

A New Synthesis of Pyrazolo[3,4-*b*]quinoline Derivatives†

D. C. HOLLA and S. SESHADRI\*

Dyes Research Laboratory, University Department of Chemical Technology, Matunga, Bombay 400019, India

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A new synthesis of pyrazolo[3,4-*b*]quinoline-4-carboxylic acid derivatives is described. This involves the Pfitzinger reaction of pyrazolone derivatives with isatic acid under controlled conditions. The pyrazoloquinolinecarboxylic acids were converted to their corresponding amides and nitriles, and their absorption and emission characteristics are recorded.

The use of pyrazolo[3,4-*b*]quinoline derivatives as fluorescent brighteners is well known.<sup>1)</sup> The major synthetic approach has been the cyclization of appropriately substituted *N*-(1-alkyl-5-pyrazolyl)anthranilic acids by phosphoryl chloride. 5-Chloro-4-formylpyrazoles and substituted aromatic amines on heating form respective 1-phenylpyrazolo[3,4-*b*]quinoline derivatives which are reported<sup>2,3)</sup> to be optical brightening agents.

An obvious alternate synthetic route would be the reaction of pyrazolone derivatives with isatin under the Pfitzinger conditions which would yield the pyrazolo[3,4-*b*]quinoline-4-carboxylic acid. Rather surprisingly, this simple synthetic scheme has not been previously described in the literature. This synthetic scheme has the advantage that different pyrazolones can be employed and further the resultant carboxylic acid could also be further converted to different derivatives such as amide or nitrile.

The Pfitzinger reaction on 3-methyl-1-phenyl-5-pyrazolone (**IIb**) was carried out under normal conditions, employing isatin (**I**) in 40% sodium hydroxide solution. Under these conditions the reaction did not occur even when the reaction mixture was heated for several hours. It was thought that the failure of the reaction might be due to the existence of the pyrazolone in the enolic form in the alkaline conditions, tending to make the pyrazolone inactive for the reaction with isatic acid (2-aminophenylglyoxylic acid). We, therefore carried out the reaction at a certain level of basicity (pH 10–11) so that the enolization would not be complete and the active methylene group would be able to react with isatic acid. Indeed, under these conditions the reaction did take place and on work-up by acidification a yellow product was obtained which was characterized as the expected 3-methyl-1-phenylpyrazolo[3,4-*b*]quinoline-4-carboxylic acid (**IIIb**). The structure of this product was established by its acidic character, infrared spectrum (carboxylic acid at 1695 cm<sup>-1</sup>) and elemental analysis and also by conversion into its derivatives like amide (**IVb**) and nitrile (**Vb**).

Rather surprisingly, the fluorescence of this acid was weak and we therefore wished to study the fluorescence of the derivatives of this acid. Thus the amide (**IVb**) was prepared by the usual method and the amide (**IVb**) was converted to nitrile (**Vb**). The nitrile (**Vb**) was expected to show enhanced fluorescence compared to the carboxylic acid (**IIIb**) but we found that

there was no improvement in the fluorescence intensity.

We then proceeded to synthesise other pyrazolo[3,4-*b*]quinoline derivatives by this route. Thus, 3-methyl-5-pyrazolone (**IIa**) was reacted with isatin and 1-unsubstituted pyrazoloquinolinecarboxylic acid (**IIIa**) was obtained. This was further alkylated by dimethyl sulfate to yield the *N*-methyl derivative (**VIa**) and by acrylonitrile to yield *N*-(2-cyanoethyl) derivative (**VIIb**). The alkylation products have been given the structures as indicated since there was only a slight bathochromic shift on alkylation. Alkylation on the 2-nitrogen atom would have yielded a quinonoid structure, which would have given a larger bathochromic shift. Thus the compounds (**IIIa**, **VIa**, **VIIb**, **IIIb**) showed absorption maxima 382, 386, 392, and 386 nm respectively whereas 2-phenyl derivative (**X**) prepared by us earlier<sup>4)</sup> had maximum at 420 nm (Chart 2).

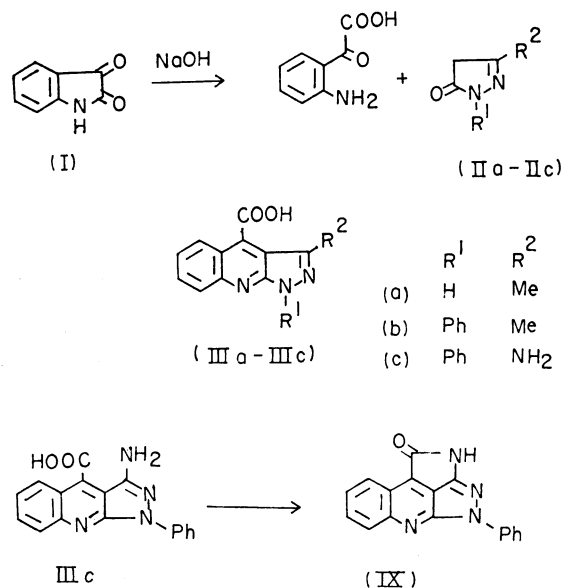


Chart 1.

We found to our satisfaction that the *N*-alkyl derivatives showed much stronger fluorescence and even the *N*-unsubstituted derivative (**IIIa**) showed stronger fluorescence than the *N*-phenyl derivative (**IIIb**). The *N*-unsubstituted pyrazoloquinolinecarboxylic acid and the two *N*-alkyl derivatives were also converted into the corresponding amides (**VIIa** and **VIIb**) and nitriles (**VIIIa** and **VIIIb**). The absorption and fluorescence efficiencies of these compounds were also studied (Table 1).

From our studies, it can be seen that the *N*-alkylpyrazolo[3,4-*b*]quinoline derivatives are strong

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| Compound                                              | Yield<br>% | Mp<br>$\theta_m/^{\circ}\text{C}$ | Recrystalliza-<br>tion solvent | $\lambda_{\text{max}}$<br>absorption/nm | $\log E$ | $\lambda_{\text{max}}$<br>emission/nm |
|-------------------------------------------------------|------------|-----------------------------------|--------------------------------|-----------------------------------------|----------|---------------------------------------|
| <b>Carboxylic acid</b>                                |            |                                   |                                |                                         |          |                                       |
| IIIa                                                  | 65         | > 300                             | EtOH                           | 382                                     | 3.74     | 425                                   |
| IIIb                                                  | 62         | 188—190                           | EtOH                           | 386                                     | 3.81     | 480                                   |
| IIIc                                                  | 58         | 214—215                           | EtOH                           |                                         |          |                                       |
| <b>Amides</b>                                         |            |                                   |                                |                                         |          |                                       |
| IVa                                                   | 78         | 276—280                           | EtOH                           | 388                                     | 3.74     | 434                                   |
| IVb                                                   | 80         | > 300                             | EtOH                           | 394                                     | 3.54     | 494                                   |
| VIIa ( <i>N</i> -CH <sub>3</sub> )                    | 80         | 226—228                           | EtOH                           | 394                                     | 3.93     | 456                                   |
| VIIb ( <i>N</i> -CH <sub>2</sub> CH <sub>2</sub> CN)  | 82         | 246—248                           | EtOH                           | 392                                     | 3.86     | 434                                   |
| <b>Nitriles</b>                                       |            |                                   |                                |                                         |          |                                       |
| Va                                                    | 86         | 180—182                           | C <sub>6</sub> H <sub>6</sub>  | 418                                     | 3.69     | 470                                   |
| Vb                                                    | 84         | > 300                             | EtOH                           | 428                                     | 3.36     | 494                                   |
| VIIIa ( <i>N</i> -CH <sub>3</sub> )                   | 79         | 260—262                           | EtOH                           | 396                                     | 3.59     | 490                                   |
| VIIIb ( <i>N</i> -CH <sub>2</sub> CH <sub>2</sub> CN) | 83         | 166—168                           | EtOH                           | 400                                     | 3.50     | 472                                   |

All melting points are uncorrected. The IR spectra were recorded on different spectrophotometers as Nujol

treated with liquid ammonia and kept overnight at room temperature. The amide obtained was filtered. The yield, mp, recrystallization solvent, molecular formula of the various amides prepared are given in the Table.

*General Procedure for the Synthesis of Pyrazolo[3,4-b]quinoline-4-carbonitriles.* These were prepared by refluxing

the amide (1 g) with  $\text{POCl}_3$  (6 ml) in an oil bath at 110—115 °C for 2 h. After the usual work-up, the product separated was isolated. The yield, mp, recrystallization solvent, molecular formula of the various nitriles prepared are given in the Table.

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#### References

- 1) H. Gold, "The Chemistry of Synthetic Dyes", ed by K. Venkatraman, Academic Press, New York and London 1971, Vol. V, Page 659.
  - 2) A. Brack (Farben fabriken Bayer A. G.) Belg. Pat. 617180, *Chem. Abstr.* **59**, 636 (1963).
  - 3) A. Brack (Farben fabriken Bayer, Laver Kusa Ger) *Ann. Chem.*, **681**, 105—110 (1965) *Chem. Abstr.*, **62**, 11799 (1965).
  - 4) V. Purnaprajna and S. Seshadri, *Ind. J. Chem. Sect. B*, **14B**, 971—2 (1976).
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