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Near-IR region absorbing 1,4-diaminoanthracene-9,10-dione motif based ratiometric chemosensors for Cu^{2+}

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Abstract

1,4-Bis[2-aminoethylamino]anthracene-9,10-diones selectively bind with Cu^{2+} to form complexes with unusual selectivity under basic conditions. The deprotonation of the aryl amine NH in the case of these chemosensors causes a bathochromic shift in the absorption band from 585 nm and 635 nm to 725 nm and enables ratiometric estimation of Cu^{2+} between pH 8 and 12.

1. Introduction

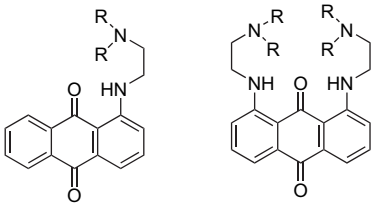
The understanding of the molecular interactions between different chemical entities is the key to the development of chemical sciences and many interdisciplinary areas, which share boundaries with chemical sciences. The availability of tools to understand and evaluate such molecular interactions has resulted in enormous expansion of knowledge in the design of new drug entities (receptor–ligand interactions)[1] and studies in new abiotic receptors (supramolecular science)[2] for the past half century.

Anthracene-9,10-diones due to their diverse chemical features depending on the substitution pattern have shown widespread potential for the development of dye stuff materials,[3] DNA-intercalating molecules,[4] redox active[5] and optical sensors.[6]

Recently, we have reported that aminoethyl functional groups bearing anthracene-9,10-diones (Fig. 1) effectively bind Cu^{2+} amongst various alkali, alkaline earth and transition metal ions.[7] The variation in substituent nature and their position on the anthracene-9,10-dione platform effectively controls the stability of their Cu^{2+} complexes across various pH ranges. The presence of the aminoethylamino moiety at position 1 (**1a** and **1b**) and positions 1,8 (**2a** and **2b**) leads to most stable complexes with Cu^{2+} between pH 6 and 8 while above pH 8, the increased concentration of hydroxyl anions, probably due to formation of $Cu(OH)_2$, results in decomplexation of the complex, which could be controlled by increasing the hydrophobic environment around anthracene-9,10-dione in **1c**.

1,4-Bis[2-aminoethylamino]anthracene-9,10-diones are one of the most effective DNA intercalators[4] and one such derivative, mitoxantrone, has been in clinical use for more than three decades. More recently, their derived systems have found applications as anion sensors.[6]

In biochemical processes, due to the presence of a large number of components, the possibility of the interaction of the molecule under study with a species other than the target receptor can significantly affect the overall interaction with



1a. R = H
1b. R = CH_3
1c. R = $CH_2CONHC_8H_{17}$

2a. R = H
2b. R = CH_3

Figure 1. Structures of sensors **1** and **2**.

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the target receptor and hence their activities. Metal ions are one of the central components of living systems and the understanding of interactions with metal ions is therefore of great significance.[8]

In the present paper, we have studied the interactions of various 1,4-substituted-anthracene-9,10-diones (**3**–**6**) (Fig. 2) towards metal ions, which depending on the substituents show highly selective bathochromic or hypsochromic effects and can find applications as Cu^{2+} sensors.[9] The molecular switching of absorption bands in the case of receptors **3** and **4** from 585 nm and 630 nm to 725 nm makes the molecules behave as ratiometric sensors, which can measure as low as 1 ppm Cu^{2+}. Significantly, **3** and **4** undergo Cu^{2+} mediated deprotonation at the aryl amine NH and in contrast to the instability of Cu^{2+}–**1a/1b** and Cu^{2+}–**2a/2b** complexes above pH 6–8, the Cu^{2+} complexes of **3** and **4** are best formed at pH >8, and even in the presence of excess of hydroxyl ions (pH 8–12) do not undergo cleavage.

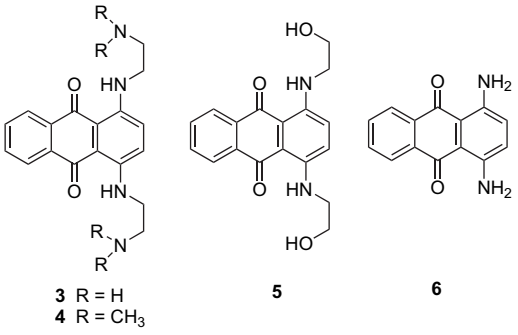


Figure 2. Structures of chemosensors **3**–**6**.

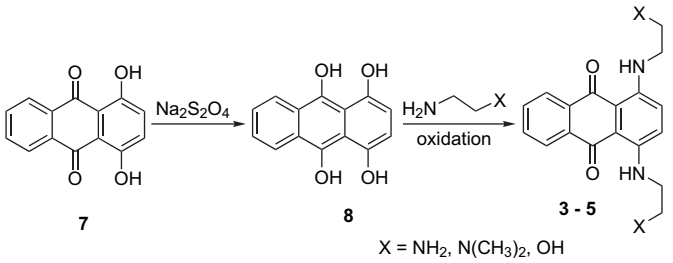
2. Results and discussion

2.1. Synthesis

1,4-Dihydroxyanthracene-9,10-dione (**7**) was reduced with sodium dithionite under alkaline conditions (pH 8) to get 1,4,9,10-tetrahydroxyanthracene (**8**). The mixture of **8** and excess of 1,2-diaminoethane on heating at 50 °C under nitrogen followed by air oxidation and usual purification gave blue solid, mp 175 °C (CH_3CN) in 60% yield. The presence of a 4H triplet at δ 3.08, a quartet at δ 3.51 and a 2H singlet at δ 7.35 confirmed the symmetrical substitution in 3. These observations along with other spectral data assigned the structure **3** for this compound. Similarly, heating of **8** with 2-dimethylaminoethylamine and 2-aminoethanol followed by air oxidation gave the respective receptors **4** (75%), blue solid, and **5** (70%), blue solid (Scheme 1).

2.2. Absorption properties

The interactions of receptors **3**–**6** with metal ions have been investigated by evaluating the changes in their absorption properties by the addition of varied concentrations of metal ions. Since all these receptors are freely soluble in methanol/water (1:1), the investigations have been performed in this medium. The visible region absorption bands of receptors **3**–**5** appear at λ_{max} 585 nm and 630 nm with the respective molar absorptivities ε 6678, 6383; 13,067, 12,204 and 3348, 2661 and receptor **6** shows λ_{max} 548 (ε 5302) nm and 588 (ε 4867) nm in methanol/water (1:1). These results clearly indicate that the non-conjugated substituents attached to anthraquinone moiety significantly affect the molar absorptivities of the receptors **3**–**6**.[10] The absorption spectra of receptors **3**–**6** (10^{-4} M) on addition of 0.01 M Na^+, K^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Sr^{2+}, Co^{2+}, Cd^{2+}, Zn^{2+} and Ni^{2+} showed only nominal changes in their respective absorption maxima and absorbance in the visible region. The addition of Cu^{2+}, even in equimolar quantities, to receptors **3** and **4** caused switching of the absorption bands from 585 nm and 630 nm to 665 nm with a respective bathochromic shift of the absorption bands by 80 nm and 35 nm. This resulted in a visible change in colour from blue to turquoise blue. However, solutions of receptors **5** and **6** on addition of Cu^{2+} showed a considerable decrease in absorbance at their λ_{max} values with concomitant broadening of the absorption band. This resulted in visible depletion of the colours of the solutions of **5** and **6**. These results clearly show that Cu^{2+} binds to receptors **3** and **4** through a different mode than it binds to receptors **5** and **6** and thus emphasizes the role of the 2-aminoalkyl unit on molecular switching behaviour of anthracene-9,10-dione derivatives.



Scheme 1.

2.3. Binding stoichiometries

Receptor **4**, due to its significantly larger ε values than **3**, was expected to exhibit more changes in absorbance on addition of analyte and thus higher sensitivities and so the studies on **4** were first initiated. The blue solution of **4** (100 μM) exhibits two absorption bands at λ_{max} 585 nm and 630 nm (pH 7.0±0.1; CH_3OH/H_2O 1:1). With gradual addition of Cu^{2+}, a new absorption band at λ_{max} 665 nm with an isosbestic point at 650 nm appeared and colour of the solution underwent visible change from blue to turquoise blue. The decrease in absorbance at 585 nm and 650 nm and increase in absorbance at 665 nm achieved limiting values up to ~150 μM of Cu^{2+} and addition of further Cu^{2+} led to only nominal changes in their absorption spectra (Fig. 3). On using 20 μM solution of **4**, <1 μM Cu^{2+} concentration could be estimated. Similar behaviour was observed on titration of solution of **3** with Cu^{2+} under identical conditions (Supplementary data, Figs. S1 and S2).

The unsymmetrical nature of Job's plot for **4**–Cu^{2+} complexation points to the formation of 3:2 (Cu^{2+}/Ligand) complex (Fig. 4).

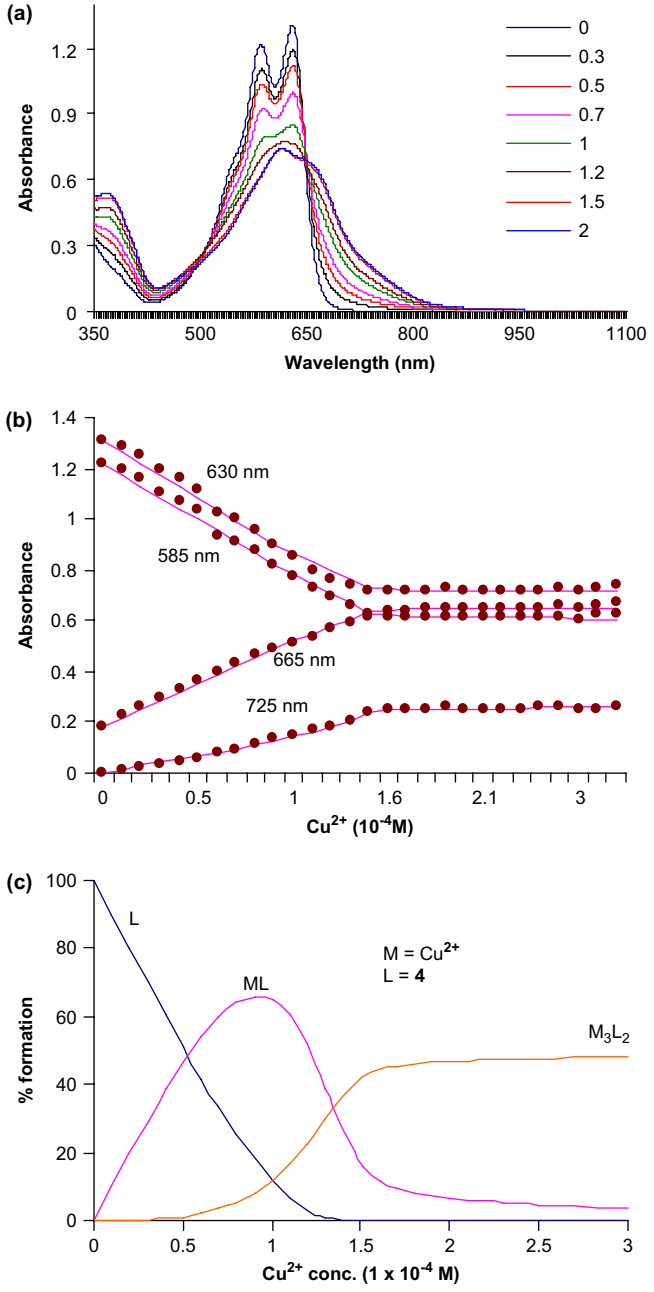


Figure 3. (a) Changes in the UV–vis spectra of **4** (100 μM, pH 7.0±0.1, CH_3OH/H_2O 1:1). (b) Plot of absorbance of **4** upon titration with Cu^{2+}. The points refer to experimental values and line to curve fit. (c) Species distribution diagram for a system containing **4** and different Cu^{2+} concentrations.

However, Job's plot with a maximum at any value besides 0.5 usually indicates complex equilibria involving more than one species.

The iteration spectral fitting of the data obtained by titration of **4** (100 μM) with Cu^{2+} at pH 7.0±0.1 in CH_3OH/H_2O (Fig. 3a) shows that at $<0.5\times10^{-4}$ M Cu^{2+} concentration, only ML species is formed. However, with incremental addition of Cu^{2+} the aggregation of ML species to M_3L_2 species takes place and this process is nearly complete at 1.5×10^{-4} M Cu^{2+}. Therefore, **4** forms ML, M_3L_2 complexes with Cu^{2+}, the proportion of which depends on the ratio of Cu^{2+}/ligand at pH 7.0 (Eq. 1, Fig. 3c).

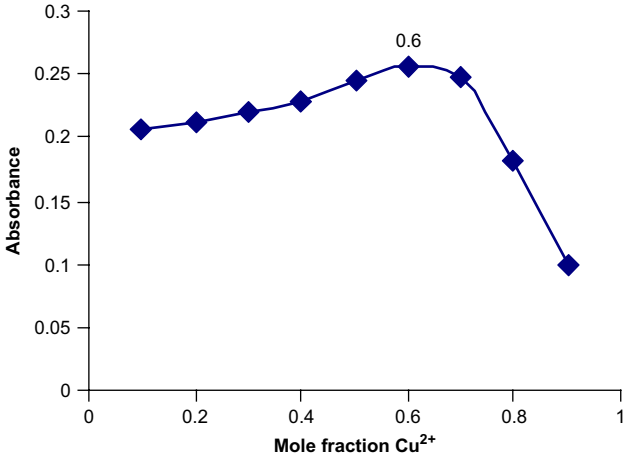


Figure 4. Job plot for receptor **4**.

The titration of chemosensor **3** with Cu^{2+} (pH 7.0±0.1, CH_3OH/H_2O 1:1) shows the formation of ML_2, ML and M_2L complexes (Eq. 2, Supplementary data, Fig. S3).

$$\mathbf{4} \xrightarrow[\log\beta\ 7.62]{Cu^{2+}} \mathbf{4}\text{–}Cu^{2+} \xrightarrow[\log\beta\ 25.56]{Cu^{2+}} (\mathbf{4})_2\text{–}\left(Cu^{2+}\right)_3 \quad (1)$$

$$\mathbf{3} \xrightarrow[\log\beta\ 15.60]{Cu^{2+}} (\mathbf{3})_2\text{–}Cu^{2+} \xrightarrow[\log\beta\ 9.69]{Cu^{2+}} \mathbf{3}\text{–}Cu^{2+} \xrightarrow[\log\beta\ 14.81]{Cu^{2+}} \mathbf{3}\text{–}\left(Cu^{2+}\right)_2 \quad (2)$$

Chemosensor **5** (100 μM, pH 7.0±0.1, CH_3OH/H_2O 1:1) on addition of Cu^{2+} (5 equiv) underwent immediate visible depletion of colour to nearly colourless. The titration of **5** against Cu^{2+} shows that with gradual increase in concentration of Cu^{2+} the absorbance at λ_{max} 585 nm and 630 nm goes on decreasing and the absorption band spreads between 500 nm and 800 nm (Fig. 5a). The analysis of the data shows the formation of only ML complex with log β_{ML} 3.77. Significantly, **5** did not undergo any colour change or change in absorbance on addition of other metal ions. Similarly, chemosensor **6** underwent selective colour discharge on addition of Cu^{2+} (Fig. 5b) with log β_{ML} 5.42.

The comparison of 1:1 complexes (Table 1) formed by chemosensors **4**–**6** shows that the order of complex stability is **4**/Cu^{2+}>**6**/Cu^{2+}>**5**/Cu^{2+}. Significantly, **6** forms a complex, which is nearly 45 times more stable than that formed by its hydroxyalkyl derivative **5**. But chemosensor **4** forms ~160 times stronger complex than **6** and ~7100 times more stable than **5**. Therefore, the presence of an alkyl group at N-1 causes a decrease in stability, probably due to increased steric constrictions but the presence of dimethylamino group in place of OH, due to increased coordination and induced deprotonation, forms a much stronger complex. Therefore, the presence of β-amino/dimethylamino moieties is desirable for highly selective Cu^{2+} mediated visible colour change and bathochromic shift of these chemosensors and allows their use as Cu^{2+} selective ratiometric sensors.

This change in absorption spectra of **3** and **4** vis-à-vis chemosensors **5** and **6** on addition of Cu^{2+} ions could be explained by considering the change in the electron-donating ability of the

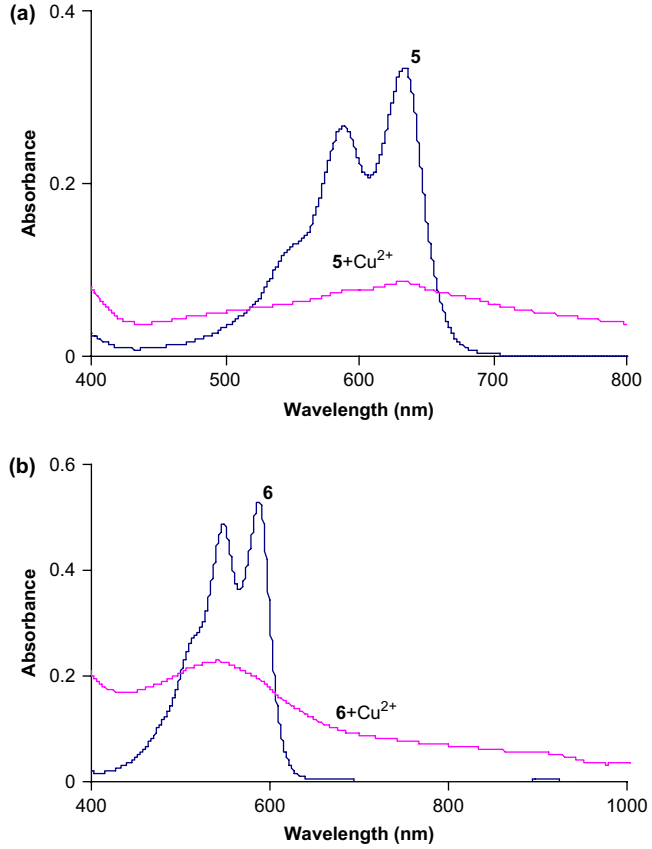


Figure 5. Changes in the UV–vis spectra of (a) **5** and (b) **6** (100 μM, pH 7.0±0.1, CH_3OH/H_2O 1:1).

aryl NH to the anthraquinone moiety. The increase or decrease in electron-donating ability of N-1 should cause the respective bathochromic or hypsochromic shift in λ_{max} of chemosensors. In the case of **3** and **4**, the distinct appearance of a new absorption band at 665 nm (pH 7.0) and 725 nm (pH 9.0) points to the increased electron-donating ability of N-1, which is assigned to the presence of negative charge on N-1 caused by deprotonation. At pH 9, due to the formation of neutral hydroxyl salt, the electron donation by N-1 anion to the ring is increased and results in a larger bathochromic shift (725 nm) of the new absorption band.

In the case of chemosensors **5** and **6**, due to broadening of the absorption bands, the increase in absorption both in longer and in shorter wavelength regions and the mode of complexation of N-1 could not be defined.

Table 1
log β values for complexation of **3**–**6** with Cu^{2+} at pH 7.0 in CH_3OH/H_2O (1:1)

Receptor	log β_{ML}	log β_{ML_2}	log β_{M_2L}	log $\beta_{M_3L_2}$
3	9.69	15.60	14.81	—
4	7.62	—	—	25.56
4[a]	6.85			24.54
5	3.77	—	—	—
6	5.42	—	—	—

[a] These log β values are at pH 9.0.

2.4. pH and UV–vis combination titrations

In order to probe the nature of species formed during complexation of **4** with Cu^{2+}, a series of pH and UV–vis titrations were performed and the respective spectral data were analyzed using an iterative method on multi-wavelength data using the programme Specfit/32.

The pK_a values of chemosensors **3** and **4** were determined by observing the changes in their UV–vis spectra upon titration of solutions of **3** and **4** (100 μM) with HCl or NaOH solutions separately. Figure 5 shows the changes for **4** upon pH titration. Receptors **3** and **4** on variation in pH from 2 to 12 showed only small changes in their λ_{max} values with ~10 nm hypsochromic shift in acidic medium (Fig. 6a). However, significant changes in absorbance values with change in pH were observed. Both chemosensors **3** and **4** showed minimum absorbance at pH 7, which on either lowering the pH to 4 or increasing the pH to 10 gradually increased and then became constant.

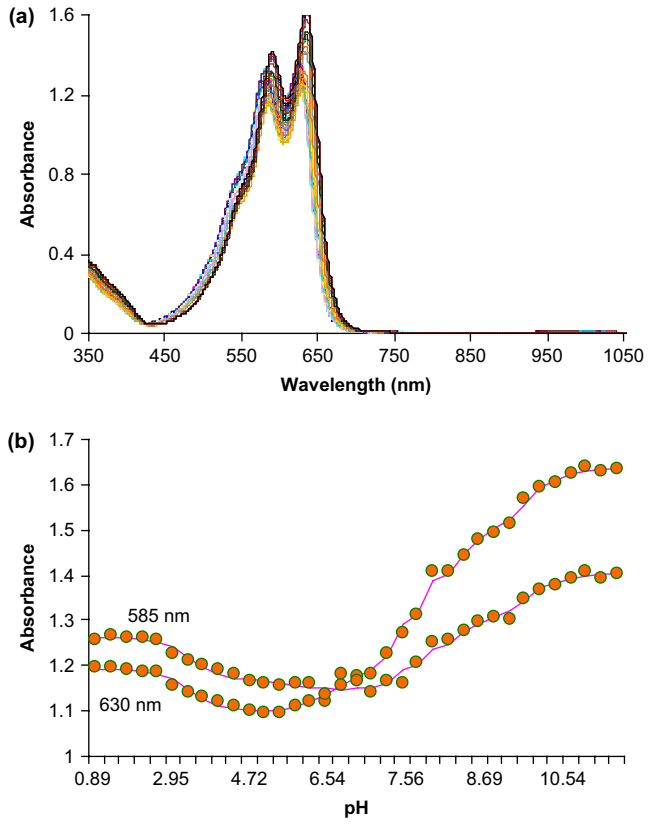


Figure 6. (a) Changes in the UV–vis spectra of **4** upon titration with diluted acid and base. (b) Plot of absorbance of **4** (100 μM) at parent absorbances with change in pH.

The absorption band at 630 nm showed only small changes (<10%) in absorbance between pH 0 and 5 but on increasing the pH the absorbance increased by ~50% up to pH 11. Similarly, the 585 nm absorption band showed larger changes in absorbance under basic conditions than under acidic conditions but the changes were significantly lower than those observed for 630 nm absorption band (Fig. 6b).

The analysis of these pH induced changes in the absorbance of **4** through iterative spectral fitting shows that at pH ≥10, the free ligand exists. At pH 5, the receptor **4** exists in tri-protonated form, which on addition of base undergoes gradual deprotonation in three steps to give free neutral receptor **4** at pH>10. At pH 7, **4** mainly exists as LH_2 (Fig. 7, Eq. 3). Chemosensor **3** undergoes stepwise tri-protonation with the formation of LH_1, LH_2 and LH_3 species (Eq. 4, Supplementary data, Figs. S4 and S5).

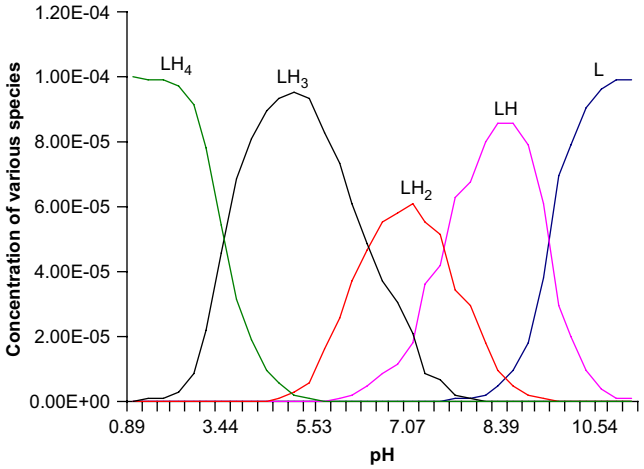


Figure 7. Species distribution diagram of **4** (100 μM, pH 7.0±0.1) as a function of pH.

The insight into the formation of various species during titration of **4** with Cu^{2+} has been provided by using a combination of pH and UV–vis titrations of solutions of Cu^{2+}–**4** (1:1) and Cu^{2+}–**4** (3:2). The evaluation of spectral data obtained by a combination of pH and UV–vis titration of solution of Cu^{2+}–**4** (1:1) (Eq. 5, Fig. 8a) shows that chemosensor **4** at pH 4.00 starts forming MLH_{-1} and above pH 6.75 forms $MLH_{-1}(OH^-)$ whereas the solution of Cu^{2+}–**4** (3:2) (Eq. 6, Fig. 8b) shows the formation of $M_3L_2H_{-2}$ and $M_3L_2H_{-2}(OH^-)_2$ species. However, the formation of M_2L species is not observed during titration of **4** with Cu^{2+} under constant pH conditions or Cu^{2+}–**4** complex solution under variable pH conditions.

$$\mathbf{4} \xrightarrow[\log\beta\ 9.95]{H^+} \mathbf{4}H^+ \xrightarrow[\log\beta\ 17.69]{H^+} \mathbf{4}H^{2+} \xrightarrow[\log\beta\ 24.45]{H^+} \mathbf{4}H^{3+} \xrightarrow[\log\beta\ 27.97]{H^+} \mathbf{4}H^{4+} \quad (3)$$

$$\mathbf{3} \xrightarrow[\log\beta\ 9.01]{H^+} \mathbf{3}H^+ \xrightarrow[\log\beta\ 17.30]{H^+} \mathbf{3}H^{2+} \xrightarrow[\log\beta\ 23.43]{H^+} \mathbf{3}H^{3+} \quad (4)$$

The evaluation of spectral data obtained by a combination of pH and UV–vis titration of a solution of Cu^{2+}–**3** (2:1) (Eq. 7, Supplementary data, Figs. S6 and S7) shows the formation of MLH_{-1} and $MLH_{-1}(OH^-)$.

Also, in contrast to di-deprotonation of **2a/2b** on addition of Cu^{2+} (2 equiv), the chemosensor **4** undergoes only mono-deprotonation. The increased electron availability on the 1,4-substituted aryl ring of **4** due to the presence of *p*-amino group causes a lowering of the electron sink acting ability of the anthraquinone moiety and so increases the availability of negative charge on aryl amine N1. Therefore, the anion of **4** forms

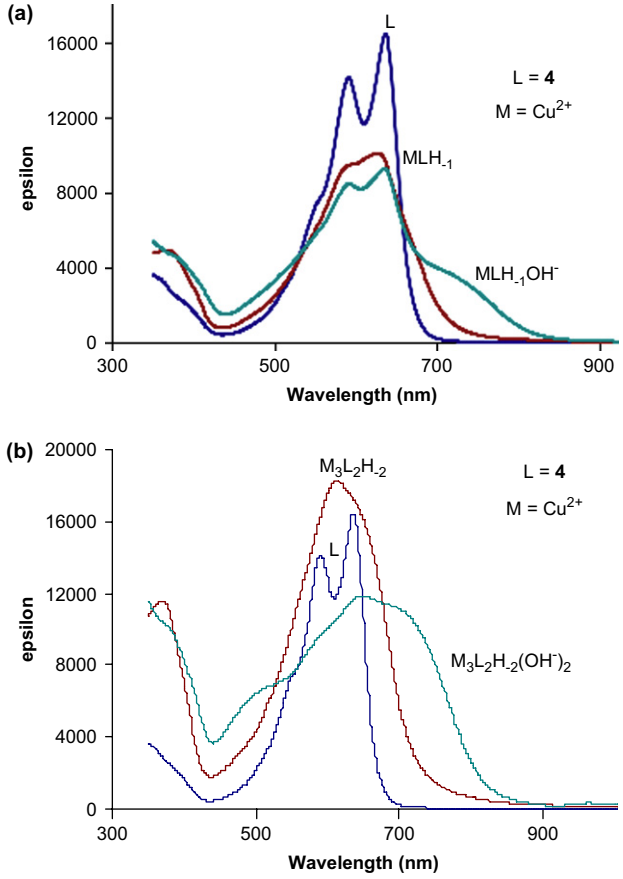


Figure 8. Absorption curves of **4** as a function of pH for a system containing (a) **4** and Cu^{2+} (1:1) and (b) **4** and Cu^{2+} (2:3).

a partially charge neutralized stable complex with Cu^{2+}, which remains stable even in the presence of excess of hydroxyl ions. In the case of 3:2 Cu^{2+}–**4** solution, the Cu^{2+} mediated aggregation of two MLH_{-1} species results in the formation of $M_3L_2H_{-2}$, which under basic conditions is converted to $M_3L_2H_{-2}(OH^-)_2$ in parallel with complexes formed in 1:1 solution.

$$\mathbf{4} + Cu^{2+} \underset{\log\beta\ 10.94}{\overset{-H}{\rightleftharpoons}} Cu^{2+}\text{–}\mathbf{4}H_{-1} \underset{\log\beta\ 3.92}{\overset{-H}{\rightleftharpoons}} Cu^{2+}\text{–}\mathbf{4}H_{-1}OH^- \quad (5)$$

$$2(\mathbf{4}) + 3Cu^{2+} \underset{\log\beta\ 32.98}{\overset{-H}{\rightleftharpoons}} (Cu^{2+})_3\text{–}(\mathbf{4})_2H_{-2} \underset{\log\beta\ 25.70}{\overset{-H}{\rightleftharpoons}} (Cu^{2+})_3\text{–}(\mathbf{4})_2H_{-2}(OH^-)_2 \quad (6)$$

$$\mathbf{3} + 2Cu^{2+} \underset{\log\beta\ 9.55}{\overset{-H}{\rightleftharpoons}} (Cu^{2+})_2\text{–}\mathbf{3}H_{-1} \underset{\log\beta\ 2.20}{\overset{-H}{\rightleftharpoons}} (Cu^{2+})_2\text{–}\mathbf{3}H_{-1}(OH^-) \quad (7)$$

At pH >8, due to neutralization of the positive charge of Cu^{2+} with hydroxyl ions, the increased availability of electron density on the amine nitrogen anion and thus its donation to anthraquinone moiety causes a further bathochromic shift from 665 nm to 725 nm. Therefore, the increased availability of negative charge in the case of **4** due to the presence of the *p*-amino group causes stability of the respective complexes

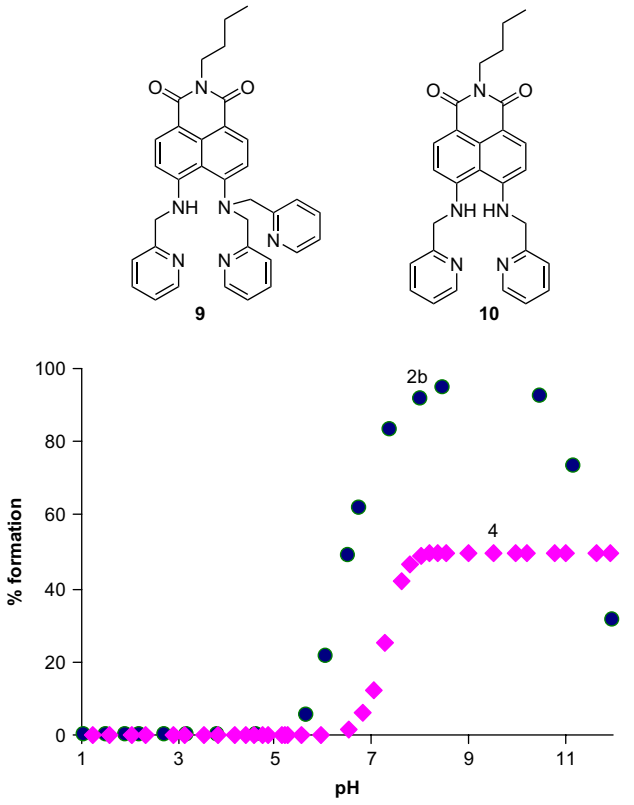


Figure 9. pH titration plots of **2b**–Cu^{2+} (1:2) and **4**–Cu^{2+} (2:3) solutions against species formation.

of its anion with Cu^{2+} even under basic conditions in comparison to the instability of the respective Cu^{2+} complexes formed by **1** and **2** where the *p*-amino group is lacking (Fig. 9). These results are in agreement with the earlier reported instability of Zn^{2+} complexes but the stability of charge neutralized Cu^{2+} complexes under basic conditions in the case of naphthalimde based receptors **9**[11] and **10**.[12]

On gradual addition of Cu^{2+} to a solution of **4** at pH 9.0±0.1 (100 μM, CH_3OH/H_2O 1:1), a gradual decrease in absorbance at 585 nm and 630 nm and concomitant appearance of new band at 725 nm with gradual increase in intensity was observed. Unlike the titration of **4** with Cu^{2+} carried out at pH 7.0, here a new band at longer wavelength is observed that is assigned to $M_3L_2H_{-2}(OH^-)_2$ (Fig. 10).

This provides the opportunity for sensor **4** to be used as ratiometric sensor. The ratiometric approach provides estimation of Cu^{2+} independent of the concentration of the sensor. Ratiometric probes have the important feature in that they permit signal rationing and thus increase the dynamic range. The dependence of absorption ratios on Cu^{2+} concentration (Fig. 11) shows that very low concentrations of Cu^{2+} can be estimated.

2.5. Competitive studies

To evaluate the potential utility of these chemosensors, the effect of other metal ions on the ability of chemosensor to sense Cu^{2+} was investigated. Importantly, chemosensor **4** completely inhibits the interference of other physiologically

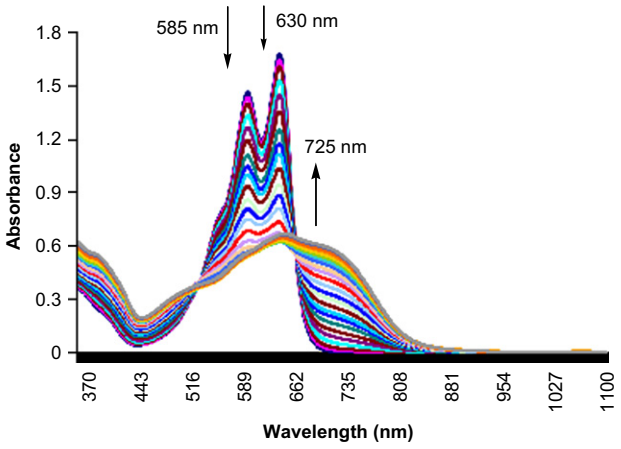


Figure 10. Changes in the UV–vis spectra of **4** (100 μM, pH 9.0±0.1, CH_3OH/H_2O 1:1) upon titration with Cu^{2+}.

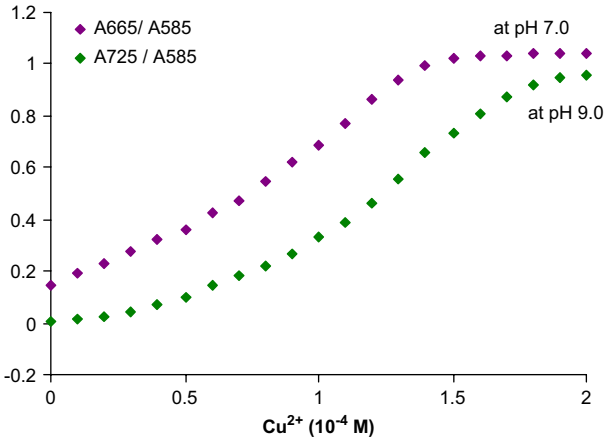


Figure 11. Plot of ratios of absorbances at pH 7.0 and 9.0 versus Cu^{2+} concentration.

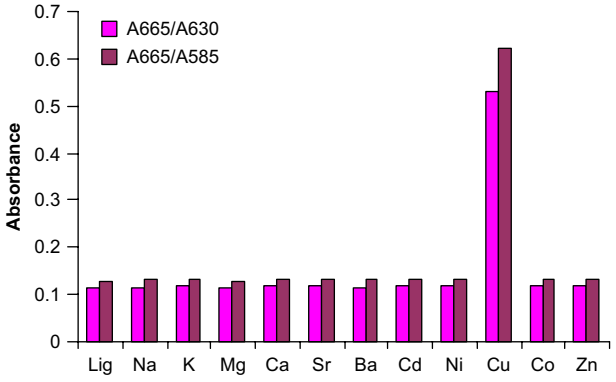


Figure 12. Responses of receptor **4** (100 μM) to selected metal ions (100 μM).

important cations such as Na^+, K^+, Ca^{2+} and Mg^{2+}, which did not give rise to any changes in the absorption spectrum of **4**. Similar results were seen for alkali, alkaline earth and other transition metal ions such as Ba^{2+}, Sr^{2+}, Co^{2+}, Cd^{2+}, Zn^{2+} and Ni^{2+} (Fig. 12).

Furthermore, for competitive analysis, a solution of **4** in the presence of Na^+, K^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Sr^{2+}, Co^{2+}, Cd^{2+}, Zn^{2+} and Ni^{2+} all in the millimolar range was titrated with

Cu^{2+} under identical conditions as described above. However, residual absorbance of **4** at λ_{max} 585 nm and 630 nm and of Cu^{2+}–**4** complex at λ_{max} 665 nm remained unaffected by the presence of these metal ions (Fig. 13). This clearly confirmed the selectivity of **4** towards Cu^{2+}.

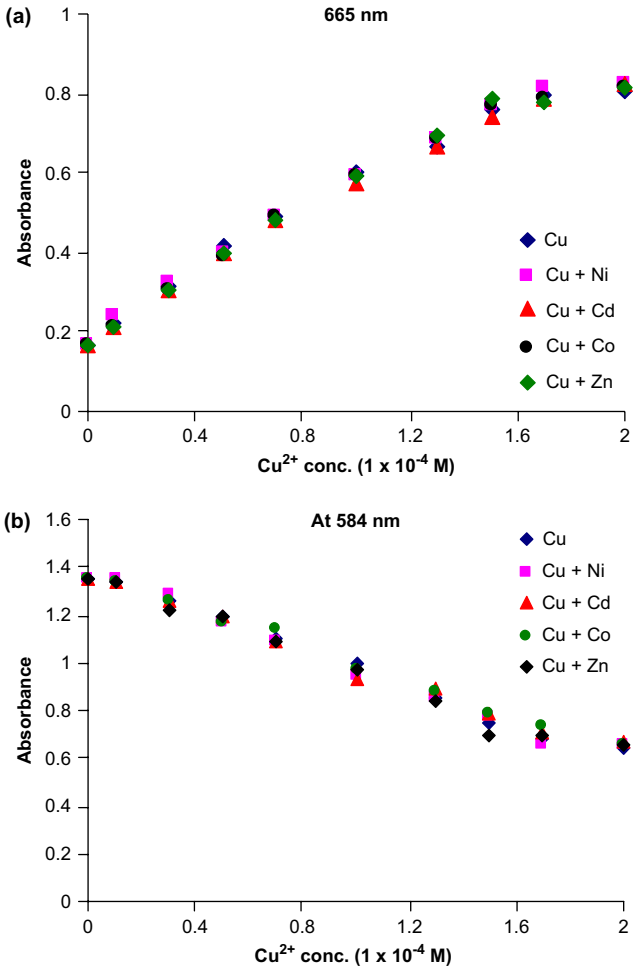


Figure 13. Plot of absorbance of **4** at (a) 665 nm, (b) 629 nm and (c) 585 nm against Cu^{2+} in the absence or presence of other metal ions (1000 μM).

3. Conclusion

Thus, 1,4-bis[2-aminoethylamino]anthracene-9,10-diones **3** and **4** in CH_3OH/H_2O (1:1) solution at pH >7 selectively bind with Cu^{2+} even in the presence of alkali, alkaline earth and other heavy metal ions. The Cu^{2+} mediated deprotonation of the aryl amine NH in the case of these chemosensors causes a bathochromic shift in the absorption band from 585 nm and 635 nm to 725 nm and enables ratiometric estimation of Cu^{2+} between pH 8 and 12.

4. Experimental

*4.1. General procedure for the synthesis of receptors **3–5***

The solution of 1,4-dihydroxyanthracene-9,10-dione (**7**) (2.4 g, 10 mmol) and sodium dithionite (5.22 g, 30 mmol) in 1,4-dioxane/water (1:1) was stirred at 25 °C for 3 h. It was extracted with ethyl acetate to get 1,4,9,10-tetrahydroxy-anthracene-9,10-dione (**8**), 85%. Compound **8** was added to excess of the respective amine (20 equiv) and the mixture was heated at 50 °C with stirring for 1 h under nitrogen and then cooled to 15 °C. This reaction mixture was oxidized at 50 °C by passing air through it for 40 min and then cooled to 15 °C. Acetonitrile was added and the precipitate formed was filtered off and washed with diethyl ether. The precipitates were recrystallized from acetonitrile to get pure chemosensors **3–5**.

*4.1.1. 1,4-Bis-(2-aminoethylamino)anthracene-9,10-dione (**3**)*

Blue solid; 60%; mp 175 °C (CH_3CN) (lit.[13a] mp 171–172 °C); FAB mass M^+ *m/z* 325 (M^++1); ^1H NMR ($CDCl_3$): δ 3.08 (t, *J*=6 Hz, 4H, 2×CH_2), 3.51 (q, *J*=6 Hz, 4H, 2×CH_2), 7.35 (s, 2H, ArH), 7.68–7.71 (m, 2H, ArH), 8.33–8.36 (m, 2H, ArH), 10.91 (br s, NH, exchanges with D_2O); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 39.17 (−ve, CH_2), 44.41 (−ve, CH_2), 118.61 (ab, ArC), 121.10 (+ve, ArCH), 124.24 (+ve, ArCH), 127.37 (+ve, ArCH), 133.79 (ab, ArC), 145.15 (ab, ArC),182.93 (ab, CO). Found: C 66.52; H 6.23; N 17.25%. $C_{18}H_{20}N_2O_4$ requires: C 66.65; H 6.21; N 17.27%.

*4.1.2. 1,4-Bis-(2-dimethylaminoethylamino)anthracene-9,10-dione (**4**)*

Blue solid; 75%; mp 170 °C (CH_3CN) (lit.[4h] mp 172–173 °C); FAB mass M^+ *m/z* 381 (M^++1); ^1H NMR ($CDCl_3$): δ 2.36 (s, 12H, 4×CH_3), 2.68 (t, *J*=6.6 Hz, 4H, 2×CH_2), 3.43 (q, *J*=6.3 Hz, 4H, 2×CH_2), 7.25 (s, 2H, ArH), 7.66–7.69 (m, 2H, ArH), 8.33–8.36 (m, 2H, ArH), 10.73 (br s, NH, exchanges with D_2O); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 40.96 (−ve, CH_2), 45.59 (+ve, CH_3), 57.47 (−ve, CH_2), 110.16 (ab, ArC), 123.42 (+ve, ArCH), 126.10 (+ve, ArCH), 131.98 (+ve, ArCH), 134.45 (ab, ArC), 145.82 (ab, ArC), 182.60 (ab, CO). Found: C 69.42; H 7.40; N 14.75%. $C_{22}H_{28}N_4O_2$ requires: C 69.45; H 7.42; N 14.73%.

*4.1.3. 1,4-Bis-(2-hydroxyethylamino)anthracene-9,10-dione (**5**)*

Blue solid; 70%; mp 230 °C (CH_3CN) (lit.[13b] mp 235 °C); FAB mass M^+ *m/z* 327 (M^++1); ^1H NMR ($CDCl_3$+DMSO): δ 3.53 (q, *J*=5.4 Hz, 4H, 2×CH_2), 3.73 (br s, 6H, 2×CH_2+2OH), 7.44 (s, 2H, ArH), 7.72–7.75 (m, 2H, ArH), 8.24–8.27 (m, 2H, ArH), 10.94 (t, *J*=5.1 Hz, NH, exchanges with D_2O); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 44.60 (−ve, CH_2), 60.08 (−ve, CH_2), 108.79 (ab, ArC), 123.56 (+ve, ArCH), 125.35 (+ve, ArCH), 131.41 (+ve, ArCH), 133.83 (ab, ArC), 145.83 (ab, ArC), 180.92 (ab, CO). Found: C 66.23; H 5.60; N 8.50%. $C_{22}H_{28}N_4O_2$ requires: C 66.25, H 5.56; N 8.58%.

4.2. Photophysical studies

UV–vis spectroscopic analysis was carried out on a Shimadzu UV-1601 PC UV–vis Spectrophotometer by using

slit width of 1.0 nm and matched quartz cells. All metal ion titrations were performed in CH_3OH/H_2O (1:1) at pH 7.0±0.1 (10 mM HEPES buffer). The pH and UV−vis combination titrations were performed with CH_3OH/H_2O (1:1) unbuffered solution. All absorption scans were saved as ASC II files and further processed in Excel™ to produce all graphs shown. Solutions of **3** and **4** were typically 100 μM.

Cu^{2+} binding characteristics, affinity and stoichiometries of different complexes were assessed via titrations with $Cu(NO_3)_2$. Titration data are fit with programme Specfit/32, which analyzes multi-wavelength data using an iterative method to obtain the association constant in terms of free or unbound Cu^{2+}.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.01.095.

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