Synthesis of New Oxindolotrimethine Meroeyanine Dyes

Zarif H. Khalil
Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt

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Meroeyanine Dyes, Synthesis

New oxindolotrimethine meroeyanine dyes (3a–l) were prepared by the reaction of 2-methyl quaternary salts with 3-acyclidene oxindole (2) in presence of a basic catalyst. The new compound were identified by IR and UV spectral determination. Bactericidal activity of selected quinoxindolotrimethine meroeyanine dyes (3e, g and l) were tested against 11 pathogenic bacterial strains.

Introduction

Extensive efforts have been made to prepare new members of meroeyanine dyes with various applications [1–15]. But, those containing an oxindolo moiety was not mentioned before in the literature. In this work, new oxindolotrimethine meroeyanine dyes (3a–l) were prepared to elucidate the effect of \( \beta \)-substituent on the absorption spectra of such compounds, taking in consideration, that, the absorption spectra of a cyanine dye is a criterion to its sensising action on silverhalidsemulsions [16]. Also, to test the bactericidal activity of selected quinoxindolotrimethine meroeyanine dyes against some pathogenic bacterial strains.

Experimental

Infrared spectra were determined with a Unicam SP 1200 Spectrophotometer using KBr wafer technique. Absorption spectra in the visible region (350–750 nm) were recorded on a Unicam SP 8000 Ultraviolet Recording Spectrophotometer. All melting points are uncorrected.

Preparation of 3-acylidene oxindole (2a–h)

The compounds were prepared in a way similar to that described earliery by Lindwall and McLennan [17]. Equimolecular proportions (0.05 mol) of isatin, acetophenone and/or its para (methyl-, ethyl-, methoxy-, chloro- and bromo-)derivatives were dissolved in ethanol (100 ml), to which ammonium hydroxide (2 ml/g isatine) was added and the reaction mixture was set aside over night at room temperature. The separated pale yellow – or colourless needles from 3-hydroxy-3-phenacyloxindole (2a and b) were obtained. 2a: Orange needles from ethanol, m.p. 254 °C, yield 37%.

Analysis for \( \text{C}_{11} \text{H}_{9} \text{NO}_2 \)

Caled C 69.36 H 4.04 N 8.09,
Found C 69.61 H 4.11 N 7.98.

2b: Yellowish-orange needles from ethanol, m.p. 254 °C, yield 37%.

Analysis for \( \text{C}_{11} \text{H}_{9} \text{NO}_2 \)

Caled C 70.59 H 4.81 N 7.48,
Found C 70.62 H 4.77 N 7.35.

Synthesis of oxindolotrimethine meroeyanine dyes (3a–l)

Equimolecular proportions (0.002 mol) of 3-acylidene-oxindole (2) and \( \alpha \)-picoline (or quinaldine) ethiodide were dissolved in ethanol (50 ml), to which piperidine (~ 1.5 ml) was added. The reaction mixture was warmed on a water bath for 3 h at 70–80 °C, then concentrated to ~ half its volume. The products (3a–l) which precipitated by water, were filtered off, washed with water and recrystallised from aqueous ethyl alcohol. Oxindolotrimethine meroeyanine dyes (3a–l) are highly coloured compounds ranging from pink to bluish-violet, readily soluble in alcohols, dioxane, acetone, pyridine, partially soluble in carbon tetrachloride and hot water and quinoxindolotrimethine meroeyanine dyes (3e, f and j) exhibit a green fluorescence in solutions. These dyes are readily soluble in concentrated sulphuric acid from which iodine is liberated on heating. The results are summarised in Table I.

Requests for reprints should be sent to Dr. Z. H. Khalil, Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt.

Dehydration of 3-hydroxy-3-phenacyloxindole derivatives

A mixture containing (2 g 1) in ethanol (10 ml) and concentrated hydrochloric acid (50 ml) was set aside for 48 h at room temperature, were fine orange-red needles from 3-phenacyclidene-oxindole derivative (2e–h) were separated. The products were filtered off, washed with aqueous ethyl alcohol and recrystallised from ethanol into orange-red needles.

The above reaction was extended to other carbonyl compounds, namely, acetaldehyde and acetone where the corresponding 3-acyclidene-oxindole (2a and b) were obtained. 2a: Orange needles from ethanol, m.p. 222 °C, yield 30%.

Analysis for \( \text{C}_{11} \text{H}_{9} \text{NO}_2 \)

Caled C 69.36 H 4.04 N 8.09,
Found C 69.61 H 4.11 N 7.98.

2b: Yellowish-orange needles from ethanol, m.p. 254 °C, yield 37%.

Analysis for \( \text{C}_{11} \text{H}_{9} \text{NO}_2 \)

Caled C 70.59 H 4.81 N 7.48,
Found C 70.62 H 4.77 N 7.35.
Table I. Oxindolotrimethine merocyanine dyes (3a-1).

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>m.p. [°C]</th>
<th>Yield [%]</th>
<th>Compound theory</th>
<th>Formula</th>
<th>Analysis [%]</th>
<th>Absorption spectra in methanol</th>
<th>Found</th>
<th>N N</th>
<th>λmax [nm]</th>
<th>εmax</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>210</td>
<td>32</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.83</td>
<td>5.76</td>
<td>538</td>
<td>14700</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3b</td>
<td>207</td>
<td>28</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.66</td>
<td>5.48</td>
<td>—</td>
<td>—</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3c</td>
<td>198</td>
<td>25</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.51</td>
<td>5.47</td>
<td>534</td>
<td>4300</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3d</td>
<td>189</td>
<td>25</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.44</td>
<td>5.38</td>
<td>534</td>
<td>4300</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3e</td>
<td>217–219</td>
<td>42</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>6.17</td>
<td>6.10</td>
<td>518 (sh); 650; 602</td>
<td>6500</td>
<td>8900; 6500</td>
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</tr>
<tr>
<td>3f</td>
<td>173</td>
<td>53</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.98</td>
<td>5.88</td>
<td>510; 560</td>
<td>16500; 16400</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3g</td>
<td>189</td>
<td>58</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.28</td>
<td>5.30</td>
<td>400; 545; 581</td>
<td>8370; 30700; 46000</td>
<td></td>
<td></td>
<td></td>
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<td>3h</td>
<td>192–194</td>
<td>47</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.14</td>
<td>5.08</td>
<td>425 (sh); 432; 472; 6300</td>
<td>6800; 6800; 548; 581</td>
<td>11800; 17100</td>
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<td></td>
</tr>
<tr>
<td>3i</td>
<td>185</td>
<td>38</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.01</td>
<td>4.87</td>
<td>401; 548; 582</td>
<td>6100; 19600; 27400</td>
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<tr>
<td>3j</td>
<td>175</td>
<td>45</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>5.00</td>
<td>5.9</td>
<td>402; 475; 550; 584</td>
<td>3500; 4000; 10000; 15600</td>
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<td></td>
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<tr>
<td>3k</td>
<td>169</td>
<td>45</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>4.96</td>
<td>4.85</td>
<td>450; 468; 550; 580</td>
<td>12200; 12200; 16000; 21300</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3l</td>
<td>166</td>
<td>38</td>
<td>C_{24}H_{23}N_{5}O_{1}</td>
<td>4.59</td>
<td>4.45</td>
<td>448; 470; 546; 582</td>
<td>7600; 7750; 7700; 9000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Exhibit a green fluorescence; sh = shoulder. All compounds gave satisfactory C, H analysis.

Bacteriological screening for selected quinoxindolotrimethine merocyanine dyes (3e, g and l)

The culture medium was normal nutrient agar (N. A.) medium [18] supplemented with one gram yeast/litre, the bacterial suspension was prepared by adding one ml of sterile distilled water to a 24 h old culture of the test organism grown on N. A. slant. One ml aliquots of bacterial suspension were added to Erlenmeyer flasks contain 150 ml of N. A. and the flasks were incubated for 24 h.

Petri dishes contain sterile modified N. A. were flooded with the bacterial suspension of the test organisms (2 plates for each organism). Two filter paper discs (one cm diameter) containing the selected compounds (3e, g and l) dissolved in aqueous ethanol (25%, 20 ml/L) were placed on each plate. The plates were incubated at 37 °C for 24 h and the diameter of the inhibition zone were measured. The experiments were repeated 3 times and the results obtained were averaged. The results are given in Table II.

Pathogenic bacterial strains were supplied by Veterinary Hospital Ministry of Agriculture, Assiut, Egypt.

Table II. Bacteriological screening of selected quinoxindolotrimethine merocyanine dyes.

<table>
<thead>
<tr>
<th>Organism used</th>
<th>3e</th>
<th>3g</th>
<th>3l</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) E. coli O26</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2) E. coli E145</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3) E. coli O78</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4) S. Derpy</td>
<td>Slight</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>5) S. Typhimurium</td>
<td>Slight</td>
<td>Slight</td>
<td>+</td>
</tr>
<tr>
<td>6) S. Thompom</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>7) Staphylococcus aureus</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>8) Staphylococcus albus</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>9) Pyocyanus</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>10) Proteus</td>
<td>Slight</td>
<td>Slight</td>
<td>+</td>
</tr>
<tr>
<td>11) Klebsiella sp.</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

* Further studies will be published later.

Results and Discussion

Interaction of 3-acrylidene oxindole derivatives (2) with α-picoline (or quinaldine) ethidione in the presence of piperidine gave the corresponding oxindolotrimethine merocyanine dyes (3a-1). The reaction is represented as follows:

Infrared absorption spectra of 3a-1 revealed an absorption band at 1740–1720 cm⁻¹ attributed to the carbonyl group and another one at 1600 cm⁻¹ attributed to C–C multiple bonds in a diene system, also, a strong absorption band at 760 cm⁻¹ was noticed in the spectra of these dyes.

The absorption spectra of 3a-1 in methanol (in the range 350–750 nm) consist of different absorption bands, their position and molar extinction coefficient are influenced by the type of the quaternary heterocyclic residue and the β-substituent at the central carbon atom within the side chain. Thus, the parent unsubstituted quinoxindolotrimethine merocyanine dye...
methine merocyanine dye (3e) possesses an absorption band at $\lambda_{\text{max}}$ 560 nm, $\varepsilon_{\text{max}} = 9800$ with a shoulder at $\lambda_{\text{max}}$ 518 nm, $\varepsilon_{\text{max}} = 6500$ and another one at a longer wavelength attributed to intramolecular charge transfer at $\lambda_{\text{max}}$ 602 nm, $\varepsilon_{\text{max}} = 5600$. Substituting the hydrogen atom by a methyl group (3f) causes a strong blue shift in the later band by 42 nm, $\lambda_{\text{max}}$ 560 nm, $\varepsilon_{\text{max}} = 16400$; while, substituting by a phenyl group (3g) causes a less blue shift by 21 nm, with strong intensification of the absorption band, $\lambda_{\text{max}}$ 581 nm, $\varepsilon_{\text{max}} = 46000$. Introducing an electron releasing group ($p$-CH$_3$, $p$-C$_6$H$_5$ and/or $p$-OCH$_3$) or electron attracting atom ($p$-Cl and/or $p$-Br) causes a minor shift in the position of the C. T. relative to 3g (c.f. Table I).

On the other hand, pyridoxindolotrimethine cyanine dyes (3a-d) possess only a single and broad absorption band in the visible region at $\lambda_{\text{max}}$ 532 to 538 nm, e.g. (3a, $\lambda_{\text{max}}$ 538 nm, $\varepsilon_{\text{max}} = 14700$). Comparing the absorption spectra of 3a and 3g, it is clear that, substituting the quaternary pyridyl by a quinolyl group causes a red shift by 43 nm with intesification of the absorption band. This, is attributed to the increase in the mass of the molecule and in conjugation, leading to the decrease in the excitation energy absorbing at a longer wavelength.

**Conclusion:** Quinoxindolotrimethine merocyanine dyes absorb light at a longer wavelength than the pyridoxindolo analogous. Substitution of the $\beta$-hydrogen atom by an alkyl or an aryl group causes a hypsochromic shift and the shift in the $\beta$-aryl substituent is less than the $\beta$-alkyl derivative. Further substitution in the para position of the $\beta$-phenyl group causes a minor shift in the absorption spectra of the C. T. band. Bactericidal activity of selected compounds against 2 pathogenic bacterial strains were tested and these dyes have a remarkable activity, specially $\beta$-($p$-bromo phenyl) quinoxindolotrimethine merocyanine dye (3l).

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