Synthesis of Novel Quinaldine Based Squaraine Dyes: Effect of Substituents and Role of Electronic Factors

Kuthanapillil Jyothish, Kalliat T. Arun and Danaboyina Ramaiah*

Photosciences and Photonics Division
Regional Research Laboratory (CSIR)
Trivandrum 695 019, INDIA

*To whom correspondence should be addressed at:

Photosciences and Photonics Division
Regional Research Laboratory (CSIR)
Trivandrum 695 019, INDIA.

Tel: +91 471 2515362. Fax: +91 471 2490186, 2491712.

E-mail : d_ramaiah@rediffmail.com or rama@csrrltd.ren.nic.in

Supporting Information

General procedure for the synthesis of quinaldines, quinaldinium salts, semisquaraines and squaraine dyes, Figures S1-S3 showing the progress of the condensation reaction between squaric acid and the quinaldinium salts **1b**, **1c** and **1e** by absorption spectroscopy and Figures S4-S7 showing the ^1H and ^{13}C NMR spectra of the representative semisquaraines and the squaraine dyes.

General methods

All melting points are uncorrected and were determined on a Mel-Temp II melting point apparatus. The IR spectra were recorded on a Perkin Elmer Model 882 infrared spectrometer. The electronic absorption spectra were recorded on a Shimadzu UV-3101 or 2401 PC UV-VIS-NIR scanning spectrophotometer. All the solvents used were purified and distilled before use. The progress of the reaction was monitored by recording absorption spectrum of the reaction mixture at various time intervals. For this 25 μL of the reaction mixture was taken out and diluted to 3 mL with distilled n-butanol and the spectra recorded.

Starting materials. 4-Aminophenol (mp 188-189 $^{\circ}\text{C}$),¹ 4-ethoxyaniline (bp 250-251 $^{\circ}\text{C}$),¹ 2-bromo-4-nitrophenol (mp 184-185 $^{\circ}\text{C}$),¹ 4-iodoaniline (mp 63-64 $^{\circ}\text{C}$),¹ 4-bromoaniline (mp 61-62 $^{\circ}\text{C}$),¹ 4-nitroaniline, (mp 148-149 $^{\circ}\text{C}$),¹ 6-hydroxy-2-quinaldine (mp 262-264 $^{\circ}\text{C}$),² 6-ethoxy-2-quinaldine (mp 71-72 $^{\circ}\text{C}$),² 6-hydroxy-7-bromo-2-quinaldine (mp 235-237 $^{\circ}\text{C}$), 6-iodo-2-quinaldine (mp 108-109 $^{\circ}\text{C}$),³ 6-bromo-2-quinaldine (mp 95-96 $^{\circ}\text{C}$),³ 6-nitro-2-quinaldine (mp 165-166 $^{\circ}\text{C}$),⁴ 6-hydroxy-N-methyl-2-quinaldinium iodide (**1a**) (mp 238-239 $^{\circ}\text{C}$),² 6-ethoxy-N-methyl-2-quinaldinium iodide (**1b**) (mp 182-183 $^{\circ}\text{C}$),² N-methyl-2-quinaldinium iodide (**1d**) (mp 195-196 $^{\circ}\text{C}$),⁵ 6-iodo-N-methyl-2-quinaldinium iodide (**1e**) (mp 222-223 $^{\circ}\text{C}$),³ 6-bromo-N-methyl-2-quinaldinium iodide (**1f**) (mp 237 $^{\circ}\text{C}$),³ 6-nitro-N-methyl-2-quinaldinium iodide (**1g**) (mp 214-215 $^{\circ}\text{C}$),⁴ and the squaraine dye (**3d**) (mp 298 $^{\circ}\text{C}$),⁶ were prepared by modifying the reported procedures. 2-Methylquinoline was purchased from Aldrich and used as such while squaric acid was a gift from Professor Waldemar Adam, University of Würzburg, Germany.

General procedure for the preparation of quinaldines⁷

To a refluxing solution of the corresponding aniline derivative (18 mmol) in 6N HCl (25 mL), crotonaldehyde (72 mmol) was added drop wise over a period of 1 h and refluxed for 6 h.

The reaction mixture was cooled to room temperature, made alkaline using ammonia solution and was then extracted with diethyl ether. Removal of the solvent under reduced pressure gave a residue, which was subjected to column chromatography over silica gel. Elution of the column with a mixture of ethyl acetate and petroleum ether (1:9) gave the corresponding quinaldine derivatives in good yields.

Preparation of 6-cyano-2-quinaldine. A mixture of 6-bromo-2-methylquinoline (600 mg, 2.7 mmol), cuprous cyanide (400mg, 4.5 mmol) and pyridine (6 mL) was heated in a sealed tube at 200 °C for 24 h. The deep brown solution was shaken with aqueous ammonia and dichloromethane and the organic layer was washed with water. Removal of the solvent gave a residue which was then subjected to column chromatography over silica gel. Elution of the column with a mixture of ethyl acetate and petroleum ether (1:9) gave 75% of the quinaldine derivative, mp 168-170 °C, IR (KBr) ν_{max} 3031, 2224, 1619 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 8.17 (1H, s), 8.10 (2H, dd, $J = 11.38$ Hz), 7.80 (1H, d, $J = 8.7$ Hz), 7.40 (1H, d, $J = 8.46$ Hz), 2.79 (3H, s); $^{13}\text{C NMR}$ (DMSO-d_6) δ 162.5, 148.8, 136.2, 133.7, 130.2, 130.1, 125.8, 123.7, 118.6, 109.3, 25.6.

General procedure for the preparation of quinaldinium salts **1a-h**

A mixture of the corresponding quinaldine (1 mmol) and methyl iodide (4 mmol) was heated in a sealed tube at 100-105 °C for 12 h. The precipitate formed was filtered, washed thoroughly with cold diethyl ether and subjected to column chromatography over silica gel. Elution of the column with a mixture of methanol and chloroform (1:4) gave the corresponding quinaldinium salts **1a-h** in good yields. **1c**: (55%, mp 296-297 °C), $^1\text{H-NMR}$ (DMSO-d_6) δ 8.68 (1H, s), 8.61 (1H, d, $J = 8.5$ Hz), 7.76 (1H, d, $J = 8.5$ Hz), 7.28 (1H, s), 4.24 (3H, s), 2.91 (3H, s); $^{13}\text{C NMR}$ (DMSO-d_6) δ 159.4, 154.4, 142.0, 131.3, 129.9, 126.8, 124.2, 122.5, 109.9, 38.6, 22.1.

1h: (75%, mp 202-204⁰C), IR (KBr) $\nu_{\max}$ 3065, 2986, 2233, 1625 cm⁻¹. ¹H-NMR (DMSO-d₆) δ 9.40 (1H, s), 9.32 (1H, d, J = 8.52 Hz), 8.82 (2H, d, J = 9.81 Hz), 8.29 (1H, d, J = 8.7Hz), 4.50 (3H, s), 3.1 (3H, s); ¹³C NMR (DMSO-d₆) δ 164.5, 145.5, 140.6, 136.2, 135.4, 127.2, 127.0, 121.0, 117.2, 111.5, 38.7, 23.6.

General procedure for the synthesis of semisquaraines **2a-c**

A mixture of the corresponding quinaldinium salt (0.06 mmol), squaric acid (0.06 mmol) and quinoline (0.5 mL) was refluxed in a mixture of *n*-butanol and benzene (6 mL each, 1:1) with azeotropic distillation of water for 24 h. The solvent was distilled off under reduced pressure to obtain a residue which was chromatographed over silica gel. Elution of the column with a mixture (1:9) of methanol and chloroform gave the semisquaraine derivatives **2a-c** in good yields calculated based on conversion.

2a: 95%, mp 150-152 ⁰C, IR (KBr) $\nu_{\max}$ 3412, 3042, 2963, 1761, 1606 cm⁻¹. ¹H-NMR (CDCl₃+DMSO-d₆, 1:4) δ 10.06 (1H, OH), 9.29 (1H, d, J = 11.4 Hz), 7.89 (1H, d, J = 9.3 Hz), 7.73 (1H, d, J = 9.4 Hz), 7.34 (1H, d, J = 9.3 Hz), 7.17 (1H, s), 6.14 (1H, s), 4.64 (2H, t, J = 6.5 Hz), 4.11 (3H, s), 1.78 (2H, m), 1.45 (2H, m), 0.93 (3H, m). ¹³C NMR (DMSO-d₆, 1:4) δ 185.2, 177.2, 175.4, 171.5, 155.8, 152.5, 137.4, 132.8, 127.1, 124.5, 123.0, 119.4, 111.5, 95.6, 70.8, 37.8, 31.7, 18.2, 13.5; FAB-MS: m/z = 325.140 (calcd 325.139 for C₁₉H₁₉NO₄).

2b: 90%, mp 184-186 ⁰C, IR (KBr) $\nu_{\max}$ 3016, 2923, 1756, 1601 cm⁻¹. ¹H-NMR (CDCl₃) δ 9.41 (1H, d, J = 9.3 Hz), 7.84 (1H, d, J = 9.3 Hz), 7.63 (1H, d, J = 9.4 Hz), 7.33 (1H, d, J = 9.5 Hz), 7.09 (1H, s), 6.15 (1H, s), 4.71 (2H, t, J = 6.6 Hz), 4.14 (2H, t, J = 6.9 Hz), 4.05 (3H, s), 1.78 (5H, m), 1.49 (2H, m), 0.96 (3H, m). ¹³C NMR (CDCl₃) δ 184.1, 176.3, 174.3, 170.2, 156.6, 153.3, 136.7, 126.6, 125.6, 122.8, 117.4, 109.5, 94.6, 71.9, 63.9, 37.1, 31.8, 18.2, 14.2, 13.5, 13.3; FAB-MS: m/z = 353.164 (calcd 353.163 for C₂₁H₂₃NO₄).

2c: 90%, mp 182-184 °C, IR (KBr) $\nu_{\max}$ 3421, 2950, 1760, 1589 cm^{-1} . ^1H -NMR ($\text{CDCl}_3 + \text{DMSO-d}_6$, 1:4) δ 9.31 (1H, d, $J = 9.2$ Hz), 8.12 (1H, s), 7.88 (1H, d, $J = 9.2$ Hz), 7.3 (1H, s), 6.15 (1H, s), 4.65 (2H, t, $J = 6.7$ Hz), 4.09 (3H, s), 1.78 (2H, m), 1.48 (2H, m), 0.96 (3H, m). ^{13}C NMR (DMSO-d_6 , 1:4) δ 185.8, 177.3, 175.4, 172.0, 156.2, 136.2, 133.3, 126.1, 124.5, 123.2, 118.0, 111.4, 97.8, 71.8, 38.8, 31.5, 18.1, 13.3; FAB-MS: $m/z = 404.256$ (calcd 404.255 for $\text{C}_{19}\text{H}_{18}\text{BrNO}_4$).

General procedure for the synthesis of squaraine dyes **3d-f**

A mixture of the corresponding quinaldinium salt (0.06 mmol), and squaric acid (0.03 mmol) and quinoline (0.5 mL) was refluxed in a mixture of *n*-butanol and benzene (6 mL each, 1:1) with azeotropic distillation of water for 24 h. The solvent was distilled off under reduced pressure to obtain a residue which was chromatographed over silica gel. Elution of the column with a mixture (1:9) of methanol and chloroform gave the corresponding squaraine dyes **3d-f** in good yields calculated based on the conversion.

3e: 85%, mp 314-315 °C, IR (KBr) $\nu_{\max}$ 2962, 1620, 1553 cm^{-1} . ^1H -NMR (DMSO-d_6) δ 9.23 (1H, d, $J = 9.4$ Hz), 9.19 (1H, d, $J = 9.2$ Hz), 7.1-8.05 (8H, m, aromatic), 5.89 (1H, s, vinylic), 5.72 (1H, s, vinylic), 3.81 (3H, s), 3.71 (3H, s); FAB-MS: $m/z = 643.944$ (calcd 643.946 for $\text{C}_{26}\text{H}_{18}\text{I}_2\text{N}_2\text{O}_2$).

3f: 86%, mp 336-338 °C, IR (KBr) $\nu_{\max}$ 3056, 1613, 1580 cm^{-1} . ^1H -NMR (DMSO-d_6) δ 9.31 (1H, d, $J = 9.5$ Hz), 9.28 (1H, d, $J = 9.3$ Hz), 7.3-8.4 (8H, m, aromatic), 5.86 (1H, s, vinylic), 5.78 (1H, s, vinylic), 3.85 (3H, s); 3.78 (3H, s); FAB-MS: $m/z = 550.246$ (calcd 550.248 for $\text{C}_{26}\text{H}_{18}\text{Br}_2\text{N}_2\text{O}_2$).

General procedure for the synthesis of squaraine dyes **3g-h**

A mixture of the corresponding quinaldinium salt (0.06 mmol), and squaric acid (0.03 mmol), tributylorthoformate (0.5 mL) and quinoline (0.5 mL) was heated in a mixture of *n*-butanol and benzene (6 mL each, 1:1) at 60-70 °C for 6 h. The solvent was distilled off under reduced pressure to obtain a residue which was then thoroughly washed with methanol to give the corresponding squaraine dyes **3 g-h** in good yields (calculated based on conversion).

3g: 86%, mp 290-292 °C, IR (KBr) $\nu_{\max}$ 3032, 1616, 1579 cm^{-1} . $^1\text{H-NMR}$ (DMSO- d_6) δ 9.49 (1H, d, $J = 9.4$ Hz), 9.45 (1H, d, $J = 9.5$ Hz), 7.4- 8.27 (8H, m, aromatic), 5.92 (1H, s, vinylic), 5.85 (1H, s, vinylic), 3.92 (3H, s), 3.84 (3H, s); FAB-MS: $m/z = 498.149$ (calcd 498.150 for $\text{C}_{27}\text{H}_{22}\text{N}_4\text{O}_6$).

3h: 84%, mp 306-308 °C, IR $\nu_{\max}$ (KBr) 3029, 2225, 1602 cm^{-1} ; $^1\text{H-NMR}$ (DMSO- d_6) δ 9.39 (1H, d, $J = 8.9$ Hz), 9.42 (1H, d, $J = 9.4$ Hz), 7.35-8.28 (8H, m, aromatic), 5.87 (1H, s, vinylic), 5.79 (1H, s, vinylic), 3.95 (3H, s), 3.82 (3H, s); FAB-MS: $m/z = 442.472$ (calcd 442.470 for $\text{C}_{28}\text{H}_{18}\text{Br}_2\text{N}_4\text{O}_2$).

Synthesis of squaraine dye 4. A mixture semisquaraine **2a** (0.06 mmol) and the quinaldinium salt **1e** (0.06 mmol), and quinoline (0.5 mL) was refluxed in a mixture of *n*-butanol and benzene (6 mL each, 1:1) for 12 h. The solvent was distilled off under reduced pressure to obtain a residue which was chromatographed over silica gel. Elution of the column with a mixture (1:9) of methanol and chloroform gave the corresponding squaraine dye **4**: 96% (based on conversion), mp 316-318 °C, IR (KBr) $\nu_{\max}$ 3442, 3046, 1729, 1621, 1579, 1560 cm^{-1} . $^1\text{H-NMR}$ (DMSO- d_6) δ 10.2 (1H, OH), 9.29 (1H, d, $J = 9.2$ Hz), 9.01 (1H, d, $J = 9.5$ Hz), 7.86-7.01 (8H, m), 5.77 (1H, s, vinylic), 5.44 (1H, s, vinylic), 3.9 (3H, s), 3.5 (3H, s); FAB-MS: $m/z = 534.040$ (calcd 534.039 for $\text{C}_{26}\text{H}_{19}\text{IN}_2\text{O}_3$).

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Figure S1. Change in absorption spectra obtained for the reaction between squaric acid and the quinaldinium salt **1b** at various time intervals. Time (a) 1, (b) 2, (c) 3, (d) 4 (e) 5, (f) 7, (g) 10, (h) 13, and (i) 24 h.

Figure S2. Change in absorption spectra obtained for the reaction between squaric acid and the quinaldinium salt **1c** at various time intervals. Time (a) 1, (b) 2, (c) 3, (d) 4, (e) 6, (f) 9, (g) 12, (h) 15.5 h.

Figure S3. Change in absorption spectra obtained for the reaction between squaric acid and the quinaldinium salt **1e** at various time intervals. Time (a) 1, (b) 3, (c) 5 h. Inset shows the change in absorption spectra obtained for the same reaction after long time intervals. Time (c) 7 (d) 9, (e) 11, (f) 16, (g) 19 h.

(A)

(B)

Figure S4. ¹H (A) and ¹³C NMR (B) spectra of the semisquaraine derivative **2a** in DMSO-d₆:CDCl₃ (1:4) mixture and DMSO-d₆ respectively.

(A)

(B)

Figure S5. ¹H (A) and ¹³C NMR (B) spectra of the semisquaraine derivative **2b** in DMSO-d₆:CDCl₃ (1:4) mixture and DMSO-d₆ respectively.

Figure S6. ¹H NMR spectrum of the semisquaraine derivative **2c** in DMSO-d₆.

Figure S7. ¹H NMR spectrum of the squaraine dye **4** in DMSO-d₆.