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Cu²⁺ metal ion

Selective quenching of benzimidazole derivatives by Cu²⁺ metal ion

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HIGHLIGHTS

G R A P H I C A L A B S T R A C T

- The decrease in the fluorescence intensity shows binding of copper with benzimidazole derivatives.
- ► FT IR spectra confirm the binding of benzimidazole derivative with Cu²⁺ metal ion.
- ► In the case of Fe³⁺, Mg²⁺, Ag⁺, K⁺, and Na⁺ metal ions the fluorescence quenching is very low.
- Crystalline benzimidazole derivatives (5) are triclinic crystals.

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ABSTRACT

It is a very big challenge to develop a Cu^{2+} selective fluorescent sensor with the ability to exclude the interference of some metal ions such as Fe^{3+} , Mg^{2+} , Ag^+ , K^+ and Na^+ . Herein, we report a fluorescence quenching of some benzimidazole derivatives (**1–6**) with Cu^{2+} metal ion. These benzimidazole derivatives have been shown to bind copper ions resulting in quenching of its fluorescence. The response to Cu^{2+} is rapid, selective and reversible upon addition of a copper chelator. These benzimidazole derivatives were characterized by ¹H, ¹³C NMR mass and elemental analysis. XRD analysis was carried out for 1-(4-meth-ylbenzyl)-2-*p*-tolyl-1H-benzo[d]imidazole.

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SPECTROCHIMICA ACTA

Introduction

The imidazole ring system is the most important substructures found in a large number of natural products and pharmacologically active compounds. For example, the amino acid histidine, the hypnotic agent etomidate [1], the antiulcerative agent cimetidine [2] the proton pump inhibitor omeprazole [3], the fungicide ketoconazole [4] and the benzodiazepine antagonist flumazenil [5] are imidazole derivatives. In recent years, substituted imidazoles are substantially used in ionic liquids [6] that have been given a new approach to 'Green Chemistry'. The imidazole compounds were also used in photography as photosensitive compound [7]. Literature survey reveals the several methods for synthesizing them, mainly using nitriles and esters [8–10] as the starting substrates.

* Corresponding author. Tel.: +91 9443940735. E-mail address: jtchalam2005@yahoo.co.in (J. Jayabharathi). An important property that makes imidazole derivatives more attractive as a chelator is the appreciable change in its fluorescence upon metal binding. Therefore, imidazole derivatives have been used to construct highly sensitive fluorescent chemisensors for sensing and imaging of metal ions and its chelates in particular those with Ir³⁺ are major components for organic light emitting diodes [11,12] and are promising candidates for fluorescent chemisensors for metal ions.

The construction of fluorescent devices for the sensing and reporting of chemical events is currently of significant importance for both chemistry and biology [13–15]. Fluorescence proffers high sensitivity among the many signal types available. Cu^{2+} is an important co-factor of several enzymes and plays a significant role in several cellular pathways and disease pathogenesis [16–18]. So the chemosensors such as benzimidazole derivatives, which can be targeted to specific organelles for detection of Cu^{2+} , would prove highly beneficial. In that regard, it is essential to understand the

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binding of Cu^{2+} to benzimidazole derivatives. In this paper we report binding effect of some novel benzimidazole derivatives with Cu^{2+} metal ion by solution spectral studies.

Experimental

Spectral measurements

The ultraviolet-visible (UV-vis) spectra of the benzimidazole derivatives were measured in an UV-vis spectrophotometer (Perkin Elmer Lambda 35) and corrected for background absorption due to solvent. Photoluminescence (PL) spectra were recorded on a (Perkin Elmer LS55) fluorescence spectrometer. NMR spectra were recorded on Bruker 400 MHz NMR spectrometer. Mass spectra were recorded on a Varian Saturn 2200 GCMS spectrometer.

General procedure for the synthesis of ligands

A mixture of corresponding aldehyde (2 mmol), *o*-phenylenediamine (1 mmol) and ammonium acetate (2.5 mmol) has been refluxed at 80 °C in ethanol. The reaction was monitored by TLC and purified by column chromatography using petroleum ether: ethyl acetate (9:1) as the eluent.

Results and discussion

Absorption characteristics of benzimidazole derivatives – Cu^{2+} metal ion

The absorption spectra of benzimidazole derivatives in presence of Cu^{2+} metal ion at different concentration and also in their absence are displayed in Fig. 1. The Cu^{2+} metal ion enhance the absorbance of benzimidazole derivatives remarkably without shifting its absorption maximum. This indicates that the Cu^{2+} metal ion do not modify the excitation process of the ligand. The enhanced absorption appeared around 290 nm observed with the Cu^{2+} metal ion are due to binding of the benzimidazole derivatives on Cu²⁺ metal ion (Scheme S1).

FT-IR characteristics of benzimidazole derivatives – Cu^{2+} metal ion

Fig. 2 shows the FT-IR spectra of benzimidazole derivative **1** (solid line) and benzimidazole derivative bound to the Cu²⁺ metal ion (broken line). The spectrum of pure benzimidazole derivative shows the >C=N stretching vibration at 1600 cm⁻¹. This band is shifted in benzimidazole derivative bound to copper metal ion a new band appears at 1619 cm⁻¹ in place of 1600 cm⁻¹. These observations show that the benzimidazole derivative bind with Cu²⁺ metal ion.

Fluorescence quenching characteristics

Addition of Cu^{2+} metal ion to the solution of benzimidazole derivatives resulted in the quenching of its fluorescence emission. Fig. 3 displays the effect of increasing concentration of Cu^{2+} metal ion on the emission spectrum of benzimidazole derivatives (**1–6**).



Fig. 2. FT-IR spectra of benzimidazole derivative **1** (solid line) and benzimidazole bound with Cu^{2*} metal ion (broken line).



Fig. 1. Absorption spectra of benzimidazole derivatives (1-6) in presence and absence of Cu²⁺ metal ion.

The apparent association constants (K_{app}) have been obtained from the fluorescence quenching data using to the following equation

$$1/(F_0 - F) = 1/(F_0 - F) + 1/K_{app}(F_0 - F) [Cu^{2+} metal ion]$$
(1)

where K_{app} is the apparent association constant, F_0 is the initial fluorescence intensity of the benzimidazole derivatives, F is the fluorescence intensity of the benzimidazole derivatives bound with Cu²⁺ metal ion and F is the observed fluorescence intensity at its maximum. A good linear relationship between $1/(F_0-F)$ and the reciprocal concentration of Cu²⁺ metal ion is seen. From the slope, the values of apparent association constants (K_{app}) have been assessed for benzimidazole derivatives-Cu²⁺ metal ion.

The fluorescence quenching behavior is usually described by Stern–Volmer relation:

$$I_0/I = 1 + K_{\rm SV} [Q]$$
 (2)

where I_0 and I are the fluorescence intensities in the absence and presence of quencher, K_{SV} is the Stern–Volmer constant related to the bimolecular quenching rate constant and Q is the quencher. Addition of Cu²⁺ metal ion to a solution of benzimidazole derivatives result in quenching of fluorescence emission. Typical linear S–V plot for steady-state fluorescence quenching of benzimidazole derivatives by Cu²⁺ metal ion is shown in Fig. S1. In case of Fe³⁺, Mg²⁺, Ag⁺, K⁺ and Na⁺ metal ions the quenching property is very low when compared to Cu²⁺ metal ion (Fig. S2).

Energy transfer between Cu²⁺ metal ion and benzimidazole derivatives

The decrease in fluorescence intensity is attributed to electron transfer between benzimidazole derivative and the Cu^{2+} metal ion. Energy transfer efficiency (*E*) is given by the following equation

$$E = 1 - (I/I_0)$$
(3)

where *I* is the emission intensity of donor in the presence of acceptor and I_0 is the emission intensity of the donor alone. From the above results it is clear that, in presence of Cu²⁺ metal ion, the

fluorescence intensity of benzimidazole derivatives is reduced (from I_0 to I) by energy transfer to Cu²⁺ metal.

According to Forster's non-radiative energy transfer theory, the energy transfer efficiency is related not only to the distance between the acceptor and donor (r_0), but also to the critical energy transfer distance (R_0). That is

$$E = R_0^6 / (R_0^6 + r_0^6) \tag{4}$$

where R_0 is the critical distance when the transfer efficiency is 50%.

$$R_0^6 = 8.8 \times 10^{-25} \, K^2 N^{-4} \varphi J \tag{5}$$

where K^2 is the spatial orientation factor of the dipole, *N* is the refractive index of the medium, φ is the fluorescence quantum yield of the donor and *J* is the overlap integral of the fluorescence emission spectrum of the donor and the absorption spectrum of the acceptor. The value of J can be calculated by using Eq. (7),

$$\mathbf{J} = \int F(\lambda)\varepsilon(\lambda)\lambda^4 d\lambda/F(\lambda)d\lambda \tag{6}$$

where $F(\lambda)$ is the fluorescence intensity of the donor and $\varepsilon(\lambda)$ is molar absorptivity of the acceptor. These experimental conditions, the calculated values of *E*, R_0 and r_0 are $\approx 0.15-0.41$, $\approx 1.69-2.08$ and $\approx 2.00-2.79$ respectively. The literature values of K^2 (=2/3) and *N* (=1.3467) are used for the calculation [19,20] and the corresponding φ values for **1–6** from the present study. Obviously, the calculated value of R_0 is in the range of maximal critical distance. This is in accordance with the conditions of Forster's energy transfer theory [21] and suggests that electron transfer occurs between the Cu²⁺ metal ion and benzimidazole derivatives (**1–6**) with high probability [22].

Crystal structure

Crystalline benzimidazole derivative (**5**) [23] are triclinic crystal. It crystallizes in the space group PT. The cell dimensions are a = 9.6610 Å, b = 10.2900 Å, c = 17.7271 Å. ORTEP diagram of (**5**)



Fig. 3. Fluorescence quenching of benzimidazole derivatives (1-6) in the presence and absence of various concentrations Cu²⁺ metal ion.

 Table 1

 Selected bond lengths (Å), bond angles (°) and torsional angles (°) of 5.

Bond lengths (Å)	Experimental XRD (Å)	Bond angles (°)	Experimental XRD (°)	Torsional angles (°)	Experimental XRD (°)
N1A-C2A	1.3782(1.4972)	C2A-N1A-C8A	106.23(101.69)	C2A-N1A-C1A-C11A	109.45(-177.75)
N1A-C8A	1.3833(1.4584)	C2A-N1A-C1A	128.33(113.71)	C8A-N1A-C1A-C11A	-81.12(-62.25)
N1A-C1A	1.4537(1.4700)	C8A-N1A-C1A	124.79(113.33)	C9A-N3A-C2A-N1A	-0.02(-13.69)
N3A-C2A	1.3163(1.3671)	C2A-N3A-C9A	104.77(105.49)	C9A-N3A-C2A-C21A	-178.71(165.91)
N3A-C9A	1.3881(1.4606)	C2B-N1B-C8B	106.27(101.69)	C8A-N1A-C2A-N3A	0.59(17.54)
N1B-C2B	1.3795(1.4972)	C2B-N1B-C1B	129.32(113.71)	C1A-N1A-C2A-N3A	171.55(139.72)
N1B-C8B	1.3863(1.4584)	C8B-N1B-C1B	123.98(113.33)	C8A-N1A-C2A-C21A	179.28(-162.06)
N1B-C1B	1.4550(1.4700)	C2B-N3B-C9B	105.12(105.41)	C1A-N1A-C2A-C21A	-9.75(-39.88)
N3B-C2B	1.3174(1.3671)	N1A-C1A-C11A	115.07(109.47)	C9A-C4A-C5A-C6A	0.1(-0.1581)
N3B-C9B	1.3866(1.4606)	N3A-C2A-N1A	113.25(113.53)	C2A-N1A-C8A-C7A	178.45(166.15)
C1A-C11A	1.5135(1.5400)	N3A-C2A-C21A	123.44(123.23)	C1A-N1A-C8A-C7A	7.08(43.71)
C2A-C21A	1.4729(1.5400)	N1A-C2A-C21A	123.30(123.24)	C2A-N1A-C8A-C9A	-0.88(13.70)
C7A-C8A	1.3921(1.3862)	N1A-C8A-C3A	131.76(130.72)	C1A-N1A-C8A-C9A	-172.25(136.15)
C8A-C9A	1.3999(1.4763)	N1A-C8A-C9A	103.49(108.25)	C6A-C7A-C8A-N1A	179.75(176.19)
C14A-C17A	1.5089(1.5400)	N3A-C9A-C4A	129.91(130.69)	C2B-N1B-C1B-C11B	108.10(-177.75)
C24A-C27A	1.5078(1.5400)	N3A-C9A-C8A	110.26(108.25)	C8B-N1B-C1B-C11B	-79.66(-62.25)
				C9B-N3B-C2B-N1B	-0.86(-13.69)
				C9B-N3B-C2B-C21B	177.35(165.91)
				C8B-N1B-C2B-N3B	1.24(17.54)
				C1B-N1B-C2B-N3B	173.85(139.72)
				C8B-N1B-C2B-C21B	-176.90(162.06)
				C1B-N1B-C2B-C21B	-4.29(-39.88)
				C9B-C4B-C5B-C6B	0.25(-0.1581)
				C2B-N1B-C8B-C7B	176.39(166.15)
				C1B-N1B-C8B-C7B	3.28(43.71)
				C2B-N1B-C8B-C9B	-1.05(-13.70)
				C1B-N1B-C8B-C9B	-174.15(-136.15)
				C6B-C7B-C8B-N1B	177.76(176.19)

Values within the parenthesis corresponds to theoretical values.

(Fig. S3) shows that the benzimidazole ring is essentially planar. The dihedral angles between the planes of the benzimidazole and the benzene rings of the 4-methylbenzyl and the p-tolyl groups are 76.64(3)° and 46.87(4)°, respectively, in molecule A. The corresponding values in molecule B are 86.31(2)° and 39.14(4)°. The dihedral angle between the planes of the two benzene rings is 73.73(3)° and 80.69(4)° in molecules A and B, respectively. Optimization of **5** have been performed by DFT at B3LYP/6-31G(d,p) using Gaussian-03. All these XRD data are in good agreement with the theoretical values (Table 1). However, from the theoretical values it can be found that most of the optimized bond lengths, bond angles and dihedral angles are slightly higher than that of XRD values. These deviations can be attributed to the fact that the theoretical calculations were aimed at the isolated molecule in the gaseous phase and the XRD results were aimed at the molecule in the solid state.

Conclusions

We have developed a simple and sensitive fluorescent probe for Cu^{2+} metal ion. Benzimidazole derivatives are bound with Cu^{2+} metal ion through azomethine nitrogen. The decrease in fluorescence intensity is attributed to electron transfer between benzimidazole derivative and the Cu^{2+} metal ion. The Cu^{2+} metal ion quenches the fluorescence intensity of benzimidazole derivatives (**1–6**) more than ten times when compared to Fe³⁺, Mg²⁺, Ag⁺, K⁺ and Na⁺ metal ions.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.saa.2012.06.012.

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