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1, 2, 4, 5-TETRASUBSTITUTED IMIDAZOLES (TSIM) FLUOROPHORE FOR SENSING APPLICATIONS

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ABSTRACT

Many studies have investigated the potential of 1,2,4,5-tetrasubstituted imidazoles (TSIM) as fluorophores for use in sensing. In regulated condensation processes facilitated by acidic or basic agents, TSIM derivatives are produced from easily accessible starting materials such 1,2-diketones and α-hydroxy ketones. Important for uses in environmental monitoring and medical diagnostics, their photophysical properties are improved by subsequent substitution at positions 1, 2, 4, and 5 on the imidazole ring. Research has shown that TSIM's fluorescence characteristics may be fine-tuned by adding various substituents, which in turn affect the emission intensities and wavelengths. The qualities are assessed by photophysical characterizations, which include measurements of absorption and emission spectra, with the use of excitation wavelengths that are optimized for absorption maxima. To further optimize TSIM derivatives for sensing applications, quantum yield measurements provide insights into fluorescence efficiency. The potential use of TSIM in sensitive and selective chemosensors is shown by the many applications that are covered, including selective detection methods such fluorescence "turn-on" responses to particular analyses like cyanide ions. The broad sensing capabilities and environmentally friendly synthesis procedures highlight the potential of TSIM derivatives as sensors for several analytical disciplines.

Keywords: fluorescence, medical diagnostics, TSIM fluorophores

INTRODUCTION

Modern sensing technologies rely on fluorescent molecules because of their sensitive and selective detection capabilities. These characteristics are vital for chemical analysis, medical diagnostics, and environmental monitoring. Because of their unusual structure and adjustable fluorescence properties, 1, 2, 4, 5-tetrasubstituted imidazoles (TSIM) stand out among them as potential fluorophores. A ring of imidazoles has two nitrogen atoms at positions one and three; these compounds are heterocyclic with five carbon atoms. A TSIM fluorophores is one that has certain imidazole ring replacements at positions 2, 4, and 5. Their photophysical characteristics are affected by this structural arrangement, which improves their solubility and stability—two qualities that are beneficial for sensing applications. A number of synthetic approaches, including condensation processes and substitution procedures, are used to accomplish the selective replacement of functional groups during the synthesis of TSIM fluorophores. The adaptability of TSIM fluorophores enables them to be tailored to individual sensing needs, guaranteeing command

over their fluorescence characteristics. A unique electronic structure of TSIM fluorophores is responsible for their fluorescence emission; specifically, the substitution pattern impacts the energy levels of molecular orbitals that are involved in the emission and absorption processes. In order to accommodate various sensing modalities, TSIM fluorophores may be tuned to emit light in the visible to near-infrared range and absorb light in the ultraviolet-visible region. It is possible to use TSIM fluorophores for environmental monitoring by testing samples of air, water, and soil for pollutants, heavy metals, and biological contaminants. Their fast fluorescence response and selective interactions make it possible to monitor complicated environmental matrices in real-time. The TSIM fluorophores have a low cytotoxicity and a high sensitivity when it comes to detecting biomolecules including nucleic acids, proteins, and enzymes in medical diagnostics. This makes them ideal for the creation of biosensors and cellular imaging, which in turn improves the diagnosis of diseases and the use of tailored medication. Latest developments aim to enhance the photostability, quantum yield, and spectrum features of TSIM fluorophores by using structural alterations and conjugation techniques. Adding recognition patterns to TSIM fluorophores or encasing them in nanomaterials increases their sensing potential, allowing for higher signal-to-noise ratios in complicated samples and multiplexed detection. Novel synthetic techniques and their potential uses in areas such as environmental monitoring networks and point-of-care diagnostics are the focus of forthcoming studies. If problems like signal interference, background noise, and biocompatibility can be resolved, the practical applicability of TSIM fluorophores in real-world sensing settings will be greatly expanded. The sensing potential of TSIM fluorophores is substantial due to their adaptability as a class of fluorescent compounds. Improving fluorescence-based sensing technologies relies on their distinctive structural characteristics, adjustable photophysical properties, and wide range of uses in environmental monitoring and medical diagnostics. Future advancements in sensing approaches and applications will be driven by ongoing research and development that further utilizes the capabilities of TSIM fluorophores. **(Alghamdi et al., 2023)**

LITERATURE REVIEW

(Mirjalili et al., 2012) Nano titanium chloride.The synthesis of 1, 2, 4, 5-tetrasubstituted imidazoles utilizing benzil, aromatic aldehyde, and an amine in the presence of ammonium acetate is facilitated by SiO2, an efficient, easily accessible, and reusable catalyst. Easy to follow and producing decent to exceptional results, the one-pot method.

(El-Remaily & Abu-Dief, 2015) The magnetic CuFe2O4 nanoparticles, which are safe for human consumption, have been engineered and studied. They have shown to be an effective catalyst in the synthesis of novel 1,2,4,5-tetrasubstituted imidazole derivatives, with high yields. It is

straightforward to work up the produced chemicals, and chromatographic procedures are not needed for product purification. Without significant loss, the catalyst may be recovered and reused for the following reactions.

(M. G. Kanawade et al., 2013) A number of imidazole derivatives with different substituents were prepared by reacting benzil with aldehyde, ammonium acetate, and aromatic primary amines in isopropanol using the catalyst tetrabutylammoniumbromide. Through the use of spectrum analysis (IR, 1 H NMR), the structures of these compounds were clarified. The antifungal and antibacterial properties of the newly synthesized compounds were tested. The activity was evaluated by comparing it to the reference medication and measuring it in terms of zone of inhibition.

(Sadeghi et al., 2019) Benzil, an aromatic aldehyde, primary amine, and ammonium acetate were combined in a one-pot, four-component reaction with tin tetrachloride supported on silica gel nanoparticles (SnCl 4 /SiO 2 NPs) to produce 1,2,4,5-tetrasubstituted imidazoles with improved yields. This process is both efficient and convenient. Long reaction durations, costly catalysts, huge quantities of catalysts, and laborious process or work-up are among the drawbacks that many of these procedures have, according to the data that was acquired. For instance, cyclic phosphoric acid and sulfonated carbon/silica composites both have longer half-lives (10 and 20 hours, respectively) and higher yields. With its low catalyst consumption, shorter reaction time, and good yields, our technology significantly outperforms alternative methods for 1,2,4,5-tetrasubstituted imidazole synthesis that are catalyzed by protic or Lewis acids.Refluxing temperature was used to react a combination of benzil, ammonium acetate, aniline or benzyl amine, and SnCl 4 /SiO 2 NPs in ethanol with aldehyde. The catalyst was filtered out of the mixture once the starting materials had vanished, which had been monitored by TLC. In order to get the pure chemical, the crude product was recrystallized from hot aq. ethanol by letting the solvent evaporate.

(Pratap Reddy et al., 2010) A four-component condensation process involving benzil or benzoin, aldehydes, amines, and ammonium acetate has been developed for the efficient synthesis of 1,2,4,5-tetrasubtituted imidazoles. This process can be carried out under microwave irradiation or classical heating conditions with the help of Aluminium Phosphate (AlPO4: a heterogeneous catalyst). The catalyst showed incredible reusability.

(Samai et al., 2009) The 3,2-dicarbonyl molecule, aldehyde, and ammonium acetate undergo a three-component cyclocondensation in methanol at moderate temperature using l-proline as a catalyst to produce 2,4,5-trisubstituted imidazoles. This process is simple, adaptable, and efficient. The method's potential was further investigated by synthesizing 1,2,4,5-tetrasubstituted imidazoles. High yields, inexpensive catalysts, simple work-up, and non-chromatographic product purification are the main benefits of this approach.

(Yamazaki et al., 1996) In moderate to high yields, 5-(1,2-dialkoxycarbonyl)hydrazino- and 5-(4-phenyl-3,5-dioxo-1,2,4-triazolidin-1 yl)imidazole derivatives were formed by electrophilic attack of azodicarbonyl compounds on the 5-position to specific 1,2,4-trisubstituted imidazoles. The reaction was quite sensitive to the kind and arrangement of imidazole ring substituents. Consequently, 2-methylsulfinylimidazoles and imidazoles that were 1,4,5-trisubstituted did not produce any response. The 1- or 1,2-cleaved product was obtained by reducing tetrasubstituted imidazoles with zinc dust-acid at different reaction temperatures; nevertheless, the hydrazino group was preserved.

(Mehrabi et al., 2021) A two-step cyclo-condensation reaction involving aryl amines, carbonitriles, and ethyl bromopyruvate or aryl amines and arylglyoxals in reflux-heated ethanol with iron (III) chloride (FeCl3) and sodium phosphate (Na2HPO4) as catalysts, respectively, was used to synthesize 1,2,5-trisubstituted and 4-amino-1,2,5-tetrasubstituted imidazoles. The spectroscopic data allowed us to determine the structures of all the compounds, and we were able to get them in high to outstanding yields.

RESEARCH METHODOLOGY

The synthesis of 1,2,4,5-tetrasubstituted imidazoles (TSIM) involves a series of carefully controlled steps designed to achieve the specific substitution patterns necessary for their unique fluorescence properties. Initially, readily available starting materials such as 1,2-diketones and α-hydroxy ketones are employed. The core imidazole ring is typically formed through condensation reactions, which are catalyzed by acidic or basic agents to facilitate the creation of the heterocyclic structure. Subsequently, functional groups are introduced at the 1, 2, 4, and 5 positions on the imidazole ring through various substitution techniques. These processes are meticulously fine-tuned to attain the desired photophysical characteristics, including specific fluorescence emission wavelengths and intensities. Different substituents are experimented with to optimize the fluorescence properties for applications like environmental monitoring and medical diagnostics. To evaluate the properties of the synthesized TSIM fluorophores, several photophysical characterizations are performed. The absorption and emission spectra of the fluorophores are recorded to determine their optical properties, with carefully selected excitation wavelengths matching the absorption maxima. Additionally, the quantum yield, which indicates the efficiency of the fluorescence process, is measured. These characterizations help in understanding and

optimizing the photophysical behavior of the TSIM fluorophores for their intended sensing applications.

DATA ANALYSIS

Tetrasubstituted imidazole core containing ESIPT Fluorescent Chemodosimeter for Selective detection of Cyanide in different medium

To detect cyanide anion (LOD 0.59 μM) utilizing fluorescence "turn-on" response in different media, the ESIPT-based tetrasubstituted imidazole core-containing organic scaffold/chemodosemeter "Rashid Ali et al., 2015" was developed and studied. Researchers have looked at synthesized polycyclic aromatic hydrocarbons' optoelectronic characteristics extensively. Molecules' photophysical behavior is improved when hetero atoms are added to the polycyclic aromatic framework, thanks to their distinct orbital interactions with the enlarged π-conjugated framework. Furthermore, fluorescence approaches outperform traditional detection techniques due to their low cost, ease of use, nondestructive nature, and exceptional sensitivity. The prospective chemodosimeter 3 showed fluorogenic and chromo responses that were visible to the naked eye, much better "turn-on" emission, and the ability to detect cyanide anion by cyclizing to generate an oxazole derivative 4. Deprotonation and isomerization of the potential phenolic protons to chelate cyanide anion is the initial step in this process. Consequently, the imine function was activated by the generated H+ ions in the medium, which facilitated the addition of cyanide to create the cyclic product 4 via a nitrile intermediate (a), as proposed in Scheme.1.**(Ali et al., 2015)**

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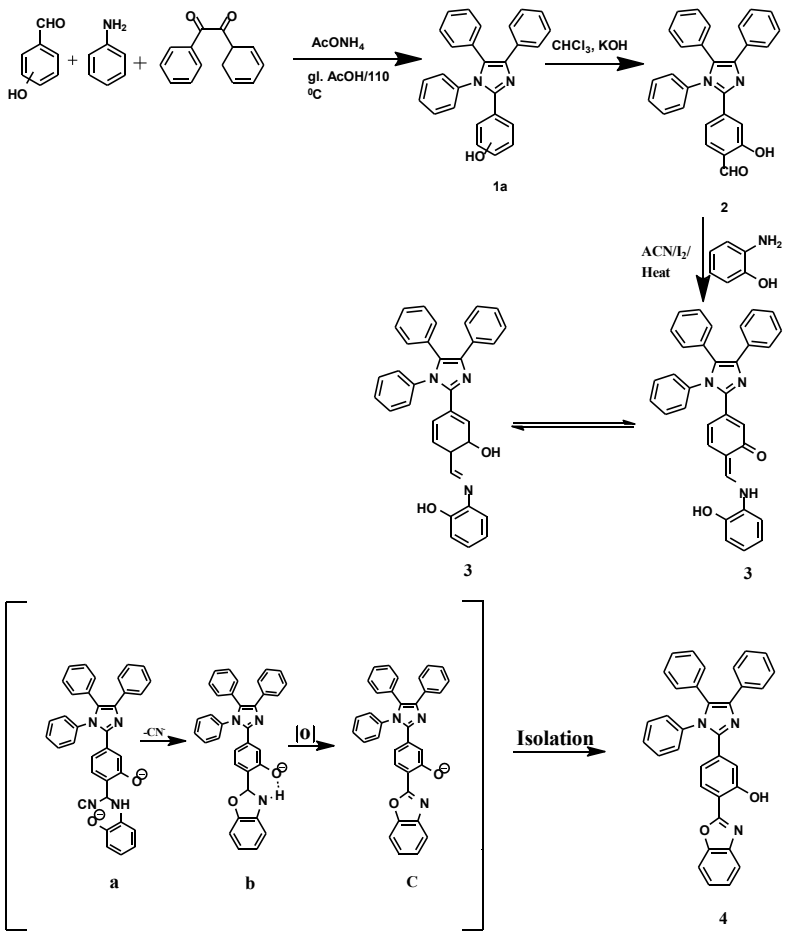

Scheme.1

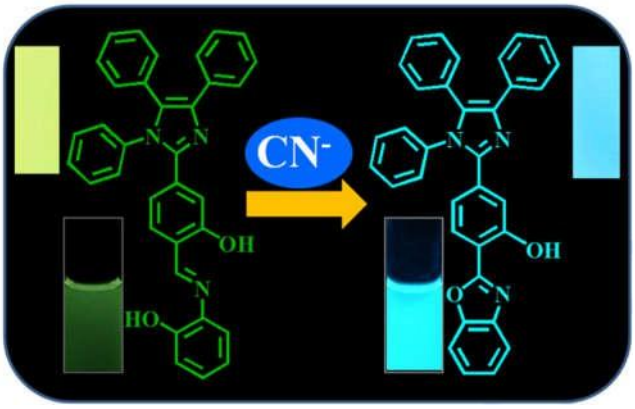

Fig.1

Polysubstituted Imidazoles as LysoTracker Molecules: Their Synthesis via Iodine/H_2O and Cell-Imaging Studies

Recently, numerous organic processes have been successfully examined in a water medium, avoiding the use of organic solvents due to their hazardous nature. Because water is a non-volatile, non-toxic, and non-flammable solvent, all reactions in aqueous media are naturally occurring. In light of the serious environmental pollution caused by many toxins, the "green chemistry" approach

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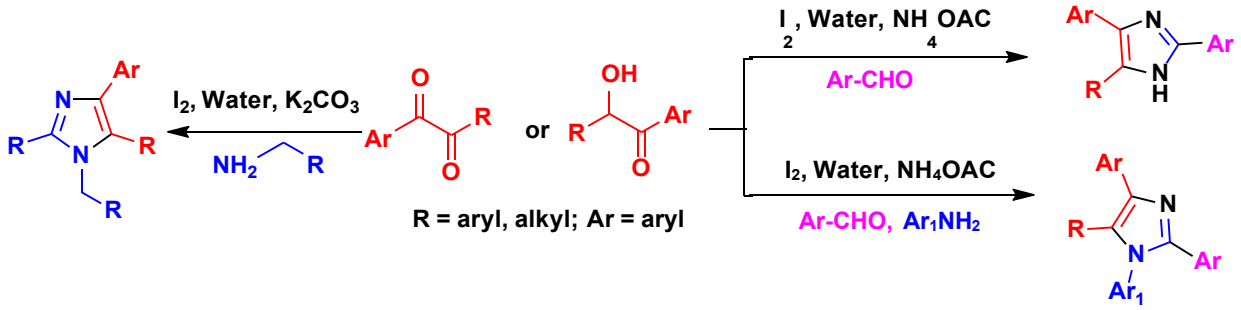
is now trending. Water is a green reaction medium, which is why there is a lot of interest in convergent processes that are synthetically simpler. "Saswati Adhikary et al., 2020" set out to address the worldwide need for ecologically friendly organic syntheses by creating a method for iodine-catalyzed small heterocycle synthesis using readily available starting materials. Their goal was to synthesize highly substituted imidazoles in an aqueous medium. This approach is regioselective, has a wide substrate range, and can manage synthesis on a gram scale. They looked at the photophysical properties of imidazole derivatives with three and four substituents. Substituted imidazole compounds showed strong blue fluorescence responses when subjected to 365 nm light. Some imidazole derivatives fluoresced when placed in dimethyl sulfoxide (DMSO). The imidazole derivatives exhibited improved fluorescence responses when combined with electron-donating groups like OH and NMe2, as well as highly conjugated groups like naphthyl. Three of them—3l, 8c, and 8f—had the most impressive fluorescence responses. Using 365 nm light, photographs were taken of the solid-state fluorescence of selected substances. **(Adhikary et al., 2020)**



Scheme 2.

Synthetic Strategies for Imidazoles from 1,2-Diketone and α-Hydroxy Ketone

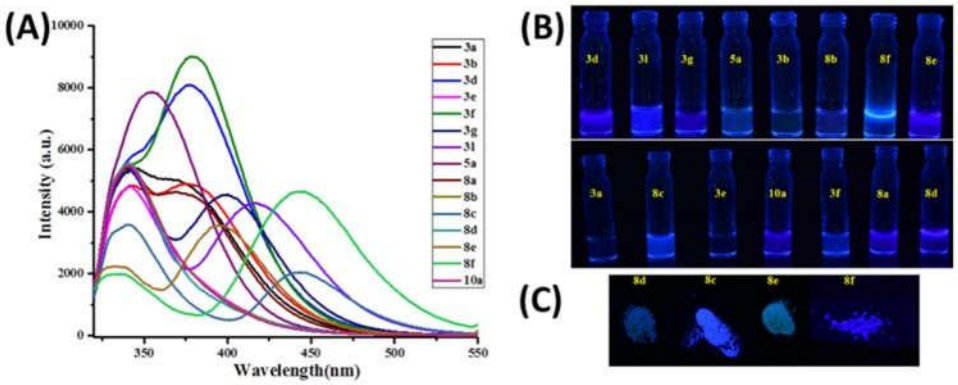


Fig.2. (A) Fluorescence spectra of some selected imidazole derivatives (500 nM) in DMSO (λex= 290−330 nm). (B) Fluorescence of 10 μM DMSO solution of selected compounds captured by irradiating at 365 nm. (C) Solid-state fluorescence of selected compounds captured by irradiating at 365 nm.

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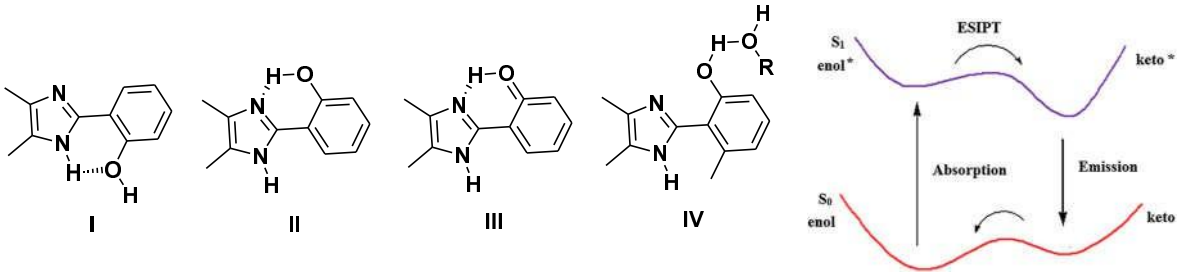
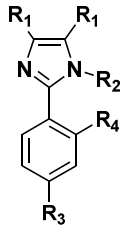
An Intramolecular Charge Transfer Fluorescent Probe: Synthesis, Structure and Selective Fluorescent Sensing of Cu^{+2}

Excited state tautomer production via ESIPT occurs in several aromatic compounds with phenolic hydroxy groups and intramolecular hydrogen bonding to adjacent heteroatoms (distance <2Å). The experimental identification of the ground state of the two separate intramolecular hydrogen-bound rotamers I and II was accomplished using the standard ESIPT-exhibiting 2-(2′-hydroxy-phenyl)benzazole compounds. When isomer II is excited by ESIPT, the synthesis of keto isomer III should take place, while isomer I should be excited to produce the usual emission for the hydroxy substituted 2-aryl imidazoles [dpip (3) and dptip (4)] in aprotic solvents. "Jayaraman Jayabharathi et al., 2011" discovered that only isomer II of dpip (3) and dptip (4) molecules remained stable in dioxane because their fluorescence spectra showed a single shorter-wavelength emission band and a small higher-wavelength shoulder peak. It was shown that the fluorescence intensity was increased by adding transition metal ions, including Co2+, Hg2+, Pb2+, and Cu2+. Accordingly, it seems that dpip (3) and dptip (4)'s radiation-less decay channel is inhibited by the binding of these ions. **(Jayabharathi et al., 2011)**





Compounds	R_1	R_2	R_3	R_4
1	CH_3	P-$C_6H_4CH_3$	F	H
2	C_6H_5	$C6H_5$	F	H
3	C_6H_5	H	H	OH
4	C_6H_5	P-$C_6H_4CH_3$	H	OH
5	C_6H_5	P-$C_6H_4CH_3$	H	OCH_3
6	C_6H_5	P-$C_6H_4CH_3$	OH	H

Fig.3. Rotameric forms of dpip (**3**) and dptip (**4**)

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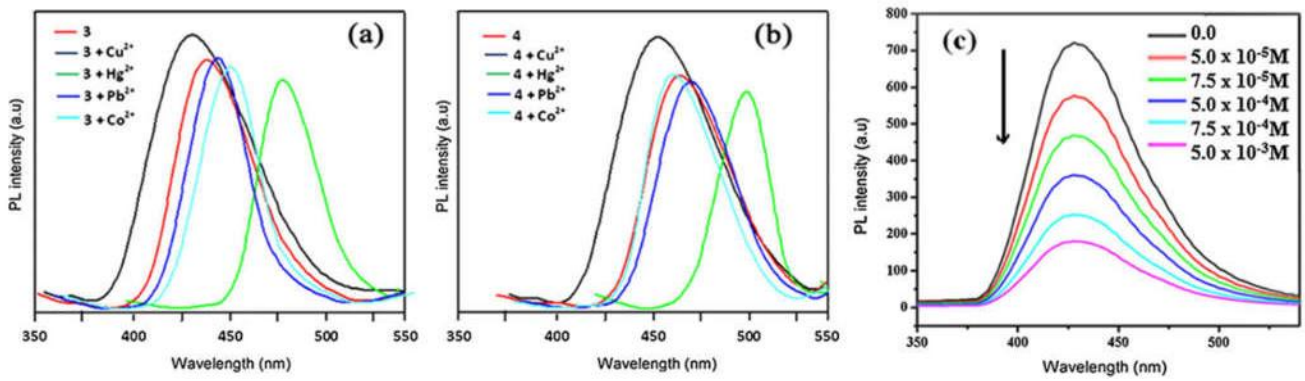

Fig.4. Fluorescence spectra of dpip (**3**) and dptip (**4**) in the presence of various metal ions.

Tetracoordinate Imidazole-Based Boron Complexes for the Selective Detection of Picric Acid

"Kunchala Dhanunjayarao et al., 2016" developed two boron compounds based on imidazole that detect PA. These complexes combine N,N-dimethylamine and N,N-diphenylamine units at the 4 position of the biphenyl group. The detection of explosives, especially PA, has not yet been demonstrated using imidazole-based N,O-chelated boron complexes, despite its investigation for electronic material applications. Figure 1 shows the boron-imidazole complexes used to create a highly sensitive and selective PA sensor. To explore the possible uses of compounds 1 and 2, they mixed 30 equiv of PA with a THF solution. Compound 2 lost its blue hue when subjected to a portable UV light, but compound 1 changed color noticeably from yellowish green to colorless (Fig.). This led us to conduct fluorometric titration studies in THF with PA, as suggested by the findings. Compounds 1 and 2's fluorescence responses to different PA concentrations are shown in Fig. To lower the emission intensity at 496 nm, compound 1 was slowly mixed with small quantities of PA. Adding 10 equiv of PA to compound 1 quenched about 90% of the emissions, while adding 26 equiv of PA to compound 1 achieved 100% emission quenching. The second compound followed the same trend. The emission response of the probes was also tested with several nitroaromatics and other analytes that may interfere, including benzoic acid (BA), phenol, nitromethane (NM), and nitrobenzene (NB), in order to ascertain the selectivity. There is no discernible quenching of fluorescence seen with other nitroaromatics and analytes in contrast to PA. Out of all these nitroaromatics, only PA showed 85% fluorescence quenching when 8 equiv of the analytes were added. **(Dhanunjayarao et al., 2016)**

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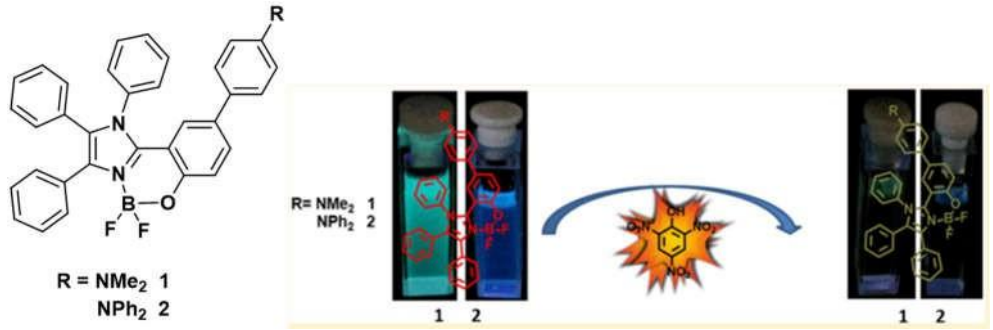

Fig.1

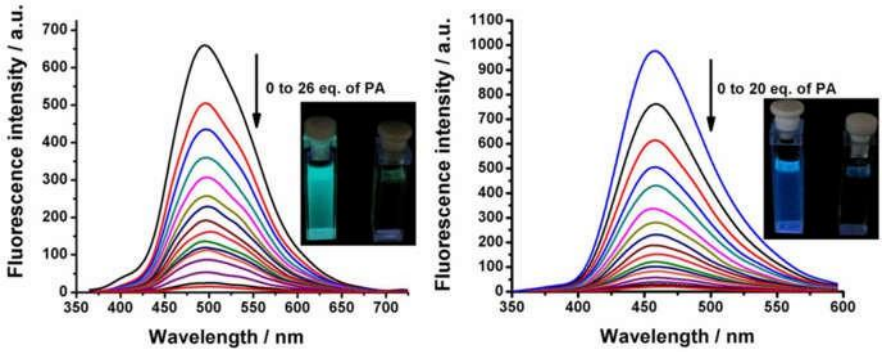

Fig.4. Fluorescence changes of probes **1** (left) and **2** (right) (43 μM) with the addition of different concentrations of PA (0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, and 26 equiv of PA) in THF when excited at 358 nm (**1**) and 327 nm (**2**) in THF. Inset. Color change under a UV lamp before (left) and after (right) the addition of PA.

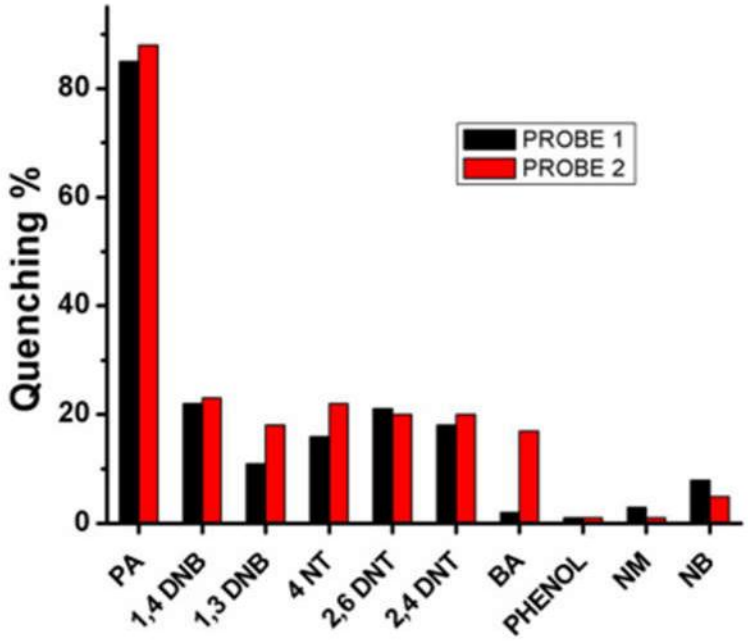

Fig.5. Fluorescence quenching efficiencies of probes (43 μM) after the addition of 8 equiv of different nitroaromatics and other analytes in THF: PA, 1,4-DNB, 1,3-DNB, 4-NT, 2,6-DNT, 2,4-DNT, BA, phenol, NM, and NB.

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Sensitive and Selective PET-Based π-expanded Phenanthrimidazole Luminophore for Zn^{2+} Ion

The newly synthesized (1-(4-methoxyphenyl)-1H-phenanthro[9,10-d]imidazol-2-yl]naphthalen-2-ol [MPPN] is described in "J. Jayabharathi et al., 2014" along with its synthesis, quantum chemistry investigations, and excited state intramolecular proton transfer (ESIPT) analyses. They also discussed a brand-new PET chemosensor for zinc ions that is based on phenanthrimidazole (MPPN). As part of their ongoing investigation into molecular hyperpolarizability, it was discovered that a phenanthrimidazole derivative creates a zinc complex that has the potential to serve as an NLO material. The luminescence of MPPN increases with the addition of zinc ions, even in minute amounts (Fig. a). As can be seen in Fig. b, the chromophore's affinity for other metal ions like Cd2+, Cu2+, and Mg2+ is substantially lower than that for Zn2+. The photo-induced electron transfer (PET) mechanism between MPPN and Zn2+, which is thermodynamically advantageous, may account for the increase in fluorescence intensity of MPPN upon interaction with Zn2+. Through the lone pair of electrons on the nitrogen atom of the azomethine and the recognition group on the phenanthrimidazole moiety, the Zn2+ ion binds to MPPN. The imidazole moiety on the nitrogen atom, where the lone pair of electrons originates, transfers electron density to the LUMO of the fluorophore, where the PET process takes place. It is evident that Zn2+ binding to MPPN via the nitrogen atom lone pair will obstruct the PET process and cause MPPN to glow more intensely when it interacts with Zn2+ ions (Scheme 1). **(Jayabharathi et al., 2014)**

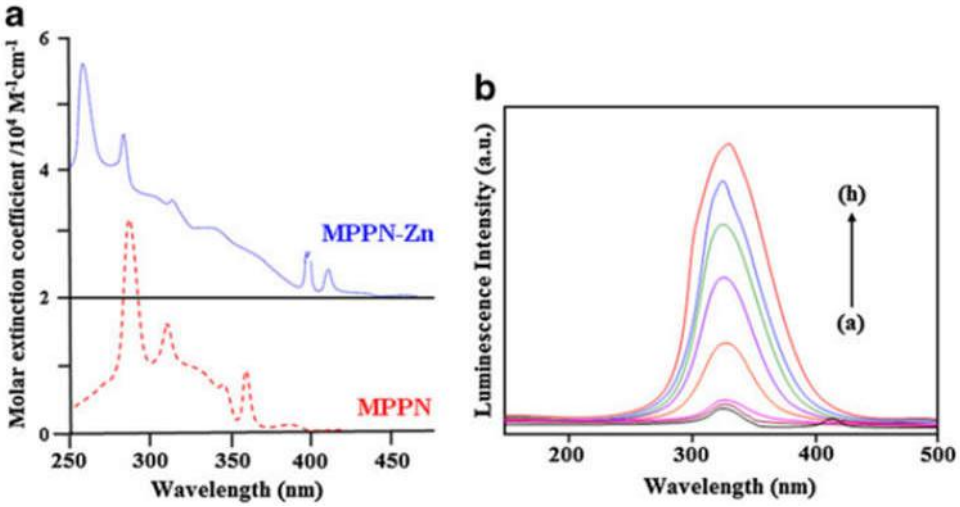

Fig. 7. Absorption spectra of MPPN and MPPN-Zn; **b.** Emission spectra of a solution of 1×10^{-5} M MPPN in the presence of different concentrations of Zn^{2+} $(NO_3)_2$.

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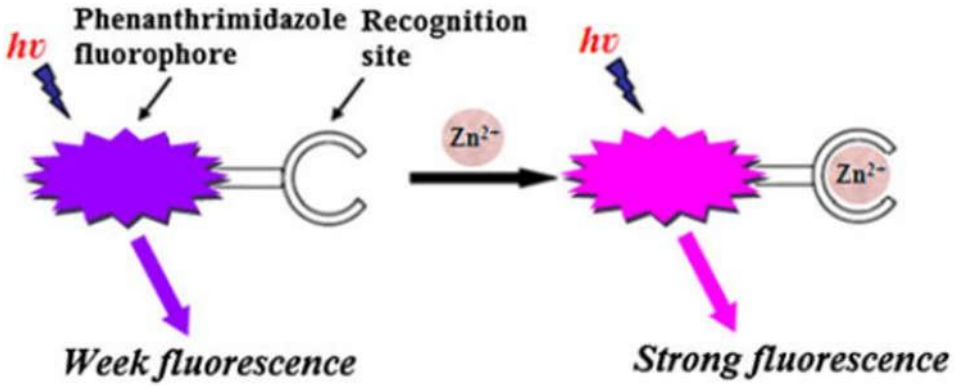

Scheme 1. Metal ion sensing by fluorescent photoinduced electron transfer (PET) indicators.

Fluoride anion detection based on the excited state intramolecular proton transfer (ESIPT) of 2-(o-hydroxyphenyl)imidazole induced by the Si–O cleavage of its silyl ether

"Xihui Li et al., 2014" presents a novel fluorescent chemosensor (SiOPI) that shows a fast, highly selective, and sensitive response to the fluoride anion. The sensor is based on the breakdown of the Si-O bond. Furthermore, the interference caused by hydroxide is effectively eliminated. The 2-(o-oxyphenyl)imidazole (OPI) group would be released from SiOPI after it was exposed to fluoride anion. This excited-state intramolecular proton transfer (ESIPT) capability of HOPI has been well-documented. Figure shows that HOPI has many potential applications beyond optoelectronic materials, one of which is as a fluorophore in fluorescent chemosensors. As the concentration of fluoride anion rose, the emission intensity at 475 nm increased as well, as seen in the inset of Figure. Increasing the concentration of fluoride anion to 100 equiv caused a reduction in emission, which was accompanied with red-shifted emission. Figure 2b shows that the emission intensity at 473 nm decreased with an astonishing red-shift of 53 nm when the fluoride concentration reached 100 equiv. Figure depicts the selectivity results achieved by adding 10 equiv of various anions (F-, Cl-, Br-, I-, OH-, NO3-, HSO4-, H2PO4-, PF6-, ClO4-, and AcO-) to the diluted THF solution of SiOPI one by one. The fluoride anion was the only one that changed the SiOPI emission spectra noticeably compared to the others. The absorption and emission spectra of SiOPI remained unaltered even after adding 10 equiv of tetrabutylammonium hydroxide, in contrast to SiOPIC, as shown in Figure. **(Li et al., 2014)**

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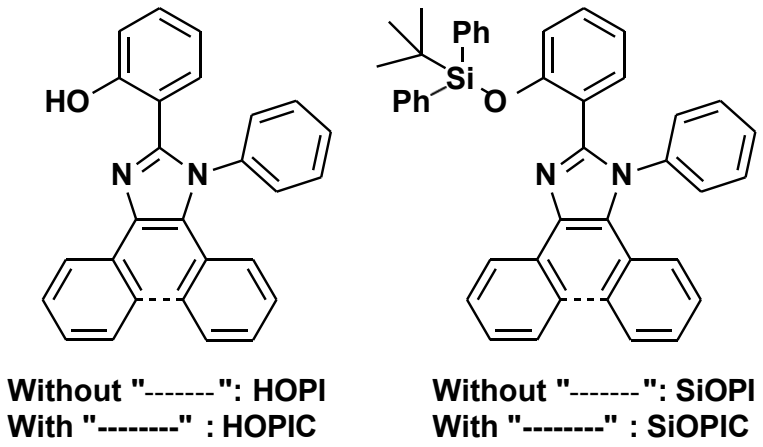


Fig.8

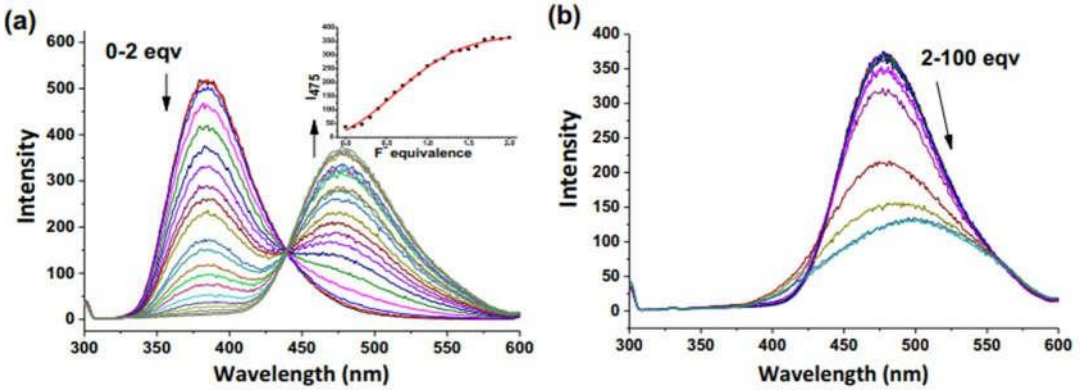


Fig.9. Emission spectra of SiOPI with the addition of F^-, (a) 0–2 equiv F^-; (b) 2–100 equiv F^-.

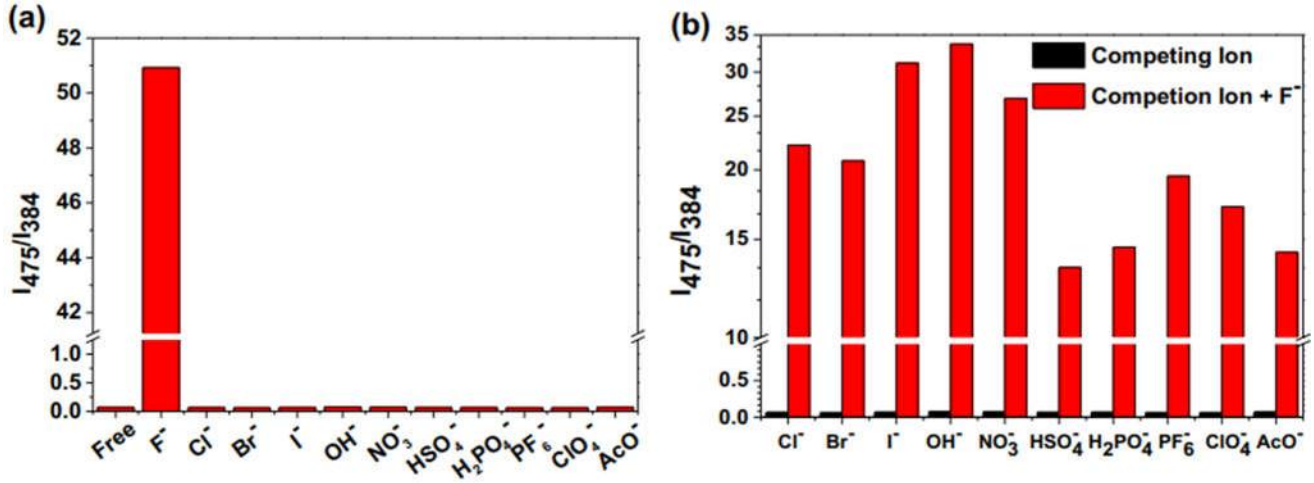
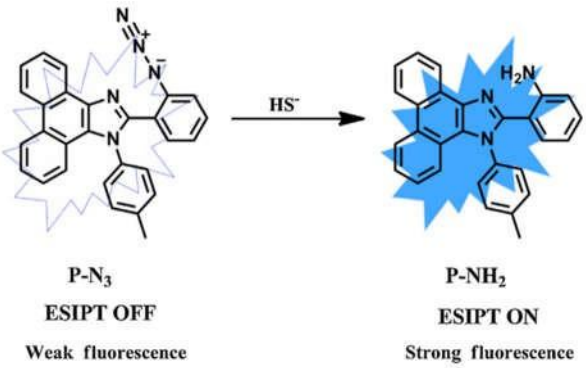


Fig. 10. (a) **I_{475}/I_{384}** of **Si–OPI** in 2 equiv F^- or 10 equiv other anions in THF; (b) **I_{475}/I_{384}** of **Si–OPI** toward other anions in THF, black bars: 10 equiv of various anions; red bars: 10 equiv of various anions plus 2 equiv of F^-.

A tetraphenylimidazole-based fluorescent probe for the detection of hydrogen sulfide and its application in living cells

"Biao Gu et al., 2015" was the first to suggest using the tetraphenylimidazole dye in conjunction with the optical probe P-N3 to detect H2S. To summarize, probe P-N3 was created by combining

the tetraphenylimidazole moiety with the azido group as the recognition unit. The azido group may be able to extinguish the fluorophore's fluorescence since the ESIPT process is impeded. The tetraphenylimidazole group released a great deal of fluorescence due to the ESIPT-regulated off-on response that followed the H2S-induced reduction of azide to amine. Proof of the proposed process was checked by comparing P-N3 fluorescence in the presence and absence of H2S. As seen in Figure, the only way to significantly amplify the fluorescence of P-N3 was to include HS-. The probe's fluorescence, however, was almost unaffected by the addition of more analytes. Furthermore, considering the relatively high concentration of the probable reducing species in the biological system or the test condition, they examined the interference of these species at a 1 mM level in the detection of HS-. These species include DTT, 2-ME, Cys, Hcy, GSH, and sulfite. Figure shows that when these species were added to the probe P-N3 solution along with HS-, there was a clear increase in fluorescence. This suggests that the interference from these chemicals was minimal and that P-N3 could be used to detect H2S even when these species are present. All things considered, probe P-N3 has excellent HS-detection selectivity. **(Gu et al., 2015)**



Scheme 1. Proposed reaction mechanism for H_2S.

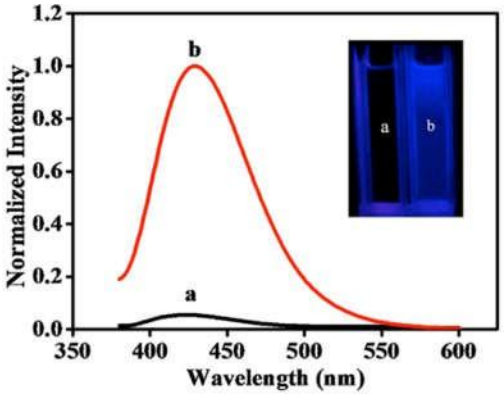


Fig. 11. Fluorescence spectra of **P-N3** (10mM) before (a) after (b) the incubation with 10 equiv. of NaHS in PBS buffer (0.01 M, pH 7.4, containing 10% ethanol, v/v) with λ_{ex} = 300 nm. The insets show the photos of samples illuminated by UV light of 365 nm.

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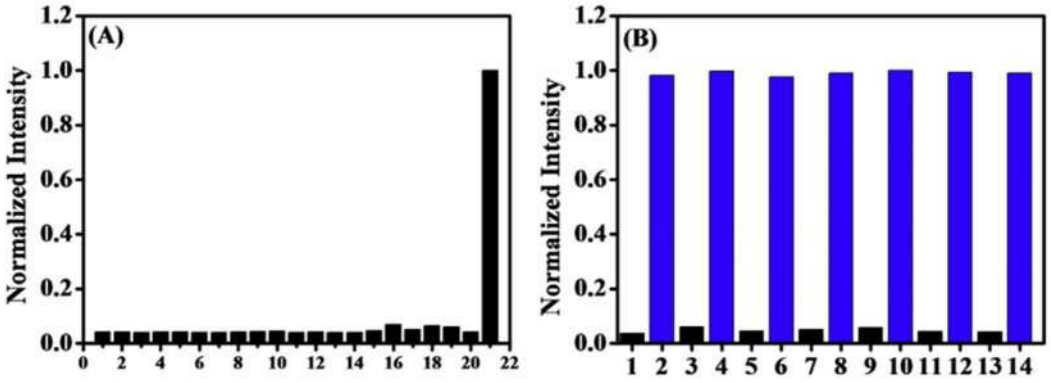

Fig.12.(a) Fluorescence responses of **P-N_3** (10mM) in the present of species (0.5 mM) in PBS buffer (0.01 M, pH 7.4, containing 10% ethanol, v/v): (1) no addition; (2) H_2O_2; (3) $S_2O_3^{2-}$; (4) citrate; (5) Cl^-;(6) CO_3^{2-}; (7) F^-; (8) HCO_3^-;(9) HPO_4^{2-}; (10) N_3^-; (11) NO_2^-; (12) NO_3^-; (13) OAc^- ; (14) SO_4^{2-};(15) HSO_3^-;(16) DTT; (17) 2-ME;(18) Cys;(19) Hcy; (20) GSH; (21) HS^-. (B) Fluorescence responses of **P-N_3** (10mM) at 436 nm toward various analytes in PBS buffer (0.01 M, pH 7.4, containing 10% ethanol, v/v). Black bars represent the addition of a single analyte (1 mM, from left to right: (1) none; (3) DTT; (5) HSO_3^{2-}; (7) 2-ME; (9) Cys; (11) Hcy; (13) GSH). Blue bars represent the mixing corresponding sulfur compounds with HS^- solution (70mM).

Supramolecular aggregates as sensory ensembles

Perylene derivatives, pyrene derivatives, tetra-phenylethylene derivatives, metallophilic species, and metal-organic frameworks are the basic building blocks of sensory materials, often taking the shape of tiny molecular sensors with a simpler structure that aggregate. Particularly, fluorescent switches, molecular transistors, and sensors have made extensive use of perylene-3,4:9,10-bis(dicarboximides) (PBIs), which have garnered a lot of interest as ideal fluorescent dyes. Their intense fluorescence in both monomeric and tiny oligomeric forms, as well as their great electron accepting capabilities, have made them effective fluorophores in sensor design. A 32-electrode H2O2-selective fluorescence sensor was developed by "Zhang et al., 2016" using a pyridinium bridge connecting a TPE core to an arylboronate ester, an H2O2-reactive group. Image 1. Since the Pyridinium Bridge renders 32 water-soluble, it may live as a monomer and does not emit any light. The extremely selective fluorescence detection of H2O2 is made possible by the oxidative hydrolysis of 32 by H2O2, which produces the much less water-soluble product 33. This product aggregates and becomes highly luminous. **(Wang et al., 2016)**

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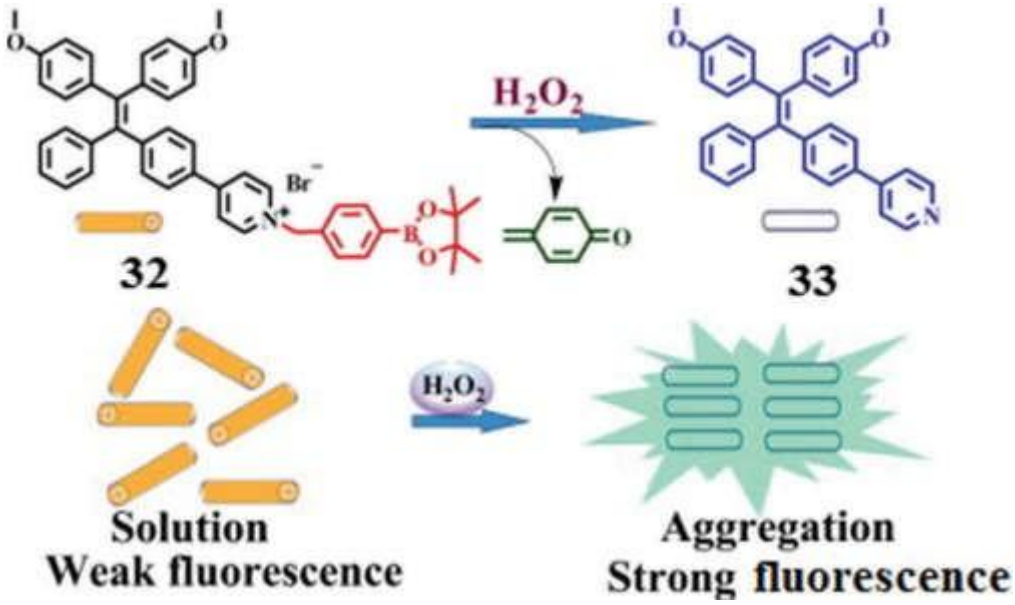

Fig.13. Rationale for the fluorescence turn-on detection of H_2O_2 using **32** which upon oxidative hydrolysis leads to the neutral TPE product **33** that undergoes aggregation.

ESIPT-capable 2,6-di(1H-imidazol-2-yl)phenols with very strong fluorescent sensing signals towards Cr(III), Zn(II) and Cd(II): molecular variation effects on turn-on efficiency

"Abiodun O. Eseola et al., 2018" states that a variety of 2,6-di(1H-imidazol-2-yl)phenols with different structures and electronic properties have been developed and tested as fluorescent chemosensors for Cr3+, Zn2+, and Cd2+. These phenols were compared to the 4,5-diphenyl-2-(3-(4,5-diphenyl-1H-imidazol-2-yl)phenyl)-1H-imidazole, which is ESIPT-incapable. Single crystal structures showed the ideal sequence of intramolecular hydrogen bonds and potential coordination states. The sensitivity experiments show that the 2,6-bis(4,5-diphenyl-1H-imidazol-2-yl)-4-methylphenol derivatives are appealing as Cd2+ sensors and show promise as Cr3+ and Zn2+ sensors.The fluorescence in Fig. 1 shows a linear rise up to one equivalent of Cr3+ is added, as shown in a titration experiment between ligand and Cr3+. With the addition of more Cr3+, the emissions become less intense over time. Job plots for the ligand versus Cr3+ or Zn2+ show that the fluorescent species responsible for turn-on emissions are produced in a 1:1 mole ratio. For instance, it is well-known that excited state intramolecular proton-electron transfer (ESIPT) increases the precision of fluorescence detection by avoiding self-absorption, thanks to the substantial Stoke-shifts it produces. It is feasible to enable ESIPT in fluorophores by pairing an active proton with a base donor. The F/Fo values for different cations, such as K+, Ca2+, Ba2+, NH4+, Cr3+, Mn2+, Fe2+, Co2+, Ni2+, Cu2+, Zn2+, Cd2+, Ag+, and Hg2+ ions are compared in the figure, with matching F/Fo values for Cr3+ and Cd2+ shown as bar charts, and λmax(Em) ~485

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nm. Figure 4 shows that the highest emission wavelength of Zn2+ is 440 nm, and the results of a similar comparative study on its F/Fo at its blue-shifted emission wavelengths are collected. **(Eseola et al., 2018)**

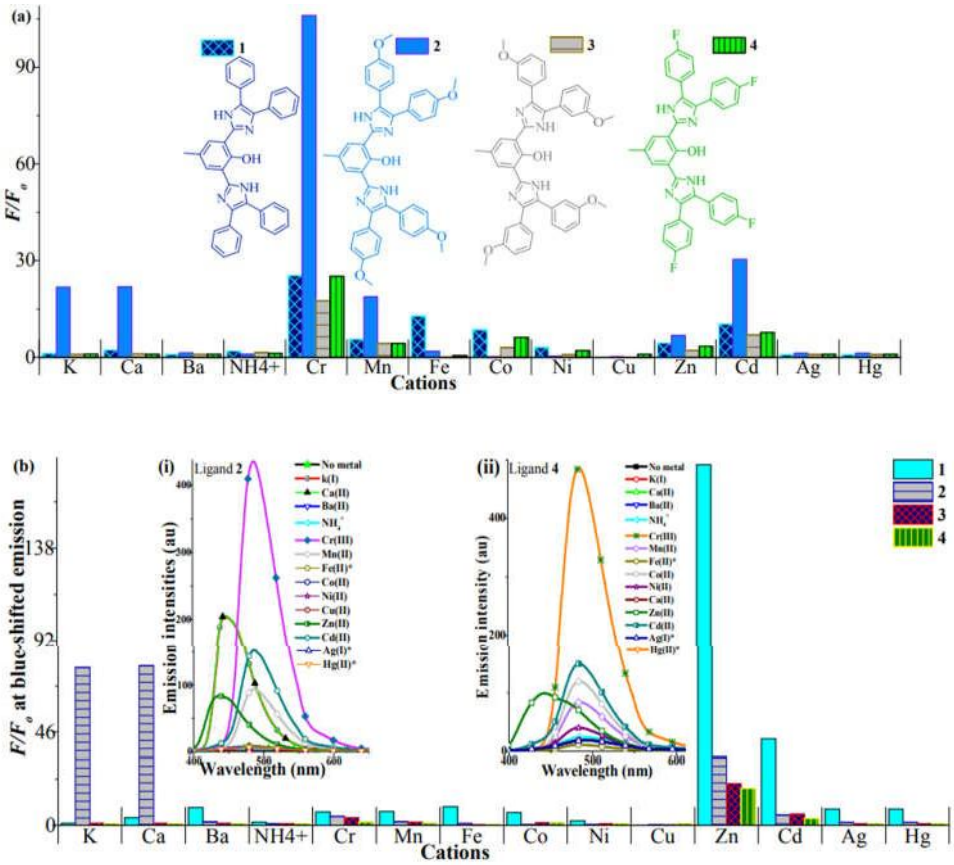

Fig.14. Bar charts comparing F/F_o values in the presence of various cations for probes **1 – 4:** (a) Shows extents of turn-on from other cations alongside Cr^{3+} and Cd^{2+} at ~485 nm; (b) Shows extents of turn-on from other cations alongside Zn^{2+} at ~440 nm while insets (i) and (ii) present the strong selectivity for Cr^{2+} as well as blue shifted Zn^{2+} emission turn-on.

Fig.15. Fluorescence of various cations showing visible sensor strength for Cr^{3+} and the weakness of interference from other cations.

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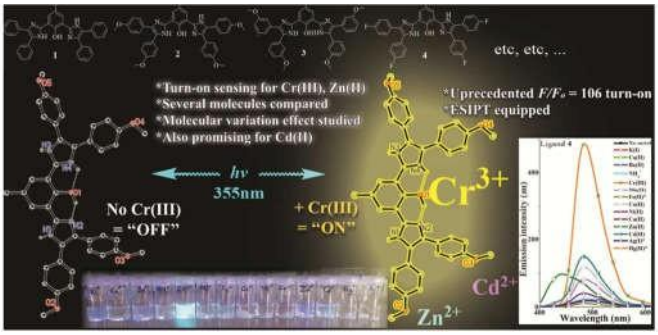

Fig.16. Derivatization influence was studied for twelve 2,6-di(1H-imidazol-2-yl)phenols, strong fluorescent sensitivity for Cr(III) is reported while Zn(II)/Cd(II) sensing potentials also appeared.

CONCLUSION

TSIMs are a promising family of fluorophores with many potential uses in sensing technologies because of their versatility. Their chemical structure can be precisely controlled by the synthesis processes described, which in turn affects their photophysical characteristics, which are important for detection systems based on fluorescence. Improving its usefulness for diverse sensing applications, researchers have used rigorous substitution techniques to adapt TSIM derivatives to display precise fluorescence emission wavelengths and intensities. In this context, studies have shown that TSIM derivatives are good chemosensors, especially for detecting target analytes with "turn-on" fluorescence responses, including metal cations and cyanide ions. Their sensitivity, selectivity, and simplicity of detection have led to several applications, which highlight their promise in environmental monitoring, medical diagnostics, and beyond. Recent developments in green chemistry, such as sustainable reaction conditions and aqueous-based syntheses, demonstrate the dedication of TSIM researchers to eco-friendly methods. To increase their usefulness in practical sensing situations, future studies may aim to better optimize TSIM derivatives for increased sensitivity. There has been great progress in sensor technology with the synthesis and use of TSIM fluorophores, which bodes well for the future of analytical chemistry that relies on fluorescence.

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