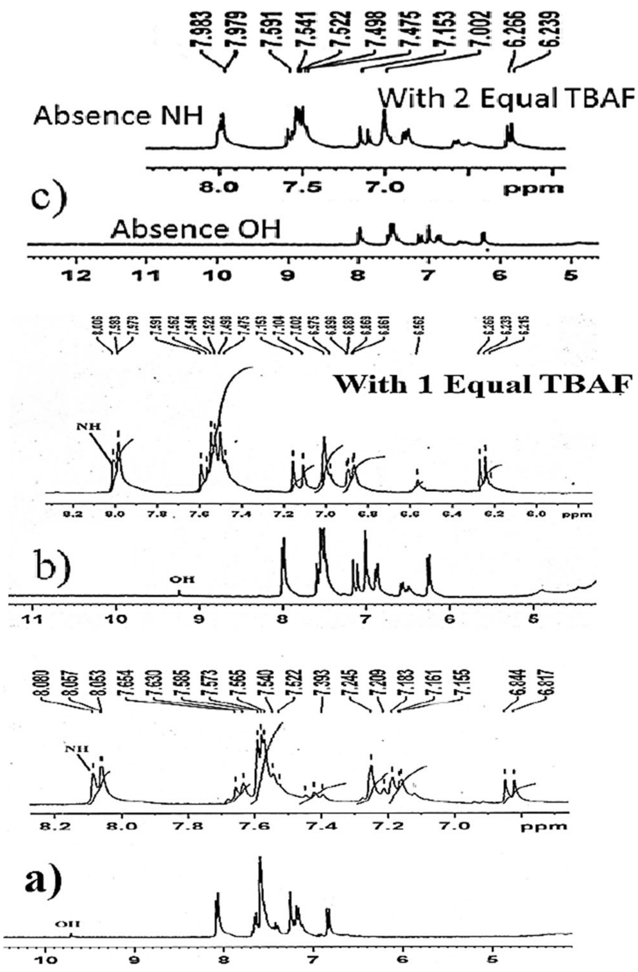


Fig. 6 Proton NMR titration of 4 with TBAF; (**a**) without addition of TBAF, (**b**) 1 equivalent of TBAF addition, (**c**) 2 equivalent of TBAF addition

Methyl Cellulose Based Bio Film

Figure 7 shows that the prepared compound **4** in methyl cellulose bio film. The prepared bio film was subjected to anion sensing. The colour of the bio film was suddenly changed dark yellow to red colour when adding the tetra butyl ammonium fluoride anion. The colour change is due to the deprotonation of compound **4** containing -NH proton and -OH proton. The obtained result confirms the potential of prepared bio film as

Fig. 7 The compound 4 in methyl cellulose for fluoride sensing

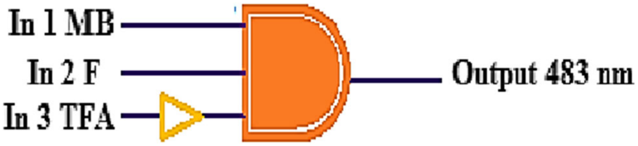


Fig. 8 Fabrication of Boolean logic gates of 4 for fluoride ion sensing

selective chemosensor for anion sensing from hazardous waste matrices

Development of Logic Gates

A basic logic representation of logic gat is showed in Fig. 8 where In 1, In 2 and In 3 as inputs are showed along with the output Y (Table 1). The introduction of fluoride anion and TFA input modes can reflect a divergent change in the UV-visible absorption spectrum. The absorbance output of this spectral reaction is demonstrating the AND gate function. We have thought about two inputs as pursues: **4** as In 1 and F^- ions as In 2. The gathering of F^- to the solution having compound **4** produces a new signal at 484 nm which thought as the output (Y) of the logic gate. As indicated by the AND Boolean arithmetic calculation, the output (Y) will be high (Y = 1) when both the inputs are high (In1 and In 2 = 1) then the output is low (Y = 0). Besides, the addition of TFA to the **4** causes protonation and is showed in the logic gate as a two-input group logic gate. To adding TFA (In 3) stops the output generated by **4** and F^-. When the compound input of In 3 (TFA) is in the ON state, then the peak at 484 nm is vanished and by Boolean arithmetic calculation, the output pinched from it turns out to be the OFF state. Yield is high only when In 2 (F^-) is the ON state (i.e., 1 or high), then the peak at 484 nm rises and consecutive accumulation of TFA to **4** and In 2 (F^-).

Conclusions

β-Amino carbonyl compound **4** was synthesized, characterized utilizing investigative methods namely, FT-IR, NMR, mass spectrometry, UV-Visible spectroscopy. The compound **4** utilized as colorimetric chemosensor for specific detection of fluoride ions over the other anions. The specific detection of fluoride is clearly visible to the naked eye with a dissimilar colour variation. The detection mechanism has been investigated by UV-visible and ^{1}H NMR titration experiments, which affirms the deprotonation of OH and NH protons by fluoride anion and the limit of detection found to be a 1×10^{-4}. The limit of quantification found to be 6×10^{-4}. The deprotonated anionic state was protonated utilizing trifluoroacetic acid, mimics the Boolean INHIBIT logic gates were developed. The prepared compound 4 mixed methyl cellulose bio film as possible candidate to sense the fluoride anions from various waste matrices.

Table 1 The truth logic gates inputs and outputs

4 (In 1)	F^- (In 2)	TFA (In 3)	Output 484 nm (Y)
0	0	0	0
0	0	1	0
0	1	0	0
1	0	0	0
1	1	0	1
1	**1**	**1**	**0**

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