SYNTHESIS AND CHARACTERIZATION OF HIGHLY FLUORESCENT NOVEL COUMARIN CHROMOPHORES

Amit Jagtap, Vijay Satam, Rajkumar Rajule, Vinod Kanetkar*
Department of Dyestuff Technology, Institute of Chemical Technology,
N. P. Marg, Matunga, Mumbai, Maharashtra-400019, India.

ABSTRACT

The novel 1,4-diethyl-1,2,3,4-tetrahydro-7-hydroxyquinoxalin-6-carboxaldehyde was synthesized, characterized and condensed with ethyl acetoacetate to obtain novel coumarin chromophore **7.** This novel coumarin derivative was further condensed with malononitrile to obtain dicyano derivative **8** which showed absorption maxima at 506 nm. This novel coumarin chromphore having 1,4-diethyl-1,2,3,4-tetraydroquinoxaline framework as electron releasing system showed red hue, exhibited brilliant fluorescence and possess remarkable thermal stability. It absorbed and emitted at higher wavelengths as compared to its 7-N,N-diethyl and Julolidine analogs. The synthesis, characterization and evaluation of spectral characteristics and thermal properties of the novel coumarin dye are reported.

Keywords: 1,4-Diethyl-1,2,3,4-tetrahydro-7-hydroxyquinoxalin-6-carboxaldehyde, Coumarin, synthesis, fluorescence, spectral characteristics, thermal stability.

CONTACT

vrkanetkar@gmail.com, vrkanetkar@udct.org

INTRODUCTION

Coumarin compounds are the most dynamic class of organic compounds which find applications in various fields of science and technology. A number of fluorescent organic chromophores derived from coumarin have been used as fluorescent brighteners, laser dyes and organic nonlinear optical materials[1-3]. They constitute the largest class of laser dyes for the 'blue–green' region[4-5]. Due to inherent photochemical characteristics, reasonable stability, good solubility and relative ease of synthesis coumarin derivatives have been extensively investigated for electronic and photonic applications such as charge-transfer agents, solar energy collectors and nonlinear optical materials[6-9]. They are widely used as fluorescent labels and pigments[10], as fluorescent probes for physiological[11-13] and enzymatic measurements, as signaling units in sensors[14-17] and in sophisticated photophysical systems[18-22]. Coumarin chromophores exhibit intense fluorescence on substitution of various functional groups at different positions[23,24] and appropriately substituted coumarins find application as fluorescent dyes for synthetic fibres and as daylight fluorescent pigments, which impart vivid brilliance to paints and printing inks[25,26]. It is well known that, the property of fluorescence in the coumarin chromophore system is significantly altered by appropriate substituents at 3 and 7 positions. Electron donors such as amino, hydroxyl and methoxy groups at 7 position and electron acceptor heterocyclic rings such as benzthiazole, benzoxazole and benzimidazole at the 3 position impart pronounced bathochromicity and strong fluorescence. Most of coumarin based chromophores reported in literature absorb in the range of 420 to 450 nm. In this communication, we report novel coumarin chromophores having 1,4-diethyl-1,2,3,4-tetraydroquinoxaline framework as electron releasing system. These chromophores absorb and emit at longer region of electromagnetic spectrum, exhibit brilliant fluorescence and possess excellent thermal stability.

The classical synthesis of quinoxalines involves condensation of aromatic 1,2-diamines with 1,2-dicarbonyl compounds. The reaction is facile and is the most widely used synthetic method for both quinoxaline and its derivatives. Quinoxalines can be easily reduced to 1,2,3,4-

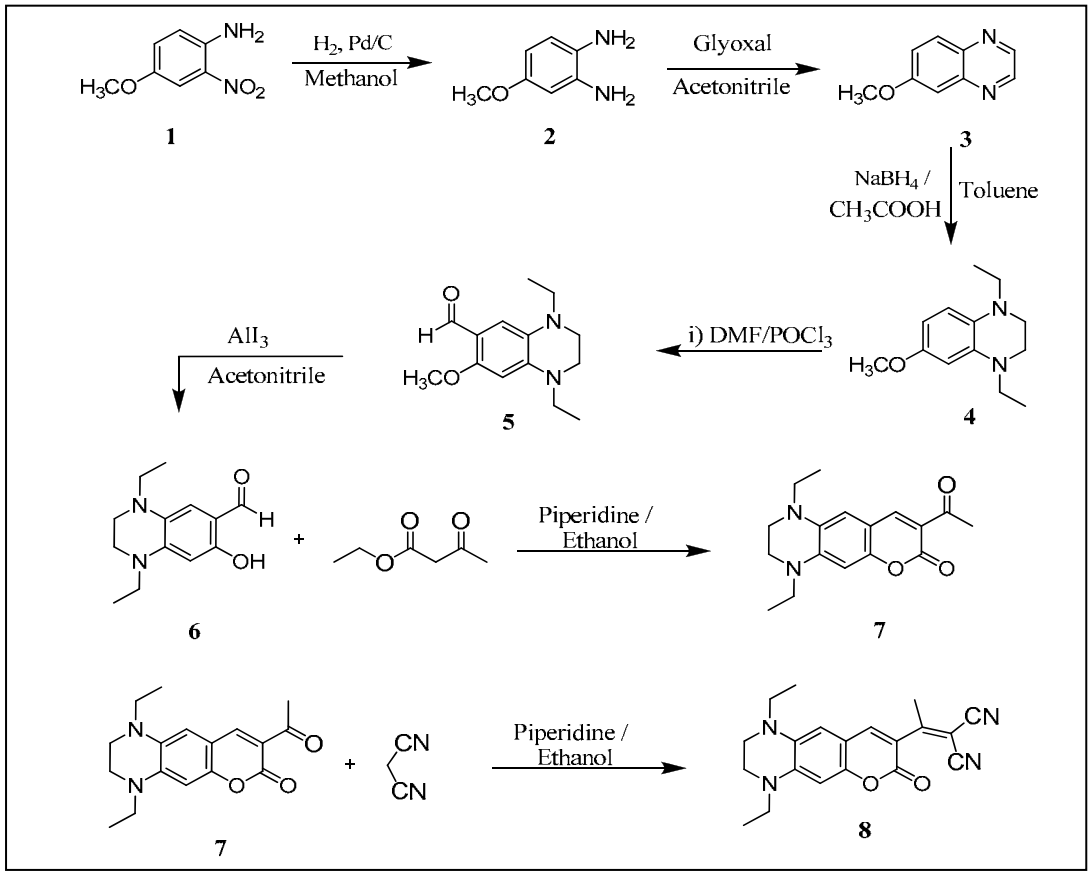
tetrahydroquinoxalines by reducing agents such as lithium aluminium hydride[27] and sodium borohydride[28] in excellent yields. Sequential reduction and alkylation of N-heterocycles such as indole to N-alkylated indoline and quinoline to 1,2,3,4-tetrahydroquinoline by sodium borohydride and trifluoroacetic acid is well known[29-32]. Quinoxalines can also be sequentially reduced and dialkylated using sodium borohydride and carboxylic acids. 6-Nitroquinoxaline has been subjected to similar reductive alkylation using sodium borohydride and glacial acetic acid to obtain 1,4-diethyl-1,2,3,4-tetrahydro-6-nitroquinoxaline[33]. The 1,4-diethyl-1,2,3,4-tetrahydroquinoxaline framework is highly electron rich. It was envisaged that, coumarins possessing such strongly electron donating and rigid system could exhibit pronounced bathochromicity and excellent fluorescence.

RESULTS AND DISCUSSION

Synthesis of Coumarin Chromophores

The novel coumarin chromophore **7** was prepared by classical Knoevenagel condensation of 1,4-diethyl-7-hydroxy-1,2,3,4-tetrahydroquinoxaline-6-carboxaldehyde **6** with ethyl acetoacetate. This coumarin derivative was further condensed with malononitrile in the presence of catalytic piperidine to yield coumarin **8**, the synthesis is outlined in Scheme 1. In the first stage, 4-methoxy-2-nitroaniline **1** was hydrogenated over palladium charcoal catalyst in methanol to obtain 4-methoxy-1,2-phenylenediamine **2** which was subsequently condensed with glyoxal in acetonitrile to afford 6-methoxyquinoxaline **3** in excellent yield. Reductive alkylation of **3** with sodium borohydride and glacial acetic acid in dry toluene yielded 1,4-diethyl-6-methoxy-1,2,3,4-tetrahydroquinoxaline **4**. The highly electron rich 1,2,3,4-tetrahydroquinoxaline derivative **4** was subjected to Vilsmeier – Haack reaction to obtain 1,4-diethyl-7-methoxy-1,2,3,4-tetrahydroquinoxaline-6-carboxaldehyde **5** which on demethylation with AlI_3 (prepared insitu) in acetonitrile gave hydroxy aldehyde **6**. The reaction mixture of aldehyde **6** and ethyl acetoacetate was refluxed in absolute ethanol and catalytic amount of piperidine to yield coumarin dye **7** which was then condensed with malononitrile in the presence of catalytic amount of piperidine to yield novel coumarin derivative **8.** The structures of the dyes were confirmed by FT-IR, ^{1}HNMR, Mass spectroscopy and elemental analysis.

Scheme 1



Spectral Characteristics of the Dyes

Basic spectral characteristics of the chromophores such as the absorption maxima (λ_{max}), emission maxima (λ_{em}) and extinction coefficient (ε) were measured in dichloromethane and are presented in Table 1. The electronic absorption spectra of the dyes **7** and **8** displayed absorption maxima in the visible region at 476 and 506 nm. Compound **8** underwent strong bathochromic shift owing to the presence another styryl group attached to two electron accepting cyano groups.

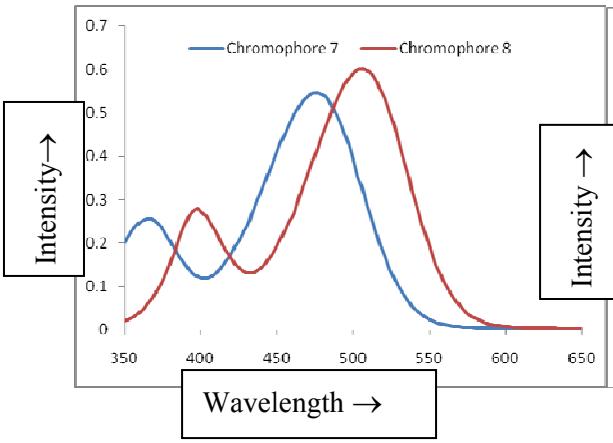


Fig1. Absorption maxima of the chromophores 7 and 8 in Dichloromethane

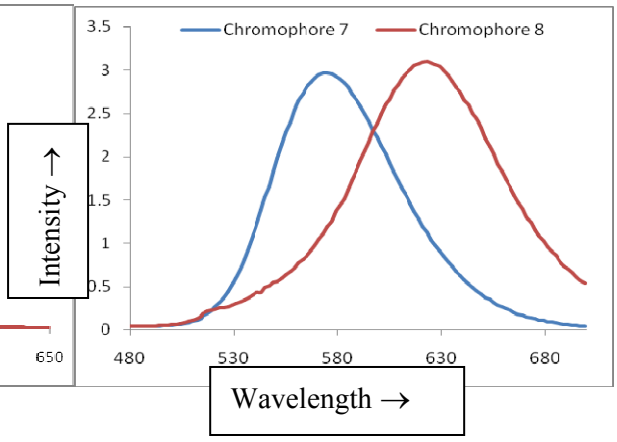
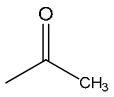
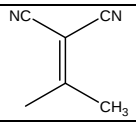
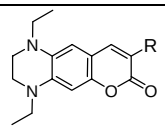
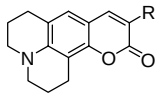
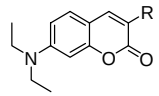


Fig2. Emission maxima of the chromophores 7 and 8 in Dichloromethane

The spectral properties of the dyes **7** and **8** were compared with analogous dyes known in the literature. The values are summarized in Table 1. It is clearly evident that the dyes **7** and **8** having electron donating 1,4-diethyl-1,2,3,4-tetrahydroquinoxaline framework showed remarkable shift towards longer wavelength. Also the Stokes shifts of the dyes **7** and **8** were found to be higher than their relative analogs.

Table1. Comparison of the spectral properties in dichloromethane of the dye 7 and 8 with analogous dyes

R						
	λmax (nm)	**λem (nm)**	**Stokes shift**	**λmax (nm)**	**λem (nm)**	**Stokes shift**
	474	568	94	506	623	117
	---	---	---	481	569	88
	435	465	30	---	---	---

Thermal Properties of The Dyes

The compounds were subjected to the thermogravimetric analysis in order to investigate their thermal stability. The change in weight of the dye was measured as a function of temperature. Figure 4 displays thermograph of the dyes **7** and **8**. The thermogravimetric curve for the dyes shows a clear plateau followed by a sharp decomposition curve. The loss in weight of the dye is

rapid when heated above 250°C. These results indicate that the dyes are stable up to 250°C after which they decompose rapidly and decomposition completes above 400°C. It is also evident that decomposition of dye **8** is faster than that of dye **7**.

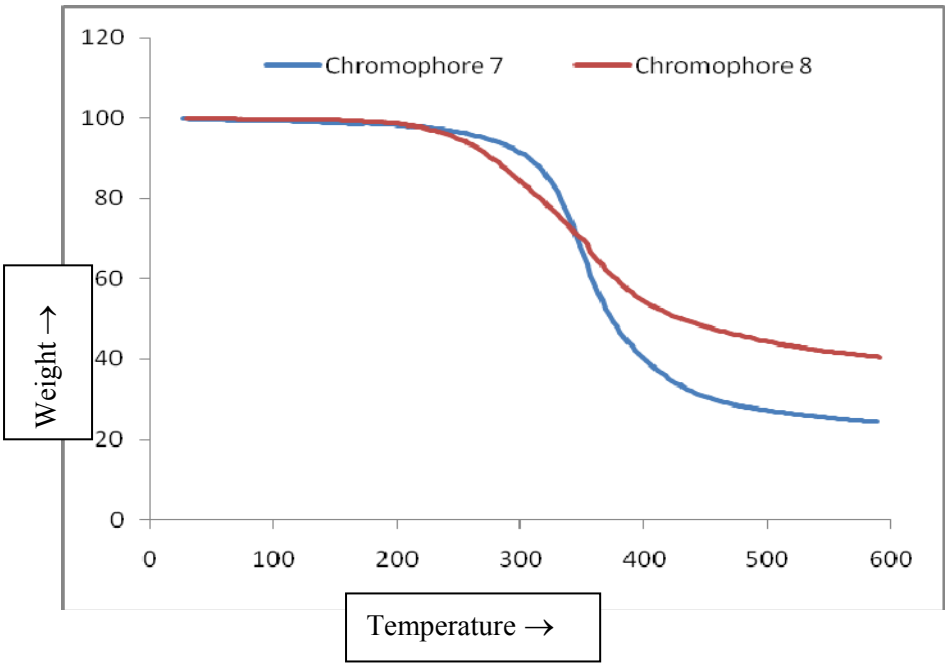


Fig3. Thermogravimetric curves of the chromophores 7 and 8

CONCLUSION

In conclusion, novel coumarin dyes **7** and **8** are valuable as new fluorescent chromophores having long wavelength of absorption and emission. The relative strength of fluorescence was affected by the substituent at 3 position of lactone ring and incorporation of another styryl group with two cyano functionalities caused pronounced bathochromic shift.

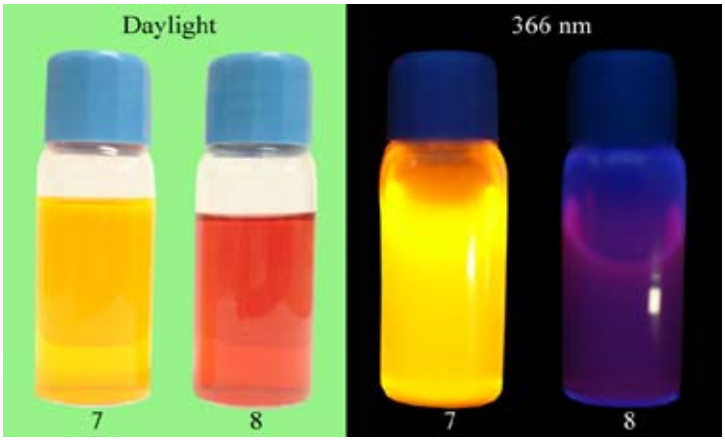


Fig 4. Photographs of the chromophores 7 and 8 in daylight and in UV light (366 nm)

EXPERIMENTAL

Materials and Equipments

All melting points were uncorrected and are in °C. FT-IR spectra were recorded on a Bomem Hartmann and Braun MB-Series FT-IR spectrometer. ^{1}H NMR spectra were recorded on Varian 300 MHz mercury plus spectrometer, and chemical shifts are expressed in δ ppm using TMS as an internal standard. Microanalysis for C, H, N and S were performed on Thermofignnin Elemental analyzer. Electronic spectra were recorded on Spectronic spectrophotometer from dye solutions in toluene, chloroform, ethyl acetate and methanol. The fluorescence maxima of the dyes were recorded on Jasco FP-1520 fluorimeter. Thermogravimetric analysis was carried out on SDT Q600 v8.2 Build 100 model of TA instruments.

Common reagent grade chemicals were procured from s d fine-chem Limited, Mumbai and were used without any further purification.

Synthesis of 6-methoxyquinoxaline 3

4-Methoxy-2-nitroaniline **1** (16.8 g, 0.1 mol) was dissolved in methanol (200 ml) and hydrogenated in Parr hydrogenator using 10% Pd/C catalyst at 60°C for 6 hrs. After cooling, reaction mass was filtered to separate catalyst and then concentrated in rotavapour. 4-Methoxy-1,2-phenylenediamine **2** so obtained was dissolved in acetonitrile (350 ml) and to this solution was added glyoxal (40%, 32.0 ml, 2.6 mol). Reaction mixture was then stirred at 60°C for 6 hrs and cooled. Solvent was removed in rotavapour and dark brown sticky solid obtained was passed over neutral alumina to remove base impurities. 6-Methoxyquinoxaline **3** was obtained as shiny white crystals (13.6 g, 85 %), m.p. 58-60°C (Lit: 60°C[34])

Synthesis of 1,4-diethyl-6-methoxy-1,2,3,4-tetrahydroquinoxaline 4

6-Methoxyquinoxaline **3** (5.5 g, 0.034 mol) was dissolved in dry toluene (150 ml) and cooled to 5°C. To this cold solution was added sodium borohydride (13.2 g, 0.35 mol) over a period of 15 minutes. Pale yellow slurry thus obtained was stirred for 10 minutes. Glacial acetic acid (57.3 ml, 60 g, 1.0 mol) was added to it drop wise over a period of one hour maintaining the temperature 5-10°C. Brownish slurry formed was stirred for another one hour at 10°C and allowed to attain room temperature. It was then heated to gentle reflux for 5 hours. On cooling, thick red resinous mass was obtained to which water (250 ml) was added. Toluene layer formed was separated and aqueous layer was extracted with ethyl acetate (3 x 100 ml). Combined extracts and toluene layer were washed repeatedly with dilute sodium carbonate solution and then with water, dried over anhydrous sodium sulphate, filtered and vacuum evaporated. Dark brown oil obtained was purified by vacuum distillation to afford golden yellow oil (6.35 g, 84%), b.p. 142-144°C at 2mm; IR (KBr) ν_{max} cm^{-1}: 2800-2900, 3000-3100, 1500, 1200; *Anal.* Calcd for $C_{13}H_{20}N_2O$: C, 70.91; H, 9.09; N, 12.73. Found: C, 70.97; H, 9.11; N, 12.64; MS: *m/z* = 221.

Synthesis of 1,4-diethyl-7-methoxy-1,2,3,4-tetrahydroquinoxalin-6-carboxaldehyde 5

Phosphorous oxychloride (8.0 ml, 0.09 mol) was added to dimethyl formamide (10.1 ml, 0.13 mol) at 5°C under stirring. After 15 minutes 1,4-diethyl-6-methoxy-1,2,3,4-tetrahydroquinoxaline **4** (11.0 g, 0.05 mol) was added to the cooled reagent under stirring. The mixture was heated at 70-80°C for 4 hrs and then poured on ice water. The clear solution obtained was neutralized by cold sodium hydroxide solution (15%) maintaining the temperature between 10-15°C. The sticky mass obtained was extracted in ethyl acetate (4 x 100 ml). Combined ethyl acetate extracts were washed with water, dried over anhydrous sodium sulphate and vacuum evaporated. Brown sticky mass was purified by column chromatography using neutral activated aluminium oxide (9.67 g, 78%); b.p. 146-148°C; IR (KBr) ν_{max} cm^{-1}: 2800-2900, 3000-3100, 1693, 1531, 1238; ^{1}HNMR: δ 1.16 (t, 6.9Hz, 3H, CH_3), δ 1.23 (t, 6.9Hz, 3H, CH_3), δ 3.13-3.18 (m, 2H), δ 3.31 (q, 6.9Hz, 2H,

CH_2), δ 3.41 (q, 6.9Hz, 2H, CH_2), δ 3.49-3.54 (m, 2H), δ 3.93 (s, 3H, OCH_3), δ 6.0 (s, 1H, phenyl proton), δ 7.0 (s, 1H, phenyl proton), δ 10.20 (s, 1H, aldehydic proton); *Anal.* Calcd for $C_{14}H_{20}N_2O_2$: C, 67.74; H, 8.06; N, 11.29. Found: C, 67.81; H, 8.14; N, 11.34; MS: *m/z* = 249.

Synthesis of 1,4-diethyl-7-hydroxy-1,2,3,4-tetrahydroquinoxalin-6-carboxaldehyde 6

Aluminium powder (0.84 g, 0.029 mol) was added to acetonitrile (30 ml) and stirred at 20°C. To the slurry, iodine (9.14 g, 0.037 mol) was added in small portions and stirred under nitrogen atmosphere till the colour changed to yellow. 1,4-Diethyl-7-methoxy-1,2,3,4-tetrahydroquinoxalin-6-carboxaldehyde **5** (6.0 g, 0.024 mol) was dissolved in acetonitrile (10 ml) and added to the slurry drop wise. The reaction mass was then gently refluxed for 10 hrs, cooled to room temperature and slowly poured in cold water (200 ml). It was then extracted with ethyl acetate (4 X 100 ml). Combined ethyl acetate extracts were washed with water, dried over anhydrous sodium sulphate and vacuum evaporated. Yellowish liquid so obtained was purified by column chromatography using silica gel (3.37 g, 60%), b.p. 158-160°C at 2mm; IR (KBr) ν_{max} cm^{-1}: 2800-2900, 3000-3100, 1683, 1521, 1338; ^{1}HNMR: δ 1.16 (t, 6.9Hz, 3H, CH_3), δ 1.23 (t, 6.9Hz, 3H, CH_3), δ 3.13-3.18 (m, 2H), δ 3.31 (q, 6.9Hz, 2H, CH_2), δ 3.41 (q, 6.9Hz, 2H, CH_2), δ 3.49-3.54 (m, 2H), δ 6.07 (s, 1H, phenyl proton), δ 6.79 (s, 1H, phenyl proton), δ 10.20 (s, 1H, aldehydic proton); *Anal.* Calcd for $C_{13}H_{18}N_2O_2$: C, 66.66; H, 7.69; N, 11.96. Found: C, 66.67; H, 7.64; N, 11.97; MS: *m/z* = 235.

Synthesis of 8-acetyl-1,4-diethyl-1,2,3,4-tetrahydro-7H-pyrano[2,3-g]quinoxalin-7-one 7

1,4-Diethyl-7-hydroxy-1,2,3,4-tetrahydro-6-quinoxalinecarboxaldehyde **6** (2.34 g, 0.01 mol) and ethyl acetoactate (1.30 g, 0.01 mol) were dissolved in absolute ethanol (10 ml). Piperidine (0.1 ml) was added to it and the reaction mixture was refluxed for 4 hrs. Orange crystals formed were filtered, washed with water and dried. The dye **7** thus obtained was purified by column chromatography using neutral activated aluminium oxide, (2.64 g, 88%), m.p. 172-174°C; IR (KBr) ν_{max} cm^{-1}: 2900-3000, 3000-3100, 1708, 1640, 1523; ^{1}HNMR (300 MHz, $CDCl_3$): δ 1.20 (t, 7.1Hz, 3H, CH_3), δ 1.26 (t, 7.1Hz, 3H, CH_3), δ 2.68 (s, 3H, CH_3), δ 3.19-3.25 (m, 2H), δ 3.33 (q, 7.1Hz, 2H, CH_2), δ 3.43 (q, 7.1Hz, 2H, CH_2), δ 3.55-3.61 (m, 2H), δ 6.41 (s, 1H, phenyl proton), δ 6.50 (s, 1H, phenyl proton), δ 8.41 (s, 1H, proton on lactone ring); *Anal.* Calcd. for $C_{17}H_{20}N_2O_3$: C, 68.00; H, 6.67; N, 9.33. Found: C, 67.96; H, 6.71; N, 9.35; MS: *m/z* = 301.

Synthesis of 2-(1-(1,4-diethyl-7-oxo-2,3,4,7-tetrahydro-1H-pyrano[3,2-g]quinoxalin-8-yl)ethylidene)malononitrile 8

8-acetyl-1,4-diethyl-1,2,3,4-tetrahydro-7H-pyrano[2,3-g]quinoxalin-7-one **7** (3.00 g, 0.01 mol) and malononitrile (0.66 g, 0.01 mol) were dissolved in absolute ethanol (10 ml). Piperidine (0.1 ml) was added to it and the reaction mixture was refluxed for 4 hrs. Red crystals formed were filtered, washed with water and dried. The dye **8** thus obtained was purified by column chromatography using neutral activated aluminium oxide, (2.81g, 81%), m.p. 180-182°C; IR (KBr) ν_{max} cm^{-1}: 2900-3000, 3000-3100, 2260, 1640, 1523; ^{1}HNMR (300 MHz, $CDCl_3$): δ 1.20 (t, 7.1Hz, 3H, CH_3), δ 1.26 (t, 7.1Hz, 3H, CH_3), δ 2.92 (s, 3H, CH_3), δ 3.19-3.25 (m, 2H), δ 3.33 (q, 7.1Hz, 2H, CH_2), δ 3.43 (q, 7.1Hz, 2H, CH_2), δ 3.55-3.61 (m, 2H), δ 6.41 (s, 1H, phenyl proton), δ 6.50 (s, 1H, phenyl proton), δ 8.41 (s, 1H, proton on lactone ring); *Anal.* Calcd. for $C_{20}H_{20}N_4O_2$: C, 68.95; H, 5.79; N, 16.08;. Found: C, 69.16; H,5.61; N,16.35; MS: *m/z* = 349.

ACKNOWLEDGEMENT
One of the authors (ARJ) is thankful to World Bank -TEQIP for providing fellowship. Authors are thankful to Chemistry Department IIT-Bombay for recording ^{1}HNMR, mass spectra and elemental analysis.

REFERENCES

1. D.F. Zhao, T.F. Zhao and Z.S. Li, *Dye Industry*, **35** (2), p. 8, 1998.
2. X.J. Luo, S.J. Luo, L.B. Cheng and D.Y. Huang, *Science in China (series B)*, **31** (6), p. 542, 2001.
3. B. Zhao and Z.H. Zhou, *Nanjing Shida Xuebao (Ziran Kexueban)*, **27** (3), p. 54, 2004.
4. K.H. Drexhage, *J. Res. National Bureau Standards, Sect A*, 80A, (3), pp. 421–8, 1976.
5. G. Jones, W.R. Jackson, C. Choi and W.R. Bergmark, *J. Phy. Chem.*, **89** (2), pp. 294–300, 1985.
6. Christie, R.M.; Lui, C.H.; *Dyes and Pigments*, 47, 79-89, **2000**.
7. N.R. Ayyangar, K.V. Srinivasan and T. Daniel, *Dyes and Pigments*, **16**, pp. 197–204, 1991.
8. C.R. Moylan, *J. Phys. Chem*, **98**, pp. 13513–6, 1994.
9. A. Fischer, C. Cremer and E.H.K. Stelzer, *Appl. Opt.*, **34**, pp. 1989-2003, 1995.
10. H. Schwander, P. Hendrix and Y.S. Yamamoto, *Ullmann's Encyclopedia of Industrial Chemistry*, **A11**. 5th Edn, VCH: Weinheim, Germany, pp. 280–1, 1988.
11. H.K. Arora, A.R. Agarwal and R.P. Singh, *Indian J. Chem.*, 21A, p. 844, 1982.
12. O.S. Wolfbeis, E. Koller and P. Hochmuth, *Bull. Chem. Soc. Japan*, **58** (2),pp. 731–4, 1985.
13. R.M. Christie, *Rev. Prog. Col.*, **23**, pp. 1–18, 1993.
14. M.T. Alonso, E. Brunet, O. Juanes and J.C. Rodriguez-Ubis, *J. Photochem. Photobio. A*, **147** (2), pp. 113–25, 2002.
15. I. Leray, J.L. Habib-Jiwan, C. Branger, J.P. Soumillion and B. Valeur, *J. Photochem. Photobiol.*, A, **135** (2–3), pp. 163–9, 2000.
16. C. Erk, A. Gocmen and M. Bulut, *Supramolecular Chemistry*, **11** (1), pp. 49–56, 1999.
17. B. Vaidya, J. Zak, G.J. Bastians, M.D. Porter, J.L. Hallman and N.A.R. Nabulsi, *Analytical Chemistry*, **67** (22), pp. 4101–11, 1995.
18. A. Adronov, D.R. Robello and J.M.J. Frechet, *J. Poly. Sci.* A, **39** (9), pp. 1366–73, 2001.
19. X. Zhou, D.S. Tyson and F.N. Castellano, *Angew. Chem. Int. Ed.*, **39** (23), pp. 4301–5, 2000.
20. A.W. Freeman, S.C. Koene, P.R.L. Malenfant, M.E. Thompson and J.M.J. Frechet, *J. Am. Chem. Soc.*, **122** (49), pp. 12385–6, 2000.
21. Z. Li, Z. Zhang, T. Emery, A. Scherer and D. Psaltis, *Opt. Express*, **14**, pp. 696–701, 2006.
22. F.J. Duarte, L.S. Liao, K.M. Vaeth and A.M. Miller, *J. Opt A: Pure Appl Opt.*, **8**, pp. 172–4, 2006.
23. C. Eggeling, L. Brand and C.A.M. Seidel, *Jpn. J. Appl. Phys.*, **41**, pp. 5801-4, 2002.
24. S. Sanghi, D. Mohan and R.D. Singh, *Asian J. Phys.*, **4**, pp. 283–8, 1995.
25. R.W. Voedisch, "Luminescent pigments, organic". In P.A. Lewis, Ed., *The Pigment Handbook*, Vol.1. 1st Edn, John Wiley: New York, NY, p. 891, 1973.
26. R.A. Ward, E.L. Kimmel, "Luminescent materials". In *Kirk-Othmer Encyclopedia of Chemical Technology*, Vol. 14, 3rd Edn, John Wiley: New York, NY, pp. 546-69, 1982.
27. J. Hamer and R.F. Holliday, *J. Org. Chem.*, **28**, p. 2488, 1963.
28. C.B. Robert and A.O. Robert, *J. Org. Chem.*, **44** (10), pp. 1719–1720, 1979.
29. G. W. Gribble, P. D. Lord, J. Skotnicki, S. J. Eaton and J. Johnson, *J. Am.Chem. Soc.*, **96**, pp. 7812–14, 1974.
30. G.W. Gribble and P.W. Heald, *Synthesis*, pp. 650–51, 1975.
31. G.W. Gribble and D. Ferguson. *J. Chem. Soc. Chem. Com.*, pp. 535–6, 1975.
32. G.W. Gribble and J. Hoffman, *Synthesis,* pp. 859–60, 1977.
33. D. F. Gloster, L. Cincotta and J. W. Foley, *J. Het. Chem.,* **36** (1), pp. 25–32, 1999.
34. W.A. Skinner, H.T. Crawford, H. Tong, D. Skidmore and H.I. Maibach, *J. Pharm. Sci.*, **65** (9), pp. 1404–07, 1976.