Tetrahydroquinoxaline based squaraines: Synthesis and photophysical properties

4 AUTHORS, INCLUDING:

Raja Siram
Weizmann Institute of Science
11 PUBLICATIONS   **81** CITATIONS

Tetrahydroquinoxaline based squaraines: Synthesis and photophysical properties

Yogesh Chandrasekaran, Gitish K. Dutta, Raja Bhaskar Kanth, Satish Patil*

Solid State and Structural Chemistry Unit, Indian Institute of Science, Bangalore 560012, India

ARTICLE INFO

ABSTRACT

Tetrahydroquinoxaline based squaraine dyes synthesized by the condensation reaction between squaric acid and different tetrahydroquinoxaline derivatives are described. The squaraines gave a strong intense peak at 700 nm and were found to exhibit good molar extinction coefficient ($>10^5$ M^{-1} cm^{-1}). Metal binding studies were carried out with different metal ions and it was found that it was selective in the case of copper metal. Using Job's plot it was ascertained that the squaraines bind to the copper metal in the ratio of 2:1.

© 2009 Elsevier Ltd. All rights reserved.

1. Introduction

The development of novel near infrared (NIR) dyes has come a long way and in particular there has been a lot of research undergone by many groups for the synthesis of squaraine dyes [1–5]. Squaraine dyes (Fig. 1) have polarised donor–acceptor–donor (D–A–D) structure with the central four membered ring (C_4O_2) as electron acceptor and dimethylaniline group as the donor. These dyes absorb at around 640 nm and their excellent photophysical properties make them highly suitable for a wide range of applications. These include photodynamic therapy [6–8], protein detection [9,10], as photoconductors in solar cells [11–14], nonlinear optics [15–17], fluorescence imaging [18] and chemosensor [9,19–40] etc.

The intense absorption band of squaraines is a very attractive property for sensor design. Although many research groups have shown interest on developing squaraine chemosensors, sensitivity and selectivity to a specific analyte remains as the big challenge in the development of these sensors. Sensors for Cu^{2+} has been extensively studied [41–44] as it is a significant metal pollutant due to its widespread use [45–51], and it is also an essential trace element in biological systems [52–54]. But still there is a great demand for new indicators for the copper with improved properties.

In the present study we report the synthesis of tetrahydroquinoxaline based squaraine and its metal binding studies with copper.

An elegant approach to synthesize NIR squaraine dyes is to increase the electron donating ability of the donor group. The stronger electron donating effect can cause a pronounced bathochromic shift of the absorption band. In this context, we have explored quinoxaline as an effective electron donor. Quinoxalines are a very important class of benzoheterocycles, widely used in a variety of applications which include dyes [55,56], as building blocks in the synthesis of organic semiconductors [57], pharmaceuticals [58,59], and electrical/photochemical materials [32,60]. Further quinoxalines can also be sequentially reduced and dialkylated to tetrahydroquinoxaline derivatives using sodium borohydride and carboxylic acids [61,62]. Moreover, alkyl side chains attached on these moieties should increase the solubility. These remarkable properties of quinoxalines led us to explore the utility of substituted tetrahydroquinoxalines to prepare novel squaraines.

2. Experimental

2.1. Chemicals and instrument

All the solvents were of analytical grade. The metal salts $Mg(ClO_4)_2.6H_2O$, $Li(ClO_4).H_2O$, $Cu(ClO_4)_2.6H_2O$, $Zn(ClO_4)_2.6H_2O$, $Ca(ClO_4)_2.4H_2O$, $Cd(ClO_4)_2.H_2O$, $Pb(ClO_4)_2.H_2O$ were obtained from Sigma Aldrich. Millipore water was used in all cases; O-phenylene diamine was obtained commercially and 4-Methoxy-benzene-1,2-

* Corresponding author. Tel.: +91 80 22932651; fax: +91 80 23601310.
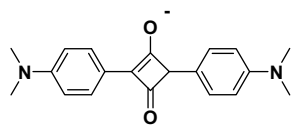 E-mail address: satish@sscu.iisc.ernet.in (S. Patil).

Fig. 1. Structure of parent squaraine dye.

diamine was prepared as described in the literature [63]. ^{1}H NMR and ^{13}C NMR spectra were recorded using Bruker 300 MHz or Bruker 400 MHz. Chemical shifts were given in parts per million and coupling constants (J) in Hertz. UV absorption spectra were obtained on Perkin Elmer UV–Vis Spectrometer. Fluorescence emission spectra were obtained using Perkin-Elmer Fluorimeter (LS 50B). Spectroscopic measurements were performed in standard quartz cells (1 cm × 1 cm). All the measurements were carried out at room temperature.

2.2. Synthesis

2.2.1. General procedure for the synthesis of quinoxaline

The diamine (7.7 mmol) was dissolved in dry acetonitrile (15 ml) and 1,2-diketone (8 mmol) was then added to the mixture, which was stirred at 60 °C for 6 h; reaction progress was monitored using TLC. Acetonitrile was removed from the ensuing compound by rotary evaporation; recrystallisation from ethanol gave the quinoxaline as a white solid.

2.2.2. General procedure for the synthesis of 1,4-diethylquinoxaline

In a 100 ml round bottom flask, quinoxaline (15 mmol) was dissolved in dry benzene (30 ml) and the reaction mixture was cooled to 5 °C to which was then added sodium borohydride (158 mmol) over a period of 15 min. The ensuing pale yellow slurry was stirred for 30 min at 5 °C and then glacial acetic acid (450 mmol) was added dropwise over 1 h. After maintaining the temperature at 10 °C for 1 h, the mixture was heated at reflux for 6 h. Upon completion of reaction, water (70 ml) was added dropwise to quench excess sodium borohydride and the mixture was extracted with ethyl acetate and the organic layer separated and dried over sodium sulfate. Column chromatography in hexane yielded the product in good yield.

2.2.3. General procedure for the synthesis of squaraines

1,4-Diethylquinoxaline (1.3 mmol) and squaric acid (0.55 mmol) was dissolved in a mixture of toluene and n-butanol (1:1) and was refluxed using Dean–Stark apparatus at 120 °C for 6 h. A notable change in colour is observed and the reaction was monitored by UV–Visible spectra for every 1 h. Then the reaction was mixture was cooled to room temperature. All the volatiles were removed in rotavapor and the dark green solid formed was precipitated out in hexane. The solid obtained is purified through column chromatography with 5% methanol/chloroform.

2.3. Compounds characterization

2.3.1. 1,4-Diethyl-1,2,3,4-tetrahydroquinoxaline (2a)

2a was purified by column chromatography with hexane as the eluent and was obtained as yellow oil. (Yield: 84%).
^{1}H NMR (400 MHz, CDCl$_3$): δ 6.54–6.51 (m, 2H), 6.48–6.46 (m, 2H), 3.24–3.19 (m, 8H), 1.09–1.02 (t, J = 6.8 Hz, 6H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 129.1, 118.9, 114.0, 57.9, 48.8, 13.3.

2.3.2. 2,3-Diphenylquinoxaline (1c)

1c was purified by passing over silica gel column to remove base impurities to get white solid. Recrystallization in acetonitrile gave needle like crystals. (Yield: 90%) ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.12–8.10 (q, 2H), 7.72–7.69 (q, 2H), 7.46–7.44 (d, J = 7.6 Hz, 4H) 7.28–7.26 (d, J = 6.8 Hz, 6H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 153.6, 141.3, 139.2, 129.9, 129.2, 128.8, 128.23.

2.3.3. 1,4-Diethyl-2,3-diphenyl-1,2,3,4-tetrahydroquinoxaline (2c)

2c was purified by column chromatography with hexane as the eluent and was obtained as white solid. (Yield: 80%) ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.08–7.05 (t, J = 6.8 Hz, 2H), 7.01–6.97 (t, J = 7.2 Hz, 4H), 6.70–6.68 (d, J = 7.2 Hz, 8H), 4.47(s, 2H), 3.34–3.29 (q, 2H), 3.04–2.99 (q, 2H), 0.94–0.91 (t, J = 8 Hz, 6H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 139.8, 135.6, 129.9, 127.9, 127.7, 118.38, 112.2, 65.4, 43.5, 11.3.

2.3.4. Squaraine dyes

3a: ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.04–8.02 (dd, J = 1.6 Hz, 2H), 7.64–7.63 (d, J = 1.6 Hz, 2H), 6.64–6.62 (d, J = 8.8 Hz, 2H), 3.62–3.60 (t, J = 4.8 Hz, 4H), 3.54–3.48 (q, J = 7.2 Hz, 4H), 3.45–3.39 (q, J = 7.2 Hz, 4H), 3.27–3.24 (t, J = 5.2 Hz, 4H), 1.27–1.22 (t, J = 7.2 Hz, 12H).
^{13}C NMR (100 MHz, CDCl$_3$): δ 184.5, 184.2, 143.1, 134.5, 126.1, 121.1, 110.2, 109.8, 48.2, 46.1, 45.1, 44.2, 11.2, 10.0.
FTIR (KBr) v: 3410, 2925, 2854, 1743, 1583, 1418, 1322, 1176 cm^{-1}.
HRMS [Found: m/z 459.271 [M + H]$^+$, Calcd for C$_{28}$H$_{35}$N$_4$O$_2$ [M + H]$^+$: 459.276].

3b: ^{1}H NMR (400 MHz, CDCl$_3$): CDCl$_3$ δ 8.21 (s, 2H), 6.02 (s, 2H), 3.59–3.50 (t, J = 5.2 Hz, 4H), 3.50–3.45 (q, J = 6.8 Hz, 4H), 3.40–3.3.35 (q, J = 7.2 Hz, 4H), 3.17–3.15 (t, J = 5.2 Hz, 4H), 1.28–1.21 (t, J = 7.2 Hz, 12H).
FTIR (KBr) v: 3474, 2969, 1667, 1520, 1352, 1280, 1181, 1049 cm^{-1}.
HRMS [Found: m/z 519.287 [M + H]$^+$, Calcd for C$_{28}$H$_{35}$N$_4$O$_2$ [M + H]$^+$: 519.289].

3c: ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.19–8.17 (d, J = 7.6 Hz, 2H), 7.96(s, 2H), 7.24–7.18 (m, 4H), 7.18–7.00 (m, 8H), 6.81–6.73 (m, 10H), 4.65–4.64 (d, J = 3.72 Hz, 2H), 4.53–4.52 (d, J = 3.76 Hz, 2H), 3.61–3.48 (m, 4H), 3.38–3.32 (m, 2H), 3.16–3.11 (m, 2H), 1.29–1.24 (m, 2H), 1.15–1.12 (t, J = 6.4 Hz, 6H,) 1.07–1.00 (t, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 184.2, 143.4, 138.5, 137.3, 135.2, 129.8, 129.5, 128.2, 128.0125.4, 121.4, 112.2, 110.9, 66.3, 62.2, 45.4, 41.9, 40.6,
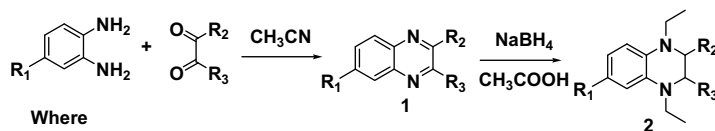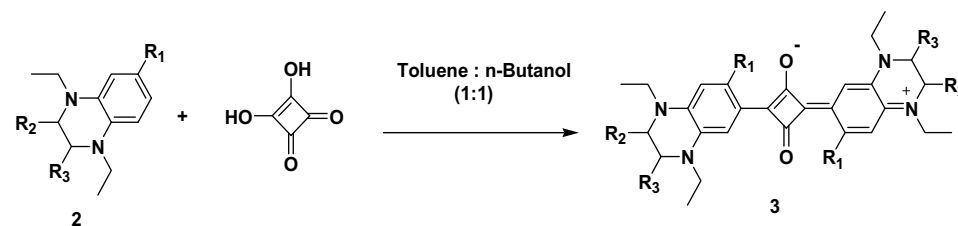

Where

1a, 2a --- R$_1$ = H, R$_2$ = H, R$_3$ = H

1b, 2b --- R$_1$ = OMe, R$_2$ = H, R$_3$ = H

1c, 2c --- R$_1$ = H, R$_2$ = Ph, R$_3$ = Ph

Scheme 1. Synthesis of tetrahydroquinoxaline.

Scheme 2. Synthesis of squaraines.

40.4, 12.2, 9.9. FTIR (KBr) v: 3342, 2931, 1723, 1583, 1414, 1341, 1260, 1169, 1073 cm^{-1}

HRMS [Found: m/z 764.409 [M + H]$^+$, Calcd for C$_{28}$H$_{35}$N$_4$O$_2$ [M + H]$^+$: 764.409].

2.4. Photophysical methods

2.4.1. Procedures of metal ion sensing
Stock solutions of the dye 3c (1.96 × 10^{-5} M) and metal ions (2.69 × 10^{-3} M) were prepared in distilled THF. Interaction with metal ions was observed by adding 1 ml of respective metal ion solution to the dye solution (5 ml). Absorption spectra of dye **3c** with different metal ions were studied. Copper showed more quenching and so interaction of the dye with different concentrations of copper was also studied.

2.4.2. Calculation of quantum yield
The fluorescence quantum yields were determined by using methylene blue as the standard ($\varphi_f = 0.52$ in CHCl$_3$). The quantum yield was calculated using the following equation.

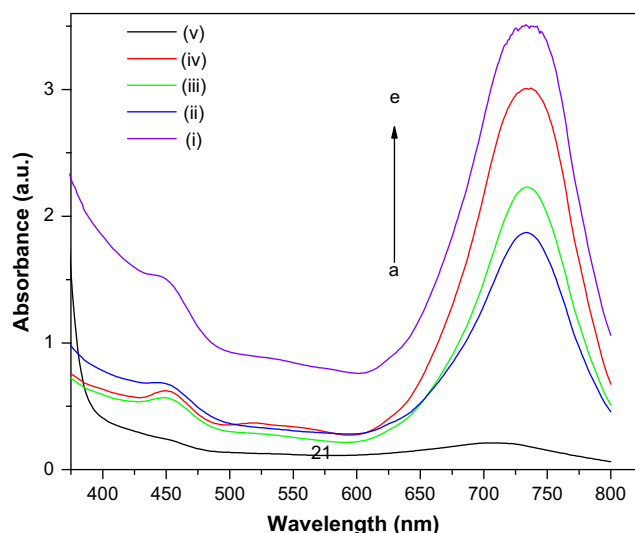$$\varphi_u = \frac{\varphi_s A_s F_u n_u^2}{A_u F_s n_s^2}$$

where φ_u and φ_s are the quantum yield of the unknown and standard, A_u and A_s are the absorbance of the unknown and standard, F_u and F_s are the integrated fluorescence intensity at the excitation wavelength of the unknown and standard, and n_u and n_s are the refractive index of the solvent of the unknown and standard, respectively.

3. Results and discussion

Initially quinoxalines were used as the donor group in the condensation reaction with squaric acid and the squaraine obtained gave an intense peak at 650 nm. But due to poor solubility of the product in common organic solvents, N-alkylation was carried out by reducing with sodium borohydride and acetic acid to obtain substituted tetrahydroquinoxalines (Scheme 1). This key intermediate was then employed to prepare novel squaraines by condensation with squaric acid. As anticipated the resulting squaraines showed a significant shift in absorbance (more than 700 nm) due to the increase in electron availability of the donor. These dyes are dark green in colour and show very high molar absorption coefficient (greater than 10^4 M^{-1} cm^{-1}).

Three different derivatives of the squaraine dye were synthesized by refluxing the electron rich tetrahydroquinoxaline derivatives with the electron deficient squaric acid (3,4-dihydroxy-3-cyclobutene-1,2-dione) in toluene/n-butanol (1:1) (Scheme 2).
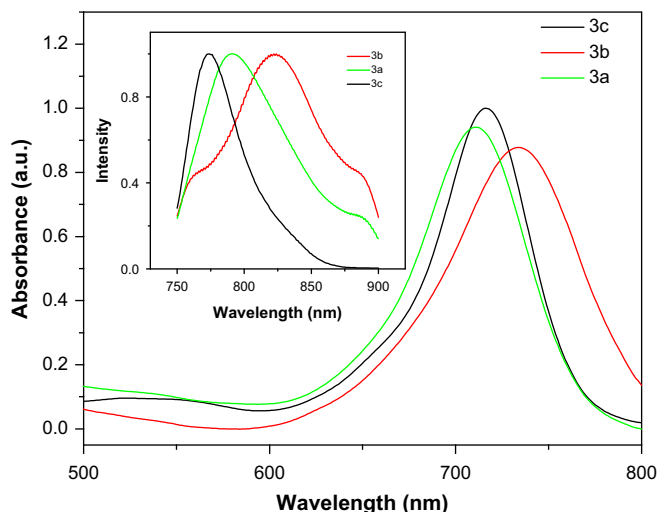

Fig. 2. Absorption spectra of dye 3 at different time intervals time: (i) 0 (ii) 1 (iii) 2 (iv) 4 (v) 6 h.

Fig. 3. Absorption spectra of dyes **3a–c** in CHCl$_3$. Inset shows the fluorescence spectra of the dyes.

Table 1
The absorption and emission properties of dyes **3a–c** in CHCl₃. Fluorescence quantum yield was calculated based on the reference, methylene blue ($\varphi_f = 0.52$ in CHCl₃).

Compound	Absorbance λ_{abs}(nm)	Molar absorbtivity ε (M^{-1} cm^{-1})	Fluorescence λ_{em}(nm)	Quantum yield φ_f
3a	711	10.30×10^4	790	9.6×10^{-3}
3b	732	2.47×10^4	823	2.98×10^{-3}
3c	717	10.44×10^4	774	2.9×10^{-2}

The reaction was monitored by UV for every 1 h and a very intense peak was obtained at around 700 nm. The absorbance was found to increase gradually for about 6 h and when there was no substantial increase in the absorbance, the reaction was stopped and the product purified by column chromatography. The change in absorption for different time intervals is obtained as shown in Fig. 2. The dyes (**3a–3c**) were characterized by FTIR, NMR, & HRMS. The results were consistent with proposed structures. All three dyes are soluble in common organic solvents like chloroform, dichloromethane and tetrahydrofuran.

The absorbance and fluorescence for the tetrahydroquinoxaline based squaraine dyes (**3a–3c**) have been studied and their normalized spectra are shown in Fig. 3. All these dyes show absorption at around 700 nm and emission at 800 nm in chloroform solution. It clearly indicates that the greater the electron donating ability of the donor group, the larger the bathochromic shift when compared to the parent dye derived from the N,N-dimethylaniline (Fig. 1). The molar absorption coefficients of tetrahydroquinoxaline based squaraine dyes are very high, ranging from 2–10×10^4 M^{-1} cm^{-1}. To understand the role of electron donating effect on squaraine dyes, we further introduced different electron donating groups on tetrahydroquinoxaline as shown in Scheme 2. When we introduced methoxy group on phenyl ring of the tetrahydroquinoxaline an even more bathochromic shift was observed (Fig. 3). The unsubstituted tetrahydroquinoxaline based squaraine **3a**, exhibits an absorption maximum at 711 nm but when the methoxy substituent is introduced **3b**, there is a red shift of 22 nm. When phenyl group was attached to pyrazine part of the tetrahydroquinoxalines, it is slightly red shifted as compared to unsubstituted tetrahydroquinoxalines. But it did not show the considerable bathochromic shift in absorbance spectra unlike methoxy group as a donor. This indicates that the electron donating group closer to central four membered ring (acceptor) shows greater overlap with rest of the chromogen. The corresponding changes in fluorescence spectra of these dyes are shown in the inset (Fig. 3). The introduction of nitro group to the tetrahydroquinoxaline moiety decreased the electron donating ability and as expected the reaction with squaric acid did not yield the corresponding squaraines. Furthermore, electron donating groups (R2 & R3 = –CH₃) were incorporated on pyrazine part of the

Table 2
Absorbance and fluorescence of **3a–c** in different solvents.

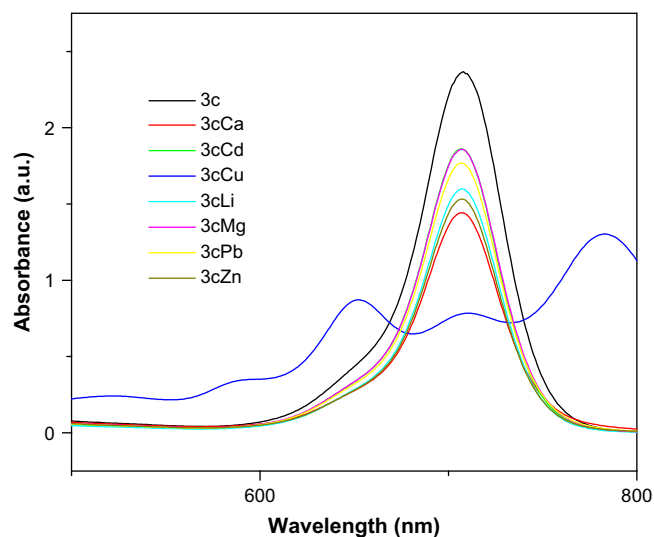| Compound	Solvent	Absorbance λ_{abs}(nm)	Fluorescence λ_{em}(nm)
3a	Chloroform	711	790
	Methanol	728	821
	Tetrahydrofuran	704	786
	Acetonitrile	713	827
3b	Chloroform	732	822
	Methanol	743	821
	Tetrahydrofuran	724	815
	Acetonitrile	733	829
3c	Chloroform	717	774
	Methanol	733	817
	Tetrahydrofuran	708	769
	Acetonitrile	716	800

tetrahydroquinoxaline but we found this compound is unstable at room temperature for structural characterization.

The high molar absorptivity (greater than 10^4 M^{-1} cm^{-1}) and good quantum yield was evident from the absorption and emission properties of the 3 dyes (Table 1). The degree of red shift in emission is modest in the case of **3c** and **3a**. A relatively large red shift in 3b indicates the donor group directly linked to central four (C₂O₄) membered ring heavily affects excited state energies of these molecules. The absorption and the emission properties of the three dyes in four different solvents like acetonitrile, tetrahydrofuran, methanol and chloroform are listed in Table 2. When polarity is changed from non-polar to polar solvent, bathochromic shift is observed for the absorbance and fluorescence of the 3 dyes. The large numbers of squaraines have been used as a probe for the detection of a variety of analytes. We have also investigated the metal interaction of tetrahydroquinoxaline based squaraine dyes with different metals ions. Complexation with different metal ions showed significant change in the absorption peak indicating the characteristics of the metal interaction involved.

The dye **3c** was selected as a representative example because of its better solubility and stability. The dye **3c** (1.96×10^{-5} M) with the addition of various perchlorate salts did not result in change in colour but when copper perchlorate was added an apparent change in colour was observed. The notable change in colour allows specific visual detection and is represented in Figs. 4 and 5. The presence of metal ions like lithium, magnesium and zinc caused less quenching in absorbance at 706 nm whereas addition of copper salt resulted in decrease in the absorption band at 706 nm, with the concomitant formation of new bands at 652 nm and 784 nm.

The above results encouraged us to explore the absorption changes with respect to different concentrations of copper perchlorate as shown in Fig. 6. As the copper concentration increases, there is a significant decrease in the absorbance peak at 706 nm and the new peaks at 652 nm and 784 nm increases in intensity. Martinez-Manez et al. [64] found blue and red shift in aniline based squaraines upon interaction with the metal ions. These findings were explained based on the coordination of nitrogen and oxygen to the metal ions. Dye **3c** possess two potential binding sites i.e. nitrogen from quinoxaline unit and oxygen from the central four membered ring. This give rise to blue shift around 652 nm and a red shift around 784 nm upon interaction with

Fig. 4. Absorption spectra of dye **3c** (1.96×10^{-5} M) in presence of metal perchlorates (2.69×10^{-4} M) in THF.

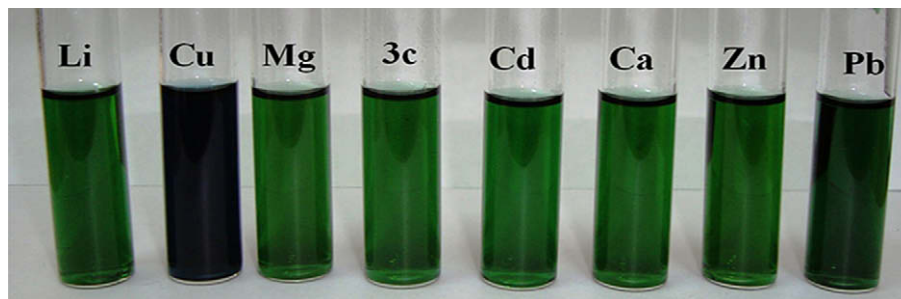**Fig. 5.** Colour of the dye **3c** solution (1.96×10^{-5} M) in the absence and presence of different metal ions (2.69×10^{-4} M) in THF.
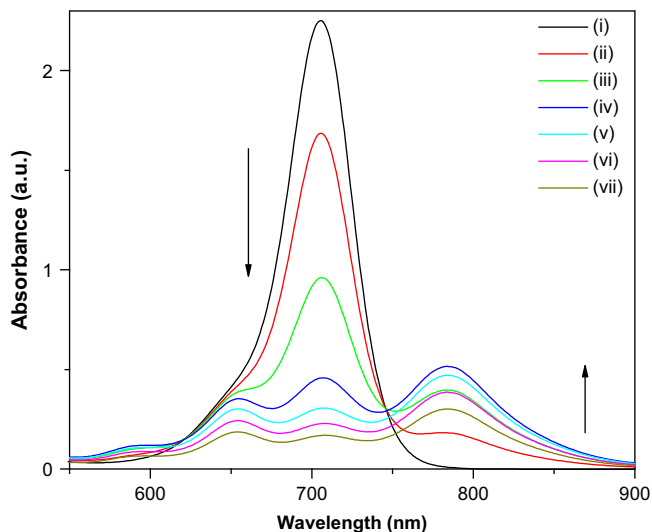

Fig. 6. Absorption spectra of dye **3c** (3.14×10^{-5} M) in THF with the addition of Cu^{2+}; $[Cu^{2+}]$ = (i) 0, (ii) 0.31, (iii) 0.62, (iv) 0.94, (v) 1.26, (vi) 1.57, (vii) 1.88×10^{-5} M.

Fig. 8. Proposed complexation mode of copper with the squaraine dye **3c**.

Job's plot (Fig. 7). The above result is conclusive of the fact that the tetrahydroquinoxaline based squaraines can be used to detect even small amount of copper selectively. The binding of Cu^{2+} with the dye **3c** could be attributed to the presence of nitrogen in the quinoxaline ring and the electron rich carbonyl group in the squaric acid as shown in Fig. 8.

4. Conclusion

A new class of NIR emitting squaraines with tetrahydroquinoxaline as the donor group has been synthesized and photophysical properties were investigated. The electron donating group shows bathochromic shift in absorption as well as in fluorescence. Interaction of squaraine with different metal ions was carried out in THF and it was found that copper ion can be detected selectively. The stoichiometry of the complex between the dye and copper was found out to be 2:1 using Job's Plot.
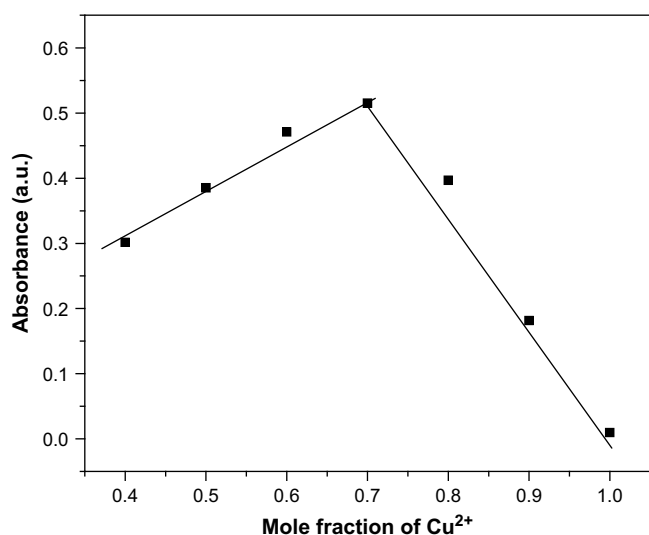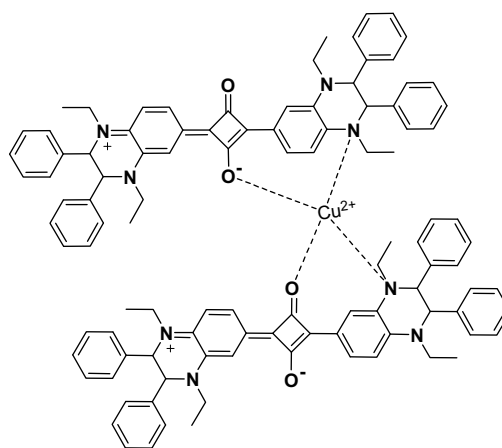
Fig. 7. Job's plot of dye **3c** (3.14×10^{-5} M) in THF with the addition of Cu^{2+}.

copper perchlorate salt as shown in Fig. 4. This clearly indicates that copper ion coordinated with both the binding sites nitrogen as well as oxygen.

The stoichiometry of the complex formed between the squaraine dye **3c** and Cu^{2+} was found to be 2:1 as evidenced from the

References

[1] Santos PF, Reis LV, Almeida P, Oliveira AS, Ferreira LFV. Singlet oxygen generation ability of squarylium cyanine dyes. J Photochem Photobiol A 2003;160:159.
[2] Santos PF, Reis LV, Almeida P, Serrano JP, Oliveira AS, Ferreira LFV. Efficiency of singlet oxygen generation of aminosquarylium cyanines. J Photochem Photobiol A 2004;163:267.
[3] Santos PF, Reis LV, Duarte I, Serrano JP, Almeida P, Oliveira AS, et al. Synthesis of fusion-isomeric imidazopyridines and their evaluation as inhibitors of syn- and anti-protonating glycosidases. Helv Chim Acta 2005;88:113.

[4] Beverina L, Abbotto A, Landenna M, Cerminara M, Tubino R, Meinardi F, et al. New π-extended water-soluble squaraines as singlet oxygen generators. Org Lett 2005;7:4257.

[5] Jyothish K, Rekha R, Avirah R, Ramaiah D. Development of squaraine dyes for photodynamic therapeutical applications: synthesis and study of electronic factors in the dye formation reaction. Arkivoc 2007;8:296.

[6] Ramaiah D, Joy A, Chandrasekhar N, Eldho NV, Das S, George MV. Halogenated squaraine dyes as potential photochemotherapeutic agents. Synthesis and study of photophysical properties and quantum efficiencies of singlet oxygen generation. Photochem Photobiol 1997;65:783.

[7] Ramaiah D, Eckert I, Arun KT, Weidenfeller L, Epe B. Squaraine dyes for photodynamic therapy: study of their cytotoxicity and genotoxicity in bacteria and mammalian cells. Photochem Photobiol 2002;76:672.

[8] Ramaiah D, Eckert I, Arun KT, Weidenfeller L, Epe B. Squaraine dyes for photodynamic therapy: mechanism of cytotoxicity and DNA damage induced by halogenated squaraine dyes plus light (>600 nm). Photochem Photobiol 2004;79:99.

[9] Suzuki Y, Yokoyama K. A protein-responsive chromophore based on squaraine and its application to visual protein detection on a gel for SDS-PAGE. Angew Chem Int Ed 2007;46:4097.

[10] Jisha VS, Arun TK, Hariharan M, Ramaiah D. Site-selective binding and dual mode recognition of serum albumin by a squaraine dye. J Am Chem Soc 2007;128:6024.

[11] Loutfy RO, Hsiao CK, Kazmaier PM. Photoconductivity of organic particle dispersions: squaraine dyes. Photogr Sci Eng 1983;27:5.

[12] Merritt VY. Organic photovoltaic materials: squarylium and cyanine-TCNQ dyes. IBM J Res Dev 1978;22:353.

[13] Piechowski AP, Bird GR, Morel DL, Stogryn EL. Desirable properties of photovoltaic dyes. J Phys Chem 1984;88:934.

[14] Liang KN, Law KY, Whitten DG. Estimation of exciton sizes in squaraine monolayers by intralayer photoinduced electron transfer. J Phys Chem 1995;99:16704.

[15] Chen CT, Marder SR, Cheng LT. Syntheses and linear and nonlinear optical properties of unsymmetrical squaraines with extended conjugation. J Am Chem Soc 1994;116:3117.

[16] Ashwell GJ, Jefferies G, Hamilton DG, Lynch DE, Roberts MPS, Bahra GS, et al. Strong second-harmonic generation from centrosymmetric dyes. Nature 1995;375:385.

[17] Ashwell GJ. A comment upon the aggregation of squaraine dyes. J Mater Chem 1998;8:373.

[18] Johnson JR, Fu N, Arunkumar E, Leevy WM, Gammon ST, Worms DP, et al. Squaraine rotaxanes: superior substitutes for Cy-5 in molecular probes for near-infrared fluorescence cell imaging. Angew Chem Int Ed 2007;46:5528.

[19] Oguz U, Akkaya EU. A squaraine-based sodium selective fluorescent chemosensor. Tetrahedron Lett 1998;39:5857.

[20] Oguz U, Akkaya EU. One-pot synthesis of a red-fluorescent chemosensor from an azacrown, phloroglucinol and squaric acid: a simple in-solution construction of a functional molecular device. Tetrahedron Lett 1997;38:4509.

[21] Akkaya EU, Turkyilmaz S. A squaraine-based near IR fluorescent chemosensor for calcium. Tetrahedron Lett 1997;38:4513.

[22] Isgor YG, Akkaya EU. Chemosensing in deep red: a squaraine-based fluorescent chemosensor for pH. Tetrahedron Lett 1997;38:7417.

[23] Thomas KG, Thomas KJ, Das S, George MV. A squaraine-based near-infrared absorbing sensor for the selective detection of transition and other metal ions in aqueous media. Chem Commun 1997:597.

[24] Ros-Lis JV, Martínez-Máñez R, Rurack K, Sancenón F, Soto J, Spieles M. Highly selective chromogenic signaling of Hg²⁺ in aqueous media at nanomolar levels employing a squaraine-based reporter. Inorg Chem 2004;43:5183.

[25] Ros-Lis JV, Marcos MD, Martínez-Máñez R, Rurack R, Soto J. A regenerative chemodosimeter based on metal-induced dye formation for the highly selective and sensitive optical determination of Hg²⁺ ions. Angew Chem Int Ed 2005;44:4405.

[26] Jiménez D, Martínez-Máñez R, Sancenón F, Ros-Lis JV, Benito A, Soto J. A new chromo-chemodosimeter selective for sulfide anion. J Am Chem Soc 2003;125:9000.

[27] Ros-Lis JV, Martinéz-Máñez R, Soto J. A selective chromogenic reagent for cyanide determination. Chem Commun 2002:2248.

[28] Ros-Lis JV, García B, Jiménez D, Martínez-Máñez R, Sancenón F, Soto J, et al. Squaraines as fluoro–chromogenic probes for thiol-containing compounds and their application to the detection of biorelevant thiols. J Am Chem Soc 2004;126:4064.

[29] Ros-Lis JV, Martínez-Máñez R, Soto J. Colorimetric signaling of large aromatic hydrocarbons via the enhancement of aggregation processes. Org Lett 2005;7:2337.

[30] Ajayaghosh A. Chemistry of squaraine-derived materials: near-IR dyes, low band gap systems, and cation sensors. Acc Chem Res 2005;38:449.

[31] Snee PT, Somers RC, Nair G, Zimmer JP, Bawendi MG, Nocera DG. A ratiometric CdSe/ZnS nanocrystal pH sensor. J Am Chem Soc 2006;128:13320.

[32] Arunkumar E, Ajayaghosh A, Daub J. Selective calcium ion sensing with a bichromophoric squaraine foldamer. J Am Chem Soc 2005;127:3156.

[33] Balbo Block MA, Hecht S. Alternating (squaraine–receptor) sensory polymers: modular one-pot synthesis and signal transduction via conformationally controlled exciton interaction. Macromolecules 2004;37:4761.

[34] Chenthamarakshan CR, Ajayaghosh A. Enhanced sensitivity and selectivity in lithium ion recognition property of an oligomeric squaraine dye based fluorescent sensor. Tetrahedron Lett 1998;39:1795.

[35] Thomas J, Sherman DB, Amiss TJ, Andaluz SA, Pitner JB. Synthesis and biosensor performance of a near-IR thiol-reactive fluorophore based on benzothiazolium squaraine. Bioconjug Chem 2007;18:1841.

[36] Ajayaghosh A, Chithra P, Varghese R, Divya KP. Controlled self-assembly of squaraines to 1D supramolecular architectures with high molar absorptivity. Chem Commun 2008:969.

[37] Jyothish K, Hariharan M, Ramaiah D. Chiral supramolecular assemblies of a squaraine dye in solution and thin films: concentration, temperature, and solvent-induced chirality inversion. Chem Eur J 2007;13:5944.

[38] Hsueh SY, Lai CC, Liu YH, Peng SM, Chiu SH. Highly selective Na⁺-templated formation of [2] Pseudorotaxanes exhibiting significant optical outputs. Angew Chem Int Ed 2007;46:2013.

[39] Ajayaghosh A, Chithra P, Varghese R. Self-assembly of tripodal squaraines: cation-assisted expression of molecular chirality and change from spherical to helical morphology. Angew Chem Int Ed 2007;46:230.

[40] Stoll RS, Severin N, Rabe JP, Hecht S. Synthesis of a novel chiral squaraine dye and its unique aggregation behavior in solution and in self-assembled monolayers. Adv Mater 2006;18:1271.

[41] Bhattacharya S, Thomas M. Synthesis of a novel thiazole based dipeptide chemosensor for Cu(II) in water. Tetrahedron Lett 2000;41:10313.

[42] Zheng Y, Orbulescu X, Ji X, Andreopoulos FM, Pham SM, Leblanc RM. Development of fluorescent film sensors for the detection of divalent copper. J Am Chem Soc 2003;125:2680.

[43] Brasola E, Mancin F, Rampazzo E, Tecilla P, Tonellato U. A fluorescence nanosensor for Cu²⁺ on silica particles. Chem Commun 2003:3026.

[44] Zheng Y, Cao X, Orbulescu J, Konka V, Antreopoulos FM, Pham SM, et al. Peptidyl fluorescent chemosensors for the detection of divalent copper. Anal Chem 2003;75:1706.

[45] Kaur S, Kumar S. Photoactive chemosensors 4: a Cu²⁺ protein cavity mimicking fluorescent chemosensor for selective Cu²⁺ recognition. Tetrahedron Lett 2004;45:5081.

[46] Kaur S, Kumar S. Photoactive chemosensors 3: a unique case of fluorescence enhancement with Cu(II). Chem Commun 2002:2840.

[47] Kumar S, Kaur S, Singh G. Photoactive chemosensors 2: 8-hydroxyquinoline based Cu(II) selective fluorescent tripod. Supramol Chem 2003;15:65.

[48] Kumar S, Pramilla Kaur S. Photoactive chemosensors. Part 1: a 9,10-anthraquinone and 2-aminothiophenol based Cu(II) selective chemosensor. Tetrahedron Lett 2002;43:1097.

[49] Frausto da Silva JJR, Williams RJP. The biological chemistry of elements: the inorganic chemistry of life. Oxford: Clarendon Press; 1993. p. 388.

[50] Sreejith S, Carol P, Chithra P, Ajayaghosh A. Squaraine dyes: a mine of molecular materials. J Mater Chem 2008;18:264.

[51] Beverina L, Crippa M, Salice P, Ruffo R, Ferrante C, Fortunati I, et al. Indolic squaraines as two-photon absorbing dyes in the visible region: X-ray structure, electrochemical, and nonlinear optical characterization. Chem Mater 2008;20:3242.

[52] Bello KA, Ajayi JO. Near-infrared absorbing squarylium dyes. Dyes Pigments 1996;31:79.

[53] Fabian J, Nakazumi H, Matsuoka M. Near-infrared absorbing dyes. Chem Rev 1992;92:1197.

[54] Law KY. Squaraine chemistry. Absorption, fluorescence emission, and photophysics of unsymmetrical squaraines. J Phys Chem 1995;99:9818.

[55] Sonawane ND, Rangnekar DW. Synthesis and application of 2-styryl-6,7-dichlorothiazolo[4,5-b]quinoxaline based fluorescent dyes: part 3. J Heterocycl Chem 2002;39:303.

[56] Dailey S, Feas JW, Peace RJ, Sage IC, Till S, Wood EL. Synthesis and device characterisation of side-chain polymer electron transport materials for organic semiconductor applications. J Mater Chem 2001;11:2238.

[57] Brien DO, Weaver MS, Lidzey DG, Bradley DDC. Use of poly(phenyl quinoxaline) as an electron transport material in polymer light-emitting diodes. Appl Phys Lett 1996;69:881.

[58] Gazit A, App H, McMahon G, Chen J, Levitzki A, Bohmer FD. Tyrphostins. 5. Potent inhibitors of platelet-derived growth factor receptor tyrosine kinase: structure–activity relationships in quinoxalines, quinolines, and indole tyrphostins. J Med Chem 1996;39:2170.

[59] Sehlstedt U, Aich P, Bergman J, Vallberg H, Norde B, Graslund A. Interactions of the antiviral quinoxaline derivative 9-OH-B220 {2,3-dimethyl-6-(dimethylaminoethyl)-9-hydroxy-6H-indolo-[2,3-b]quinoxaline} with duplex and triplex forms of synthetic DNA and RNA. J Mol Biol 1998;278:31.

[60] Basheer MC, Alex S, Thomas KG, Suresh CH, Das S. A squaraine-based chemosensor for Hg²⁺ and Pb²⁺. Tetrahedron 2006;62:605.

[61] Gloster DF, Cincotta L, Foley JW. Design, synthesis, and photophysical characterization of novel pentacyclic red shifted azine dyes. J Heterocycl Chem 1999;36:25.

[62] Cosmao JM, Collignon N, Queguiner G. Réduction alkylante de quelques composés hétéroaromatiques polyazotés. J Heterocycl Chem 1979;16:973.

[63] Mahajan SS, Nandre RG. Studies in the synthesis of 2-mercapto-5-methoxybenzimida zole. Indian J Chem Section B Org Chem 2006;45B(7):1756.

[64] Ros-Lis JV, Martinex-Manez R, Sancenon F, Soto J, Spieles M, Rurack K. Squaraines as reporter units: insights into their photophysics, protonation and metal-ion coordination behaviour. Chem Eur J 2008;14:10101.