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The Preparation of 5-Nitro-2-Aminophenol and some Derivatives

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ABSTRACT

A facile method for the preparation of 5-nitro-2-aminophenol and its derivatives is described. Starting from isatins, through Bayer–Villiger oxidation and nitration of the intermediate 2,3-dioxo-4H-1,4-benzooxazines and hydrolysis of the corresponding nitro compounds to 5-nitro-2-aminophenols, the procedure is shown to be an effective and reliable route to these compounds. From two new 5-nitro-2-aminophenols thus prepared, azo dyes from 2-naphthol and 1-phenyl-3-methylpyrazolone-5 were obtained.

1 INTRODUCTION

5-Nitro-2-aminophenol is a valuable intermediate for the preparation of *o*,*o*′-dihydroxyazodyes, which are starting materials for metal complex azo dyes.[1] Known methods[2,3] have a drawback in that they use 2-aminophenols as starting materials, and thus protection of the hydroxy and amino groups is required.

The present paper describes a facile method for the preparation of 5-nitro-2-aminophenol and some of its derivatives, starting from readily available isatins, through Bayer–Villiger oxidations, nitration of the intermediate 2,3-dioxo-4H-1,4-benzooxazines and hydrolysis of the corresponding nitro compounds to give 5-nitro-2-aminophenols. Using this procedure, the protection step of the intermediate reaction products is avoided. The

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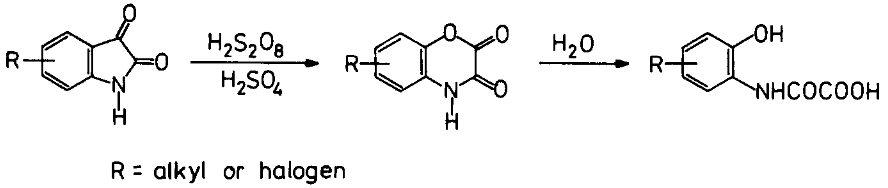
procedure proves to be an effective and reliable method for these valuable dye intermediates.

2 RESULTS AND DISCUSSION

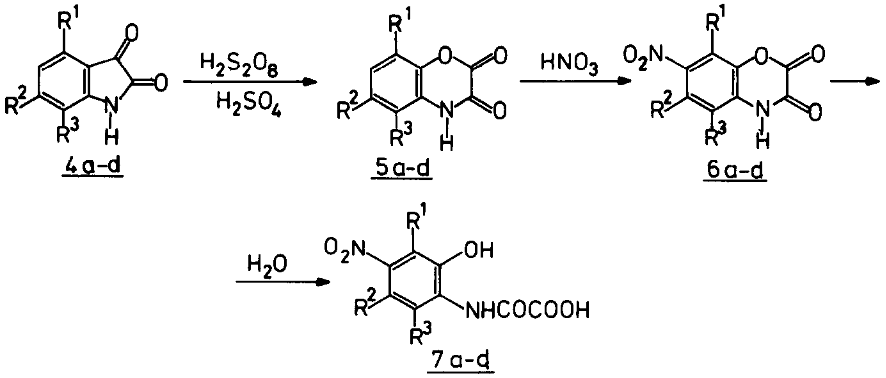
Several methods are known for the preparation of 5-nitro-2-aminophenol, by nitration of 2-aminophenol with protected (acylated) amino and hydroxy groups. Nitration of 2-/3H/-benzoxazolone gives 6-nitro-2-/3H/-benzoxazolone.[2] However its hydrolysis is difficult and the yield is very low. Another method, nitration of 2-acetoxyacetanilide, gives 2-acetoxy-4-nitroacetanilide. Both methods use 2-aminophenol with a protected amino and hydroxy group, and in some cases the deprotection step is difficult to perform.

Recently, Reissenweber and Mangeld[4] gave a relatively simple method for the preparation of 2,3-dioxo-4H-1,4-benzooxazines **2** by Bayer–Villiger oxidation of isatins **1** in acid media. The heterocyclic ring of these compounds is opened very easily by hydrolysis, even at room temperature, thus giving N-(2-hydroxyphenyl)oxamide acids **3**, which actually represent acylated 2-aminophenols (Scheme 1).

Bearing this method in mind, we now propose a facile and effective



Scheme 1

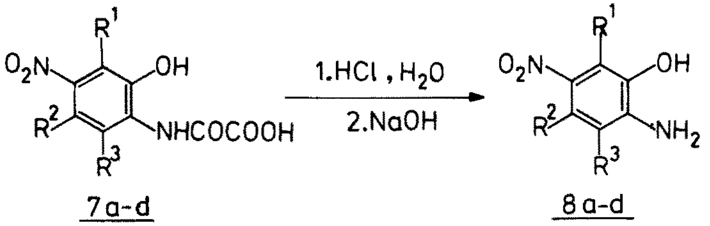


Scheme 2

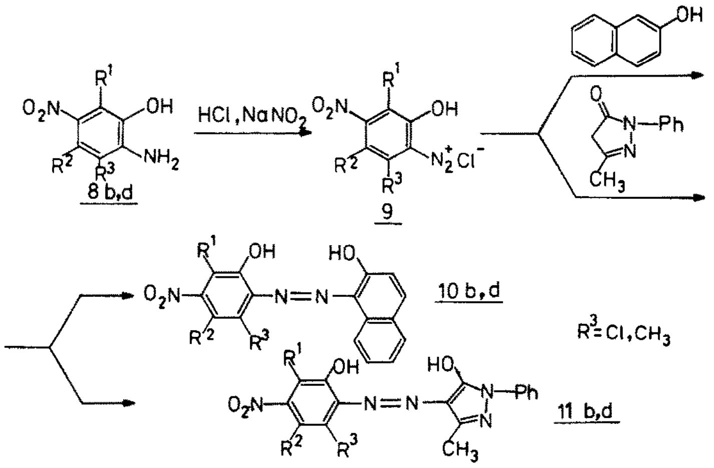
TABLE 1
Substituents in Compounds **4a–d–7a–d** and **8b,d–11b,d**

Substituent	***a***	***b***	***c***	***d***
R_1	H	Cl	H	H
R_2	H	H	Cl	H
R_2	H	H	H	CH_3

method using nitration of the 2,3-dioxo-4H-1,4-benzooxazines to the corresponding nitro derivatives, which can then be easily hydrolysed. The first step is Bayer–Villiger oxidation of the isatins **4a–d** to 2,3-dioxo-4H-1,4-benzooxazines **5a–d**. Without isolation, **5a–d** were nitrated giving 7-nitro-2,3-dioxo-4H-1,4-benzooxazines **6a–d**. The hydrolysis of **6** proceeds smoothly at room temperature, and in the initial stages the precipitated product was a mixture of **6** and **7**. After 24 h hydrolysis was complete, and the only product was **7** (Scheme 2, Table 1). Some of the compounds are



Scheme 3



Scheme 4

identified as N-(2-hydroxy-phenyl)oxamide acids. Refluxing of **7a–d** in 10% hydrochloric acid for 2 h gave the corresponding 5-nitro-2-aminophenols **8a–d** (Scheme 3).

The new 5-nitro-2-aminophenols were diazotized and coupled with 2-naphthol and 1-phenyl-3-methyl-pyrazolone-5 giving the dyes **10b,d** and **11b,d** (Scheme 4).

The one-pot steps of oxidation and nitration, i.e. with no necessity for protection steps, the very facile hydrolysis and high yields of the final 5-nitro-2-aminophenols are indicative of the advantages of this new method.

3 EXPERIMENTAL

3.1 General

Melting points were determined on a Koffler apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on a Tesla BS-487 80 MHz instrument in DMSO-d_6 with TMS as internal standard.

3.2 Preparation of 7a–c (General procedure)

Concentrated sulphuric acid (100 ml, $d = 1{\cdot}84$) was charged into a three-necked round bottomed flask equipped with a mechanical stirrer and a thermometer. Potassium persulphate (40 g, 0·15 M) was added with vigorous stirring. The reaction mixture was then cooled (ice–salt bath) to 15°C and 0·1 M of the corresponding isatin was slowly added keeping the temperature at 15–20°C. The reaction mixture was stirred for 30 min at the same temperature. Sodium nitrate (9·5 g, 0·1 M) was added gradually below 20°C. The viscous suspension was stirred for 2 h at 20–25°C and then poured onto ice (400 g). The resultant precipitate was filtered and dried. The product was a mixture of **6** and **7**; to obtain **7**, after adding to ice, the reaction mixture was either kept for 24 h or made alkaline and then acidified.

(7a) Yield 85–91%, m.p. 259°C (water).
Elemental analysis for $C_8H_6N_2O_6$:
Found: C% 42·7; H% 3·2; N% 12·3.
Calculated: C% 42·5; H% 2·7; N% 12·4.
^{1}H-NMR (DMSO-d_6) δ, 7·87–8·62 (m, 3H, 2Ar); 9·95 (s, 1H, OH).

(7b) Yield 75–80%, m.p. 313–314°C (water).
Elemental analysis for $C_8H_5ClN_2O_6 . H_2O$:
Found: C% 35·0; H% 2·3; N% 10·3.
Calculated: C% 34·5; H% 2·5; N% 10·0.
^{1}H-NMR (DMSO-d_6) δ, 7·67–8·56 (m, 2H, Ar); 9·85 (s, 1H, OH).

(7c) Yield 75–80%, m.p. 242–243°C (water).
Elemental analysis for $C_8H_5ClN_2O_6 . H_2O$:
Found: C% 34·6; H% 3·0; N% 10·3.
Calculated: C% 34·5; H% 2·5; N% 10·0.
^{1}H-NMR (DMSO-d_6) δ, 7·72–8·62 (m, 2H, Ar); 9·90 (s, 1H, OH).

2.3 Preparation of 5-nitro-2-aminophenols 8 (General procedure)

Hydrochloric acid (100 ml 10%) and the respective N-(hydroxyphenyl)-oxamide acids **7** (0·1 M) (or wet cake containing the same amount) were charged into a flask equipped with a mechanical stirrer and reflux condenser. The reaction mixture was stirred and refluxed for 2 h. The dark solution was filtered hot to remove undissolved material; the filtrate was cooled to room temperature and neutralized with sodium hydroxide solution to pH 7. The resultant solid was filtered and dried.

(8a) Yield 90–95%, m.p. 199–201°C (ethanol); literature m.p. 201–202°C.[3]
(8b) Yield 90–95%, m.p. 243–244°C (acetone: water, 1:1).
Elemental analysis for $C_6H_5ClN_2O_3$:
Found: C% 38·7; H% 3·0; N% 14·9.
Calculated: C% 38·2; H% 2·7; N% 14·8.
(8d) Yield 90–95%, m.p. 191–192°C (acetone: water, 1:1).
Elemental analysis for $C_7H_8N_2O_3$:
Found: C% 50·1; H% 5·1; N% 16·5.
Calculated: C% 50·0; H% 4·8; N% 16·7.

3.4 Preparation of dyes 10b,d and 11b,d

Compound **8b** or **8d** (0·01 M) was dissolved in dilute hydrochloric acid (prepared from 5 ml 37% HCl and 50 ml water). The reaction mixture was cooled to 0–5°C. Sodium nitrite (0·7 g, 0·01 M) dissolved in 5 ml water was added dropwise to the suspension formed. The pH of the reaction mixture at the end of diazotization was 1–2; it was then adjusted with sodium bicarbonate solution to pH 3–4. 1-Phenyl-3-methylpyrazolone-5 or 2-naphthol (0·01 M) was dissolved in NaOH (0·4 g) and water (30–40 ml). The alkaline reaction mixture was cooled to 0–5°C and added slowly to the diazo suspension, with stirring, at the same temperature. The coupling reaction was completed at pH 8 over about 2 h. At the end of the process, the pH was adjusted to 7 and the dye filtered and dried.

(10b) Yield 95%, m.p. 283–284°C (1-propanol).
Elemental analysis for $C_{16}H_{10}ClN_3O_4$:
Found: N% 12·07.
Calculated: N% 12·26.

(10d) Yield 96%, m.p. 232–234°C (1-propanol).
Elemental analysis for $C_{17}H_{13}N_3O_4$:
Found: C% 62·7; H% 4·4; N% 12·6.
Calculated: C% 63·1; H% 4·0; N% 13·0.

(11b) Yield 96%, m.p. 278–279°C (1-propanol).
Elemental analysis for $C_{16}H_{12}ClN_5O_4$:
Found: C% 52·1; H% 3·7; N% 18·4.
Calculated: C% 51·4; H% 3·2; N% 18·7.

(11d) Yield 94%, m.p. 273–274°C (1-propanol).
Elemental analysis for $C_{17}H_{15}N_5O_4$:
Found: C% 58·5; H% 4·5; N% 20·3.
Calculated: C% 57·8; H% 4·2; N% 19·8.

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