Organic & Supramolecular Chemistry

An AIE-Active Tetraphenylethylene-Based Cyclic Urea as a Selective and Efficient Optical and Colorimetric Chemosensor for Fluoride Ions

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Anion sensing is a very challenging and important issue in many diverse fields, including biological, medical and environmental sciences. In this paper, we report the serendipitous synthesis of a tetraphenylethylene (TPE) bearing a cyclic urea (coded as: **1**). This easy-to-make, simple chemosensor shows high selectivity towards fluoride (F^-) ions. Importantly, this work demonstrates two important factors: firstly, the use of cyclic urea for ion sensing and secondly, the use of aggregation induced emission (AIE)- TPE signalling units. This selective fluoride sensing can be observed by the naked eye, UV-vis absorption, fluorescence spectroscopy, and ^{1}H-NMR spectroscopy. Solutions of sensor **1** are fluorescent in DMSO with fluorescence quantum yield $\Phi = 1.3$ and upon addition of fluoride ions the emission is quenched with $\Phi_F = 0.07$. Notably, other anions, such as CN^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, I^-, OH^-, ClO_4^-, SCN^- and Cl^-, do not show any quenching effect. The binding constant (K) between sensor **1** and fluoride was found to be $4.90 \times 10^8\ M^{-2}$ with a detection limit of 30 μM. We also studied AIE-activity of 1 in THF/water mixture. As such the fluorescence quantum yield (Φ_F) of **1** in pure THF solution shown to be 0.05% which was enhanced 22-fold to 1.98 and 6.65% at $f_w = 90$ and 99%, respectively. This is clear confirmation that compound **1** is AIE active due to decreased solubility and increased molecular self-assembly as the water fraction is increased.

1. Introduction

In recent years, anion sensing has been a very challenging and important issue in many diverse fields, including biological, medical and environmental sciences.[1] Many chemosensors consist of an optical-signalling unit covalently linked (or bonded) to a neutral receptor such as urea,[2] thiourea,[3] amides,[4] phenols,[5] pyrroles,[6] dipyrrolyl-bis-sulphonamide,[7] imidazolium salt, triazole, azide,[8] and quinoxaline[9] subunits. These groups provide one or more H-bonding donor sites for sensing of anions, typically, F^-, AcO^-, $H_2PO_4^-$, etc. The selectivity of the sensor, however, is highly dependent on the properties of the H-bonding moiety and the basicity of the anion. Fluoride anions (F^-) are of particular importance as they play a main role in the inhibition of tooth decay and as a treatment for osteoporosis.[10] Thus, it is essential to design and develop new approachs for the selective recognition of F^-. Fluoride ions form strong H-bonds with the NH or OH fragments of the artificial receptor, which may lead to proton transfer reactions, depending on the inherent acidity of the H-bond donor group of the receptor.[11,12] This is true for amide-, phenol-, and urea-based receptors bearing electron-withdrawing substituents.[2] Nevertheless, a clear distinction in the optical properties of the chemosensor in the presence and absence of ions should be observed, either under UV irradiation or with the naked eye .

Tetraphenylethylene (TPE) has recently been used as a versatile luminophore due to its aggregation induced emissive (AIE) behaviour,[13] and its lack of the other chromophores, such as naphthalene diimide, porphyrin etc., which are often used for sensing applications.[14] The AIE-active receptors used in this study can be used for the naked eye detection of fluoride ions. The influence of selective fluoride binding can also be detected by both optical and naked eye, which is difficult to do with other receptors, which generally show one, but not both the signalling properties.[7,11]

2. Results and Discussion

2.1. Synthesis

Herein, we report a simple and easy-to-make chemosensor based on a cyclic urea as a proton-transfer signalling unit for the selective detection of F^- ion. The synthesised cyclic urea was discovered by accidentwhile attempting to prepare diamino-TPE (**7**) for other purposes (Scheme 1). Attempts to dehydrate the product from the reaction of lithium diphenylmethanide and *N,N′*-di-(tert-butoxycarbonyl)-3,4-diamino benzophenone with *p*-toluenesulfonic acid (p-TSA) gave the partially deprotected TPE compound **6**. Reaction of **6** with trifluoroacetic acid to complete the deprotection reaction failed to give the expected diamino-TPE compound **7**, but rather the cyclic urea compound **1**.

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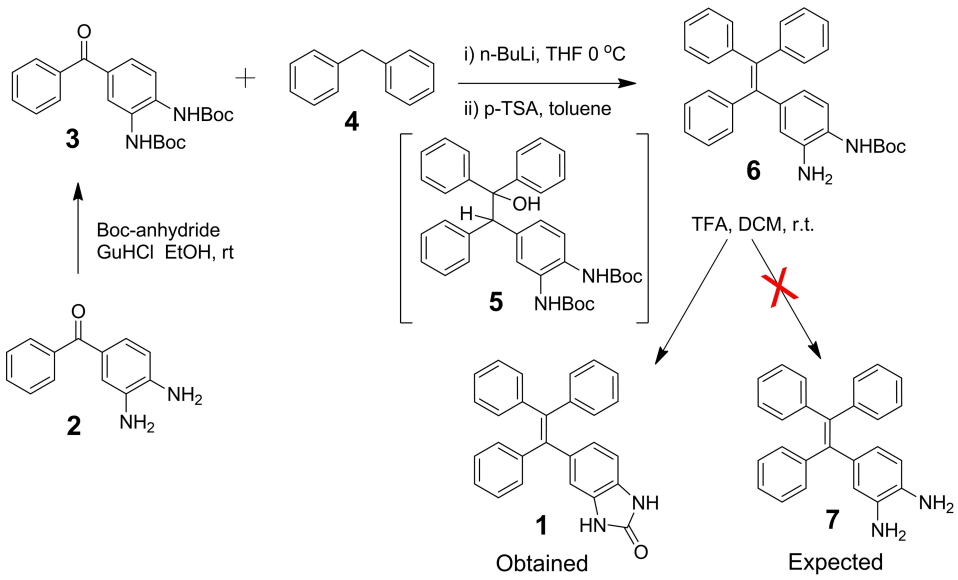

Scheme 1. Synthesis of the tetraphenylethylene-cyclic urea **1**.

In the course of characterizing compound **1**, we observed a color change in the presence of fluoride ions, prompting us to further investigate this behaviour. Various anions as their tetrabutylammonium (AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, I^-, Cl^- and F^-) or tetraethylammonium (CN^-) salts were used for the anion-detection studies with chemosensor **1**. Compound **1** was poorly soluble in many common organic solvents, including $CHCl_3$, CH_2Cl_2 and CH_3CN, therefore DMSO was selected for further studies.

2.2. Optical properties

Initially, we treated dilute DMSO solutions of **1** (20 μM) with 5 equiv. of various anions. As shown in Figure 1A,a pronounced effect was only observed for receptor **1** in the presence of F^- ion, in which the color of the solution changed from colorless to yellow-green; none of the other anions tested caused a similar observable color change. It is well known that TPE is an AIE-active luminophore and under UV-light (365 nm) receptor **1** in the presence of F^- showed a diminished fluorescence emission whereas the other anions did not show any effect (Figure 1B).

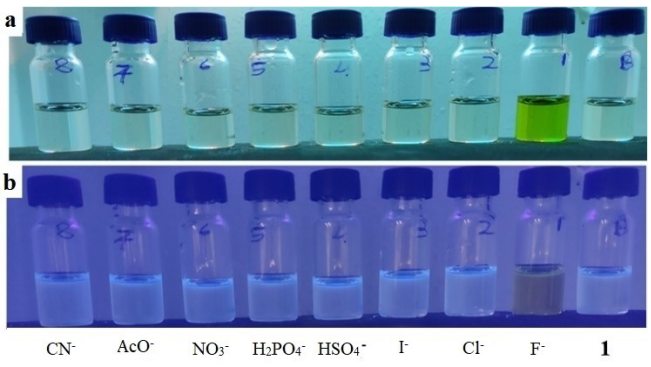

Figure 1. Solutions of **1** (20 μM) in DMSO upon addition of 5 equiv. of CN^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, I^-, Cl^-, F^-, and only **1** without any anions: A) under ambient light and B) under UV light 365 nm.

2.3. UV-vis absorption and ^{1}H-NMR titration

UV-vis absorption spectroscopy was used to study the anion sensing properties of receptor **1**. Typically, the UV-vis absorption spectrum of a 20 μM solution of receptor **1** in DMSO displayed a very strong absorption band at 330 nm, as shown in Figure 2a. The UV-vis absorption spectrum of **1** in the presence of CN^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, I^- and Cl^- (as their TBA salts, except CN^- used as TEA salt) showed no noticeable changes even at high concentrations of anion (up to 100 equiv.) Importantly, a significant red-shift of 55 nm for the peak maxima was observed, i.e. a band at 385 nm along with the appearance of new peak 290 nm (possibly related to intermolecular hydrogen bond interactions), was only observed in the spectrum of **1** after the addition of 5 equiv. of F^- ion (as its TBA salt). The interaction of **1** (20 μM) in DMSO with fluoride ion was also investigated by means of UV-vis spectroscopy titration experiments (Figure 2b). Upon addition of F^- (0-2.0 equiv.), the intensity of the band at 330 nm decreased, while the peak at 385 nm increased. Upon further addition of F^-, from 2.5-5.0 equiv., the band at 330 nm reaches the maximum. Thus, we believe that initially the F^- ions form a H-bonding complex with receptor **1**, disturbing the intermolecular H-bonding between neighbouring molecules. Upon further addition of F^- ions, the band at 385 nm reaches a maxima with a clear isosbestic point at 355 nm, thus, the new band at 385 nm.

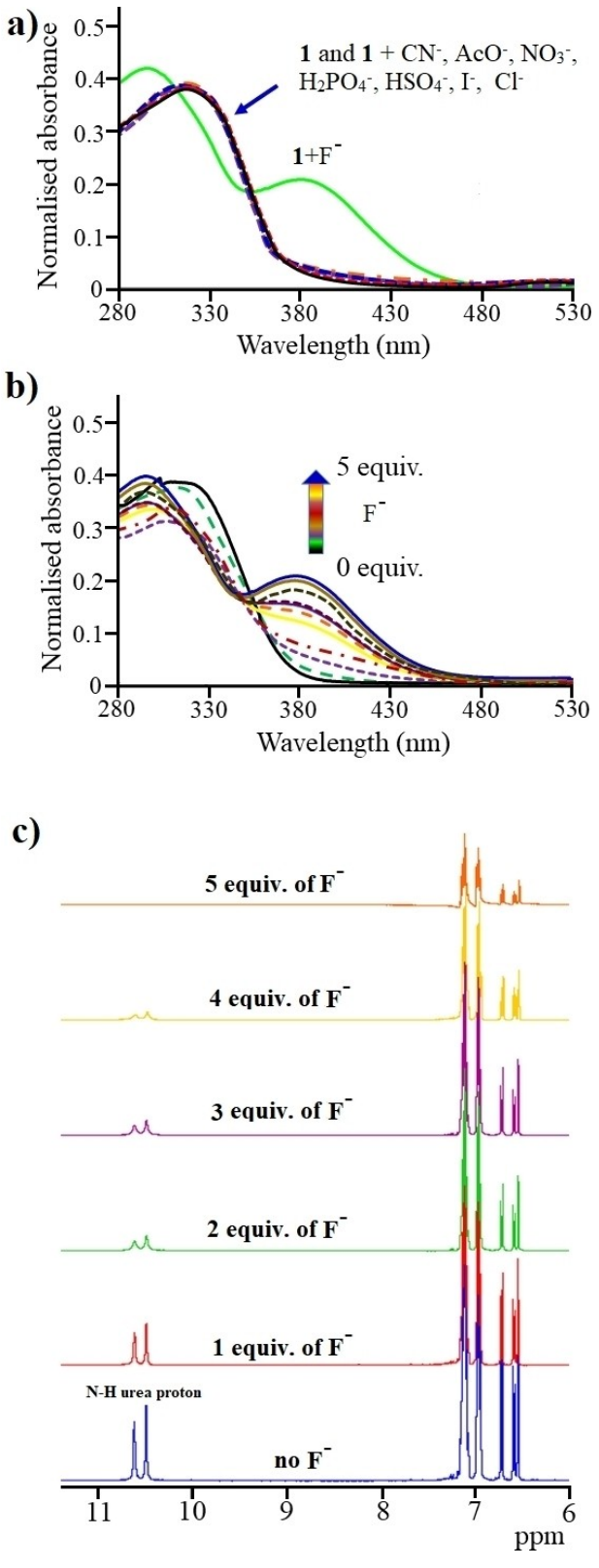

Figure 2. a) UV-vis spectra of **1** (20 μM) in DMSO and upon addition of 5 equiv. of various anions, such as CN^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, I^-, Cl^- and F^- (as their TBA salts except for CN^-, which was a TEA salt) b) UV-vis spectra of **1** (20 μM) in DMSO upon gradual addition of 0–5 equiv. of fluoride ion and c) ^{1}H NMR spectra of **1** in DMSO-d_6 upon addition of 0, 1, 2, 3, 4 and 5 eqiuiv. of fluoride ion, respectively.

To confirm complex formation of receptor **1** by F^- ion, ^{1}H NMR spectroscopic titration experiments were carried out in DMSO-d_6. As shown in Figure 2e, the two N–H protons of receptor **1** appeared at 10.52 and 10.61 ppm.Upon addition of 2.0 equiv. of F^- ions, the resonances were broadened and became less intense, and further addition of F^- up to 5.0 equiv. resulted in the complete disappearance of N–H proton resonances. These results are in agreement with the UV-vis absorption spectroscopic data in that the first equiv. of added F^- establishes a H-bond interaction with the N–H group in **1**, while further addition make the two hydrogen bifluoride ion complex. This, further confirm in the addition to the broadening and disappearance of the N–H resonances, the appearance of a new broad peak at 16.46 ppm was also observed (see ESI, Figure S1.), consistent with the formation of the hydrogen bifluoride ion, $[FHF]^-$.[17,18]

2.4. Fluorescence properties

To gain a deeper understanding of the optical properties of **1** in the presence of various anions, fluorescence emission spectroscopy was undertaken. As shown in Figure 3a, the fluorescence emission spectrum of a DMSO solution of receptor **1** (20 μM) shows a strong band at 445 nm (λ_{ex} = 330 nm, with quantum yield $\Phi = 1.3$), the intensity of which was significantly decreased by the addition of fluoride ion ($\Phi = 0.07$) and red-

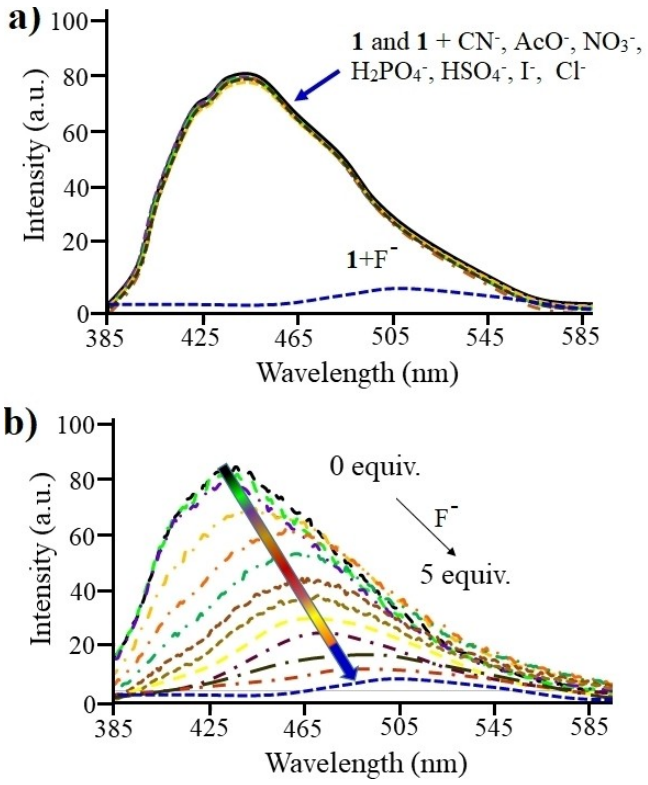

Figure 3. a) Fluorescence emission spectra of **1** in DMSO (20 μM, λ_{ex} = 330 nm) after addition of various ions (as TBA salts), and b) fluorescence titration spectra of **1** in DMSO (20 μM, λ_{ex} = 330 nm) upon gradual addition of F (0–5 equiv.)

shifted by 80 nm. In contrast, no decrease in fluorescence intensity was observed upon addition of CN^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, I^- and Cl^-. Similarly, no observable change was observed in the UV-vis absorption spectrum of **1** in the presence of other anions such as OH^-, ClO_4^- and SCN^-, (see ESI Fig. S2). To evaluate the selectivity of receptor **1** for F^- ion, the changes in emission upon gradual addition of F^- (0–5 equiv. λ_{ex} = 330 nm) in DMSO were measured, it clearly shows shift with quenching of the fluorescence (Figure 3b). Based on this experiment and supported by the UV-vis experiments (Figure 1a and 1b) and ^{1}H NMR spectroscopy (Figure 1c), the preferred interaction of receptor **1** to F^- through the strong hydrogen bonding with the urea N–H.

To further confirm that the detection of fluoride ion by receptor **1** was *via* strong hydrogen bonding with N–H groups, the polar protic solvent methanol was added to a solution of **1**-F^-. An immediate recovery of the fluorescence and reversion of the greenish-yellow color of the solution to its original bluish color (see Figure 4a) confirmed the reverse process, i.e. protonation of **1**-F^- by methanol. The binding stoichiometry of the final complex between **1** and F^- was determined using the Job's plot method of continuous variation (Figure 4b). The final concentration of receptor **1** and F^- was kept constant at 50 μM, with a continuous variation of the molar fraction of receptor **1**. The sharp peak confirms that the dominant species is the 1:2 complex with respect to receptor **1** and F^-, which is in agreement with the titration data from the UV-vis, ^{1}H NMR and fluorescence spectroscopic experiments. The association constant (K) of **1** for F^- ions from the fluorescence titration experiments was calculated to be 4.90×10^8 M^{-2} (Figure 3b and Figure S3) and the detection limit (LOD), calculated using 3δ/S, to be 30 μM, confirming the high selectivity of receptor **1** at low F^- concentrations in DMSO.[15]

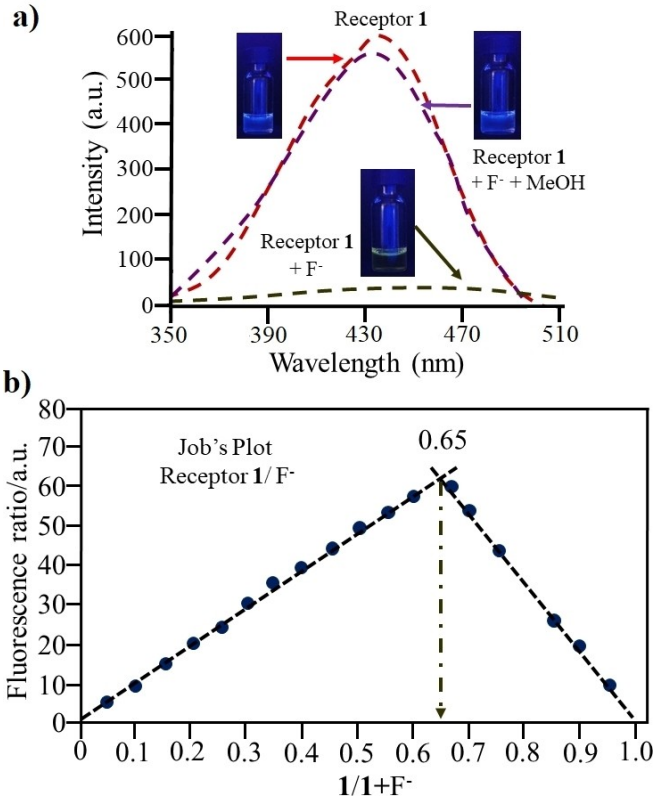

Figure 4. a) Fluorescence emission spectra of **1** (30 μM, λ_{ex} = 330 nm), after the addition of F^- (10 equiv.) and addition of methanol to complex **1**-F^- in DMSO, and b) Job's plot for the association of **1** with F^- in DMSO.

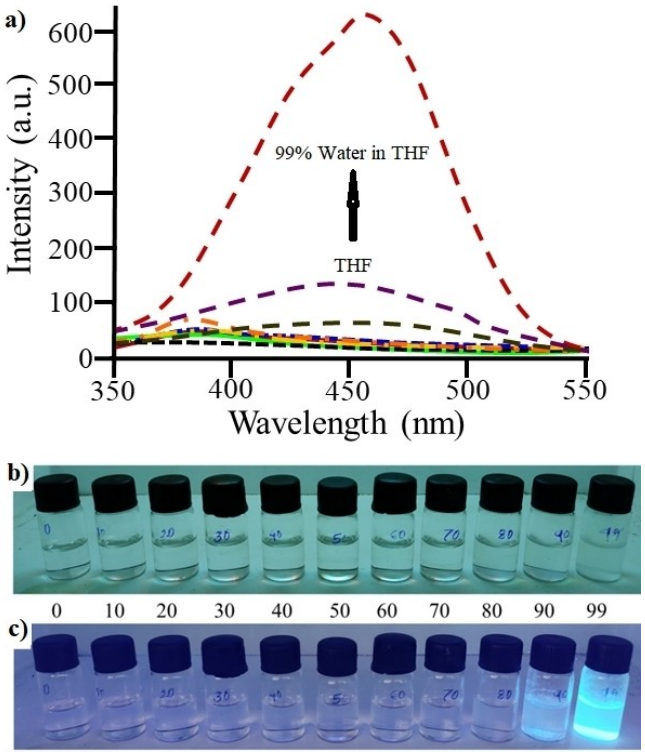

Figure 5. a) Fluorescence emission spectra of **1** (30 μM, λ_{ex} = 330 nm), after addition of water fraction 0–99% v/v in THF. Naked eye color changes of **1** (30 μM) after addition of water fraction 0–99% v/v in THF: b) under ambient light and c) under UV irradiation (365 nm).

The deprotonation and protonation effect was studied in the presence of NaOH and HCl, it can be seen that with NaOH deprotonation of N–H was observed and reverse in the presence of acid i.e. HCl (see ESI Fig. S4) and also supported by support by ^{1}H NMR, in which upon addition of NaOH (0.1 M) deprotonation was observed and addition of HCl recovered the protonal singnal of N–H to original position **1** (ESI Fig. S5). As expected only small changes was observed in UV-vis and fluorescence spectras, we believe deprotonation of N–H of urea with base doesnot affect on the structural TPE core, however, ^{1}H NMR (Fig. 5) shows complete deprotonation in the presence of base and reverse with HCl.

Further, a simple strip-based sensor was developed, as shown in Figure S6 of the ESI, which clearly shows that, under UV irradiation (365 nm), the fluorescence emission of receptor **1** is quenched when the strip is placed in fluoride solution, whereas solutions of other anions have no effect. Thus, this experiment clearly demonstrates the applicability of receptor **1** for the selective detection of fluoride anion.

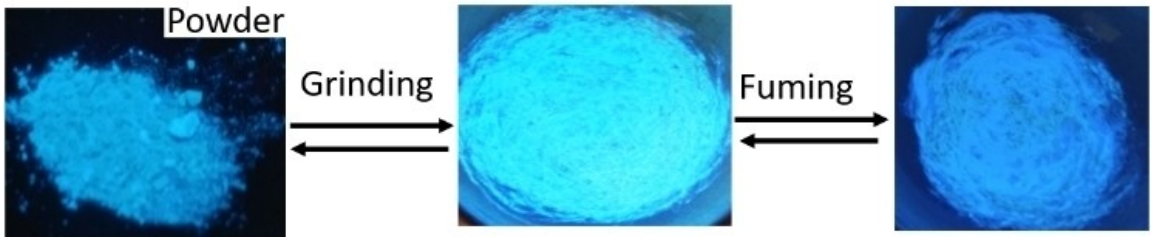

Figure 6. Fluorescence color changes of **1** upon grinding and fuming with methanol vapor. Iimages taken under UV excitation at 365 nm.

In THF solution, receptor **1** is non-emissive which can be 'switched on' by the addition of water. Therefore, the solvatochromic properties of **1** was evaluated at various water fractions (f_w). Compound **1** is non-fluorescence in water fractions between 10 and 70% but interestingly, **1** was shown to be emissive (λ_{max} 450 nm) when $f_w = 80\%$ (Figure 5a) (Figure 5a). Increasing f_w to ~99% resulted in an emission at 465 nm with a red-shift of 15 nm, which is an enhancement of 73 times compared with $\mathbf{f}_w = 0\%$. The quantum yield (Φ_F) of **1** in pure THF solution was 0.05% which was enhanced 22-fold to 1.98 and 6.65% at $\mathbf{f}_w = 90$ and 99%, respectively, calculated using Rhodamine B as a standard with $\Phi_F = 70\%$ in ethanol. This is clear confirmation that compound **1** is AIE active due to decreased solubility and increased molecular self-assembly as the water fraction is increased (Figures 5b and 5c). The AIE-activity of **1** can be seen under UV irridation at 365 nm by the naked eye, as shown in Figure 5c. Important to mention that compound **1** is non-emissive in THF ($\Phi = 0.05\%$) due to high solubility (Fig. 5a), however, **1** in DMSO partially aggregates, thus, produce fluorescence emission ($\Phi = 1.3\%$) in DMSO (Fig. 3a), comparable to emission produced from 90% water in THF (Fig. 5a). Since the TPE and their derivatives are highly emissive in polar solvents, so depending polarity of solvents fluorescence emission intensity increases due to which our compound was found to be highly emissive in DMSO compared to that of THF as the relative polarity of the DMSO is (0.444) found to be twice to that of THF (0.207). The results are similar to described by Chen *et al.* that TPE derivative shown to be higher fluorescence in DMSO as compared to other solvents such as DCM, ether, acetone, and DMF, respectively.[19]

Compound 1 also displays multicolored mechanochromic luminescence. In powder form, UV irradiation (365 nm) of **1** emitted a sky-blue fluorescence, which, upon grinding with a pestle turned bluish-green. Interesting, the original sky-blue colored fluorescence of **1** was recovered when the ground mixture was fumed with thevapor of a polar solvent such as methanol, as shown in Figure 6.

3. Conclusions

In summary, the new cyclic-urea based receptor **1** was synthesised and its utility in anion sensingand AIE-activity investigated. Receptor **1** was shown to highly selective for the detection of fluoride anions. The selective and sensitive recognition of fluorides anion over other anions, such as CN^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, I^-, OH^-, ClO_4^-, SCN^- and Cl^-, was confirmed by UV-vis absorption spectroscopy, a decrease in fluorescence and strip-based sensing. The disappearance of the N–H proton resonances in the ^{1}H NMR spectrum of the cyclic urea was attributed to formation of hydrogen bonding complex of fluoride iona with urea i.e. HF_2^-. Interestingly, reversible anion sensing was demonstrated upon addition of a polar solvent (methanol) to the complex of **1**-F^-. Finally, a strip test to detect F^- anions by receptor **1** was also developed. Thus, we believe that these types of cyclic urea derivatives may have real practical applications in sensing as well as for the preparation of fluorescence devices in solid state. Thus, we believe this and similar types of cyclic urea receptors may have real practical applications in the future.

Supporting Information Summary

The following data are available online: synthetic details, ^{1}H NMR, ^{13}C NMR spectra, The Benesi–Hildebrand analysis, strip based selective detection of fluoride anion can be found in ESI.

Author Contributions: D.N.N. synthesised the target molecules and fully characterised them by means of NMR, IR and mass spectroscopy; D.N.N. and G.A.Z. performed the UV-vis and fluorescence spectroscopy; S.V.B. (GU) outlined and supervised the work, analysed the data and drafted the manuscript. All co-authors contributed to and read the manuscript.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: colorimetric chemosensor · cyclic urea · fluoride ions · nuclear magnetic resonance · tetraphenylethylene

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