SHORT COMMUNICATION

Bis(2-Hydroxy-3-Isopropyl-6-Methyl-Benzaldehyde) Ethylenediamine: A Novel Cation Sensor

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Abstract Novel substituted phenol-based new symmetrical bis(2-hydroxy-3-isopropyl-6-methyl-benzaldehyde) ethylenediamine (**1**) has been designed and synthesized. The compound **1** fluorometrically recognized Cu^{2+} ion in CH_3OH/H_2O (90:10, v/v) by exhibiting an increase in emission upon complexation. In addition, Cu^{2+} gave rise to a change in colour of the solution of compound **1**, which was clearly visible to the naked eye under UV irradiation. The association constant (K) of compound **1** with Cu^{2+} ion was computed with the Benesi-Hildebrand plot and Scatchard plot at 43,000 M^{-1} and 43,011 M^{-1} respectively.

Keywords Phenol substituted receptors · Cu^{2+} binding · Fluorometric sensor · Association constant

Introduction

The design and synthesis of new cation binding agents is an important area of current research interest due to the growing awareness of the environmental and clinical importance of cations. The different size and shapes of cations are responsible for the fast growth in the development of cation binding agents as compared to anion binding agents [1]. Noncyclic compounds containing plural bonding sites have gained considerable attention recently because of their ability of complexation towards ionic and/or neutral molecules [2]. We have so far synthesized non-cyclic compounds with plural hydroxyl groups and imine function groups have been proved to serve not only as cation sensors but also as precursors for constructing supramolecular system, e.g. metallo-supramolecular complexes [3]. So the precise design and efficient synthesis of noncyclic compound has continued to play a very important role in the area of supramolecular chemistry. Although many kinds of noncyclic compounds are prepared, development of a cost effective synthetic route under mild conditions to this type of compound still remains a smart and demanding subject for synthetic chemists.

The discriminating strap of chemical species upon molecular recognition can express bulky perturbation in the host environment, particularly when the ionic or neutral guest is used. Fluoroionophore can offer chemical information on the ion concentration, which constituted important area in metal ion analysis [4]. The development of particular chemosensor for the recognition, discovery and enhanced capacity of transition metal ions extraction have drawn particular interest as these ions play important roles in nature [5].

Copper, the third most plentiful important trace element in the human body and commonly founds as Cu^{2+} ion in natural water [6]. However, free Cu^{2+} ions potentially toxic to aquatic life, both acutely and chronically. For example, micro-organisms affected by submicromolar concentrations of Cu^{+2} ions [7]. Even if a variety of aspects of copper transportation and metabolism have been investigated in the last few decades [8] very little is known about the specifics of intracellular copper transfer. Cloning of the genes may be liable for the two major genetic disorders of copper metabolism in human, it has been seen that Menkes and Wilson diseases were resulted due to excessive intracellular copper transport [9, 10].

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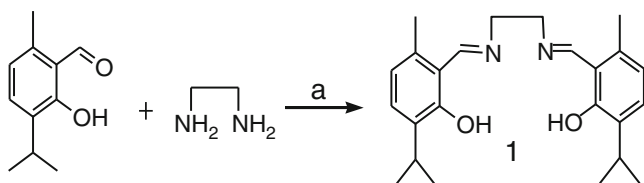
Scheme 1 Synthetic route to receptor **1** (a=Ethanol, 1 h)

As a part of our work in the molecular recognition, we reported here design and synthesis of novel chemosensor bis(2-hydroxy-3-isopropyl-6-methyl-benzaldehyde) ethylenediamine (**1**) and studied its inclusion phenomenon with various cations.

Experimental

All commercial grade chemicals and solvents were procured and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Varian NMR mercury System 300 spectrometer operating at 300 and 75 MHz in CDCl$_3$ with Me$_4$Si as an internal standard, respectively. The Fluorescence and UV-visible spectra of the receptor compound **1** with selected metal ions were recorded in CH$_3$OH/H$_2$O (90:10, v/v) namely on HORIBA JOBIN YVON Fluoromax-4 spectrofluorometer and Shimadzu UV-24500 at room temperature using 1 cm pathlength cell.

Bis(2-Hydroxy-3-Isopropyl-6-Methyl-Benzaldehyde) Ethylenediamine (1)

A solution of 1,2-diamino ethane (0.06 g, 0.001 mol) was added to a solution of 2-hydroxy-3-isopropyl-6-methyl-benzaldehyde (0.356 g, 0.002 mol) in ethanol (50 mL) and mixture was stirred at ambient temperature up to 1 h. There by deposited yellow crystals at room temperature were filtered and recrystallized from ethanol, 83 %, mp 112–115°C. (Refer Scheme 1)

IR (KBr, cm^{-1}): 1623, 1340; ^{1}H NMR (CDCl$_3$, δ ppm): 1.27 (d, J=1.2 Hz, 12H, gem 4CH$_3$), 2.34 (s, 6H, 2Ar-CH$_3$), 3.32 (heptet, 2H, 2CH), 3.91 (s, 4H,CH$_2$-CH$_2$), 6.58 (d, 2H,

2Ar-H, ortho to isopropyl gr), 7.09 (d, 2H, 2Ar-H ortho to methyl gr), 8.66 (s, 2H, 2CH=N); ^{13}C NMR (CDCl$_3$, δ ppm): 17.2, 21.8, 27.3, 66.2, 120.1, 123.3, 126.4, 133.8, 136.9, 156.2, 162.3; MS (ESI): m/z (%): 403 (22), 380 (100); Elemental analysis calculated for C$_{24}$H$_{32}$N$_2$O$_2$: C, 75.8; H, 8.48; N, 7.35 %. Found: C, 75.75, H, 8.23; N, 7.15 %.

The yellow colour product obtained was purified by recrystallization from ethanol and characterized by IR, ^{1}H and ^{13}C NMR, mass spectroscopic techniques and was confirmed by elemental analysis. The elemental analysis and spectral data were in good agreement with chemical structure of compound **1**. The assigned structure for **1** was supported by an X-ray crystallographic structure determination (Fig. 1). Supplementary crystallographic data for **1** was shown in CCDC 870837 [11]. The crystal structure of compound **1** is shown in (Fig. 1). Selected bond lengths and angles are summarized in Table 1.

Crystal Data for C$_{24}$H$_{32}$N$_2$O$_2$ (M =380.53): triclinic, space group P-1 (no. 2), a=8.4604(4) Å, b=10.4538(5) Å, c=13.9426(5) Å, α=99.479(3)°, β=107.165(4)°, γ=108.166(4)°, V=1073.80(9) Å^3, Z=2, T=120.0 K, μ(Mo Kα)=0.075 mm^{-1}, D$_{calc}$=1.1768 g/mm^3, 18363 reflections measured (5.2≤2Θ≤55), 4917 unique (R$_{int}$=0.0379) which were used in all calculations. The final R$_1$ was 0.047732 (I>=2σ(I)) and wR$_2$ was 0.113297 (all data).

Hydrogen bonding of the phenolic –OH shown in (Fig. 1) was major advantageous feature in host guest complexation. Invariability, phenolic hydrogen atom formed an intramolecular hydrogen bond to N atom of the azomethine group, giving a six membered ring. This interaction was usually characterized in terms of phenolic oxygen to ethylenediamine nitrogen separation [12]. This distance varies little between the two molecules. In all free ligand structure, the molecular association was via intramolecular hydrogen bonding. The compound **1** exhibits intramolecular hydrogen bonding (Table 1), where the H atom of phenolic hydroxyl group formed a strong O-H····N intramolecular hydrogen bond with O····N distance 2.55 Å which was in the middle of expected range of such hydrogen bonds[13].

Fig. 1 The structure contains two independent 'half-molecules'. The full molecules are generated by an inversion centre located in the middle of the bond between C1A and its symmetry equivalent atom C1A^1. The geometry of the molecule that is not shown is very similar to the geometry exhibited by the one shown above
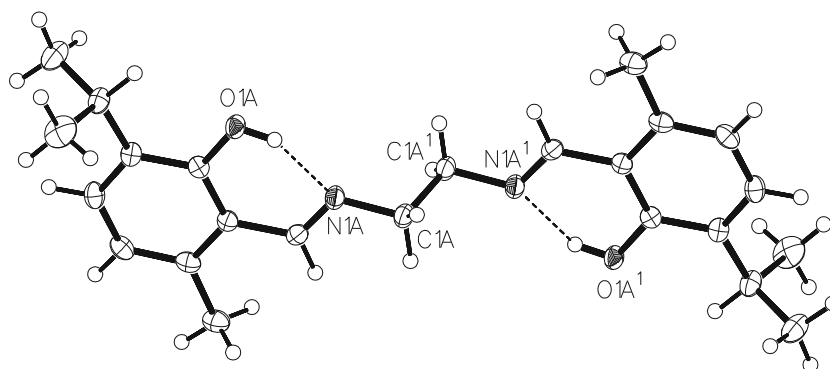
Table 1 Distances and angles around the hydrogen bonded D- A atoms. The X-ray distances were derived from the model where the O-H distance was fixed to 0.840Å and the values adjusted for the neutron-corrected hydrogen position used a restrained distance of 0.983Å

	O1A-N1A/Å	H1A-N1A/Å	O1A-H1A-N1A	O1B- N1B/Å	H1B-N1B/Å	O1B-H1B-N1B
X-Ray	2.55627(10)	1.801(10)	148.6(9)	2.53326(13)	1.776(7)	148.8(5)
Neutron	–	1.638(8)	153.9(17)	–	1.629(9)	150.5(16)

Determination of the Binding Constant by Spectroflourometric Titration

The fluorescence titration experiments were carried out with a HOSHIBA JOBIN YVON Fluoromax-4 spectrofluorometer in CH_3OH/H_2O (90:10, v/v, mole fraction≈0.8) at room temperature (298 K) and then the association constant (K_a) was computed for receptor compound **1**–cation complexation. The selectivity of various metal ions towards receptor **1** was studied. The titration of the selective metal ion was talented through addition of changeable amount of metal salt solution (0.005 ml, 1×10^{-3} M) to a fixed amount of receptor compound **1** solution (2 ml, 1×10^{-4} M) in CH_3OH/H_2O (90:10, v/v) in the cell. This was followed by a 5 min interval (in which the reaction cell was left under continuous stirring to ensure mixing). Then the fluorescence data was collected and processed to calculate the association constant (K_a) of the appropriate cation and receptor **1** complex.

Result and Discussion

The response of receptor **1** towards various metal ions was recorded in CH_3OH/H_2O (90:10, v/v) using fluorescence spectroscopy. The change in fluorescence of compound **1** was observed upon addition of selected metal salts solution prepared in CH_3OH/H_2O (90:10, v/v). As can be seen from (Fig. 2), the broad emission peak centered at 600 nm for compound **1** in CH_3OH/H_2O (90:10, v/v), progressively increase with the addition of increasing amount of metal

salt solution for which the receptor was selective, accompanied by the emission peak height enhancement. It was well understood from (Fig. 2) that receptors were highly sensitive and selective towards Cu^{2+} ion by exhibiting a distinct mode of emission. It was well known that copper compound have paramagnetic nature with +2 oxidation state and the great stability [14]. In our precise analysis, the enhancement of compound **1** after binding with Cu^{2+} ions was fairly remarkable and mentionable along with other few related accessible systems.

The binding mode of compound **1** exposed the importance of the hydroxyl group in Cu^{2+} binding. Generally hydroxyl group acts as a good binding site and also plays an effective role in binding of transition metal ions such as Cu^{2+} metal ion. Therefore, it was appeared that the core functionality required for compound **1** to efficiently bind with Cu^{2+} ion were imine association and hydroxyl groups. However, due to binding of Cu^{2+} ion in the gap, the metal–fluorophore interaction was modulated [15] and the excitation energy transfer from the receptor to the metal d orbital and/or receptor to metal charge transfer was inhibited. Fluorescence ratiometric response of receptor compound **1** and interference toward the surveyed metal ions are displayed in (Fig. 3a, b). The results showed a highly selective response of compound **1** towards Cu^{2+} ions as compared to the other metal ions. Although Zn^{2+}, Cr^{3+}, Mn^{2+} and Ni^{2+} gives fluorescence enhancement but in the presence of Cu^{2+} ion, there intensity is negligible. The data presented here will be helpful for the researcher to expand the new function of compound **1** in analytical and environmental science.

Fig. 2 Changes in fluorescence intensity of compound **1** (1×10^{-4} M) upon the addition of fixed amount of metal ion solution (1×10^{-3} M) in CH_3OH/H_2O (90:10, v/v)
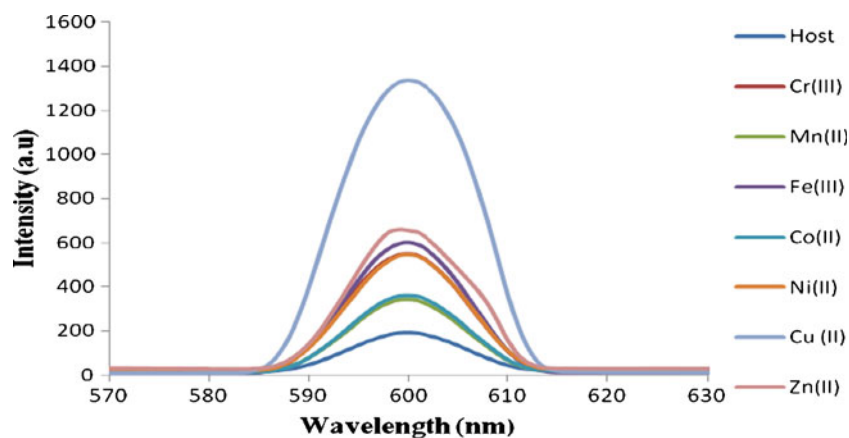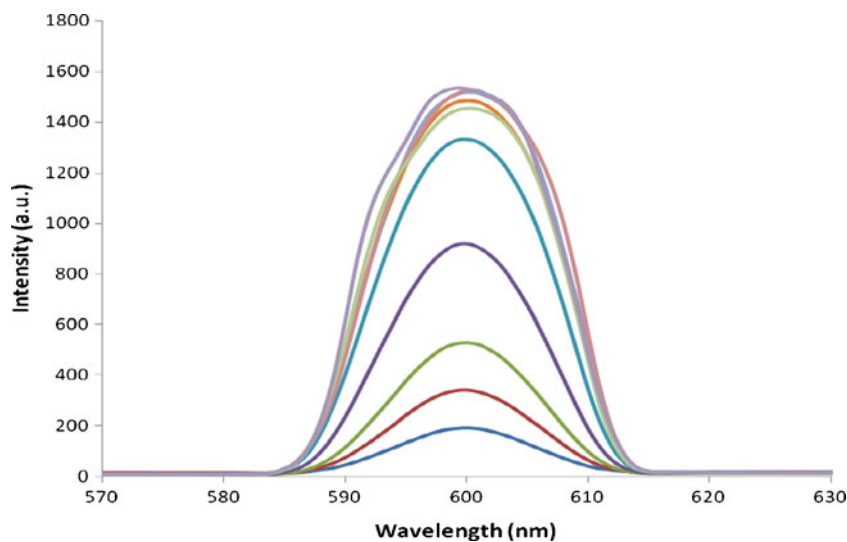
Fig. 3 **a** Fluorescence ratiometric response (I_0-I/I_0) of compound **1** (1×10^{-4} M) upon the addition of a particular metal salt (1×10^{-3} M) in CH_3OH/H_2O (90:10, v/v). **b** Respective interference of metals at the time of detection of Cu^{2+} ion
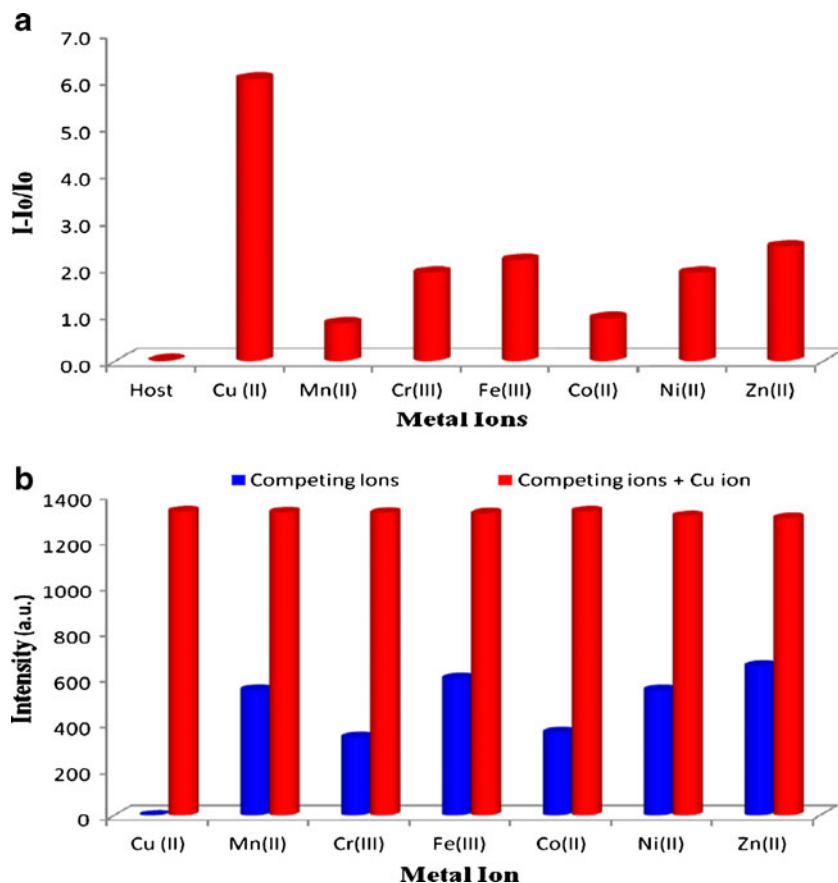
When receptor **1** was titrated with Cu^{2+} in CH_3OH/H_2O (90:10, v/v), a progressive fluorescence enhancement was observed with Cu^{2+} ion and the development reached up to saturation as seen in (Fig. 4) observed change may be due to the chelation followed by prevention of the photoelectron transfer. Normalized response of fluorescence signal to change Cu^{2+} ion concentration in the CH_3OH/H_2O (90:10, v/v) solution is shown by (Fig. S2 in Supplement data).

The fluorescence intensity was gradually increased (Fig. S2 in Supplement data) with increasing the guest concentration. To determine the binding stoichiometry between receptor **1** and Cu^{2+}, the continuous variation method was used [16]. (Fig. S3 in Supplement data) shows the Job plot of the fluorescence intensity of free receptor **1** and the intensity of the system with the molar fraction of the host {[H]/([H]+[G])} for a series of solutions, in which the total concentration of host and guest was constant, with the molar

Fig. 4 Changes in fluorescence spectrum of receptor **1** (1×10^{-4} M) upon the addition of Cu^{2+} salt of (1×10^{-3} M) in CH_3OH/H_2O (90:10, v/v)

Fig. 5 Changes in absorbance spectrum of receptor **1** (1×10^{-4} M) upon the addition of metals (1×10^{-3} M) in CH_3OH/H_2O (90:10, v/v)
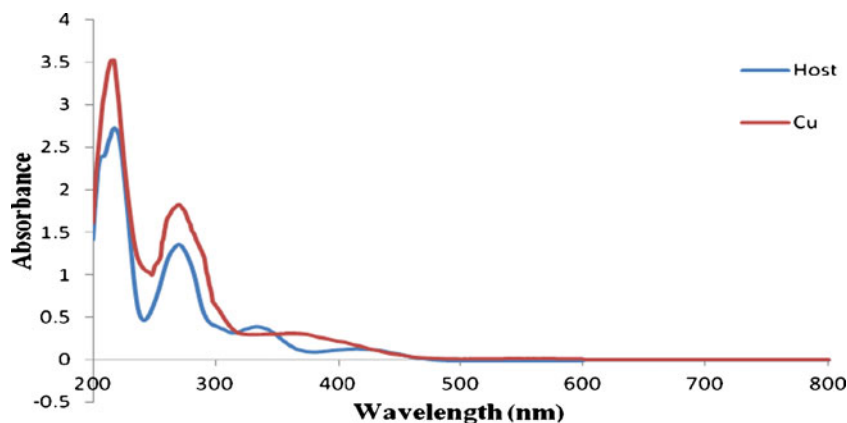
fraction of host continuously varying. The results indicate the formation of a 1:1 (Host: Guest) complex. Using the equation: $[G]tot = a/2K_{11}(1-a)^2[H]tot + a[H]_{tot}/2$, where $[G]_{tot}$ is total concentration of guest, [H]tot is the total concentration of host, $a = (I - I_0)/(I_i - I_0)$ with I being the fluorescent intensity at a particular Cu^{2+} concentration while I_0 and I_i are the intensities at zero and infinite Cu^{2+} concentrations, respectively, the association constant K_a was determined as $4.3 \times 10^4 \pm 0.1$ M^{-1}.

Using the Benesi-Hildebrand [17] (Eq.1) and the Scatchard [18, 19] (Eq.2) methodologies and we made the calculation of association constant (K_a).

$$1/F - F_0 = 1/(F\infty - F_0)K[G] + 1/(F\infty - F_0) \qquad (1)$$

$$F - F_0/[G] = (F\infty - F_0)K - (F - F_0)K \qquad (2)$$

Applying both equations two lines were obtained in the plot of $1/(F-F_0)$ verses $1/[G]$ for Benesi-Hildebrand equation and in the plot of $(F-F_0)/[G]$ versus $(F-F_0)$ for Scatchard equation, as illustrated in (Fig. S4 in Supplement data) and (Fig. S5 in Supplement data). Where F_∞ was the fluorescence intensity in the absence of Cu^{2+} ions, F was the fluorescence intensity in presence of Cu^{2+} ions and [G] was the concentration of guest. The association value (K_a) obtained from Benesi-Hildebrand plot and Scatchard plot was found to be in good agreement and were 43,000 M^{-1} and 43,011 M^{-1} respectively.

The absorption spectrum of receptor compound **1** with various metal salts was shown in (Fig. 5) Receptor exhibited λmax at 273, 328 and 428 nm in CH_3OH/H_2O (90:10, v/v) solution together with a swelling at 273 nm and a shoulder at 310 nm. The longer wavelength band at 428 nm and shoulder at 478 nm may be assigned to transitions associated with phenol substituted ring (Fig. 5). This observation clearly indicated towards a charge transfer from nitrogen (donor) of imine to Cu^{2+} (acceptor) metal ion.

In addition, the selective recognition of compound **1** by Cu^{2+} ion was visualized by the naked eye owing to the fluorometric change. Visual detection studies of receptor compound **1** (1×10^{-4} M) were conducted with all cations such as metal chlorides of Cr^{3+}, Mn^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}. The receptor compound **1** in mixed solutions of CH_3OH/H_2O (90:10, v/v) was appeared to be almost colourless at room temperature. With the addition of these cations (10.0 equivalents) to receptor compound **1**, only Cu^{2+} ion shown spectacular colour change from colourless to fluorescent green colour, which was noticeable in the presence of UV light compared to other cations (Fig. S1 in Supplement data). In general, the cations such as Fe^{3+}, Ni^{2+} and Co^{2+} interfere in Cu^{2+} ion detection. However, in our study, we did not find any significant colour change to the solution of compound **1** even after the addition of these interfering anions. The probable reason for the colour change in presence of Cu^{2+} ion over other cations may probably be attributed to the fact that the copper have +2 oxidation state and the observable bathochromic shift. All the attempts failed to grow a single crystal of Copper complex of compound **1**.

Conclusion

In summary, we have designed and developed a selective and sensitive fluorescent chemical sensor compound **1** for the detection of Cu^{2+} ion in organic and aqueous medium. The detection of Cu^{2+} ion gave rise to major colour change from colourless to fluorescent, which can easily be detected by the naked eye under UV irradiation. The selective detection of Cu^{2+} ion in water was generally complicated in the presence of other metal ions. But we successfully detected Cu^{2+} ion in aqueous environment. The 1:1 stoichiometry of the host guest complexes in methanol containing 10 % water was confirmed from job plot. The association constant (K_a) of compound **1** with Cu^{2+} ion was calculated with the Benesi-Hildebrand plot and Scatchard plot and were found to be 43,000 M^{-1} and 43,011 M^{-1} respectively.

Most of the reported sensors for these metal cations are often structurally complicated and required tedious synthetic

procedures. Herein, this reported sensor which was easy-to-make. We believe that this sensor, with sensitive and selective naked eye responses can be used for many practical applications in chemical, environmental and biological systems.

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