Oxazole Ring Cleavage in the Course of the Synthesis of Heterocyclic Azo Dyes

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The formation of azo dyes by coupling the diazonium salts of aminophenyloxazolopyridines with N,N-diethylaniline was shown to be a suitable probe to check the stability of the oxazole ring in the course of their preparation. Depending on experimental conditions, "closed" and "opened" systems could be obtained separately.

In the course of our work on disperse heterocyclic dyes obtained in the usual way, i.e. by coupling the diazonium salts of aminophenyloxazolopyridines 1-4 with N,N-diethylaniline, we observed an undesired reaction leading to


1 = meta
2 = para

3 = meta
4 = para
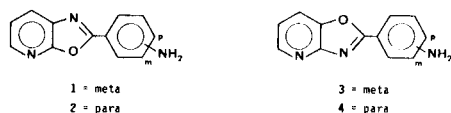
dyes in which the oxazole ring underwent cleavage. The reaction was influenced by the acidity of the mixture during the diazotization and, to a greater extent, by the temperature. We checked the reactions using the formation of azo dyes as a probe, since our final goal was to obtain these substances.

The patterns described in the experimental section may be schematically represented as follows: 1. The way to be sure of obtaining the expected azo dyes, such as dye 5, is

5
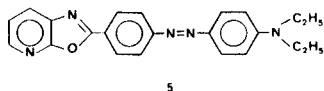
represented by the use of a mixture of hydrochloric acid-isoamyl nitrite, preventing the temperature to exceed 12-14°. 2. When the classic mixture hydrochloric acid-sodium nitrite is used, the temperature plays a determining role during the formation of the amine hydrochlorides; (i) at low temperature the oxazole dyes are obtained, but the approach described in 1 above is preferable from a practical point of view; (ii) at higher temperature, para-amines (2 and 4) give o-hydroxyamido dyes, such as dye 6,

6
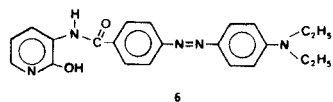
as a consequence of oxazole ring cleavage, whereas meta-isomers 1 and 3 decompose and no trace of coloration is observed. In fact, dyes from isomers 3 and 4 have been previously described [1], but it was sheer chance that their synthesis was performed using the hydrochloric acid-

sodium nitrite mixture at low temperature. Using isomers 1 and 2, we have now carefully examined the problem and we have extended our attention to the whole series.

The problem of the assignment of structures 5 and 6 is, a posteriori, similar to a textbook case. The complete set of data is reported for the latter dyes, derived from amine 1, but some representative tests on other isomers, chromatography for example, ensure the validity of the above general statements.

Chromatography.

On RP-18 plates, the general behaviour is represented in Scheme 1.

Scheme 1
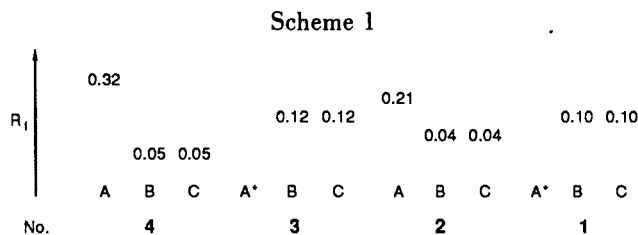
A: Amine + hydrochloric acid + sodium nitrite + DEA (hydrochloride formed at high temperatrue). B: Amine + hydrochloric acid + sodium nitrite + DEA (hydrochloride formed at low temperature). C: Amine + hydrochloric acid + isoamyl nitrite + DEA (the entire mixture at low temperature). A* No coloured spots.

The data in the scheme clearly confirm the above reported reaction patterns. In order to have more suitable R_f values the chromatography for dyes 5 and 6 have also been performed on silica gel plates, obtaining R_f values of 0.91 and 0.87 respectively.

Electronic Spectra.

The main absorptions in the spectra of dyes 5 and 6 in ethanol lie at 479 nm (log ϵ, 4.64) and at 460 nm (log ϵ, 4.50) respectively. These data are consistent with the view of a donor-acceptor substituted azobenzene chromogen [2] in which the bathohyperchromic effect of dye 5 compared to dye 6 is dependent on the stronger electron-attracting power of the pyridooxazolyl moiety compared to its open-chain counterpart.

NMR Spectra.

Figure 1 shows the spectra of dye **5** (1a) and dye **6** (1b) in the region of the aromatic protons. The aliphatic region is not reported being obviously the same for the two dyes (a triplet, 6H, 1.25 ppm and a quartet, 4H, 3.48 ppm). When the oxazole ring is cleaved, two signals in the low field portion of the spectrum appear, giving rise to exchange by addition of deuteriomethanol. The first, at 9.15 ppm, has been attributed to OH, the latter, at 11.65 ppm, which disappears at 50° and subsequently reappears, strengthened, at 5°, has been attributed to NH [3]. In Table 1 are reported the proton chemical shifts and $\Delta\delta$ values for dye
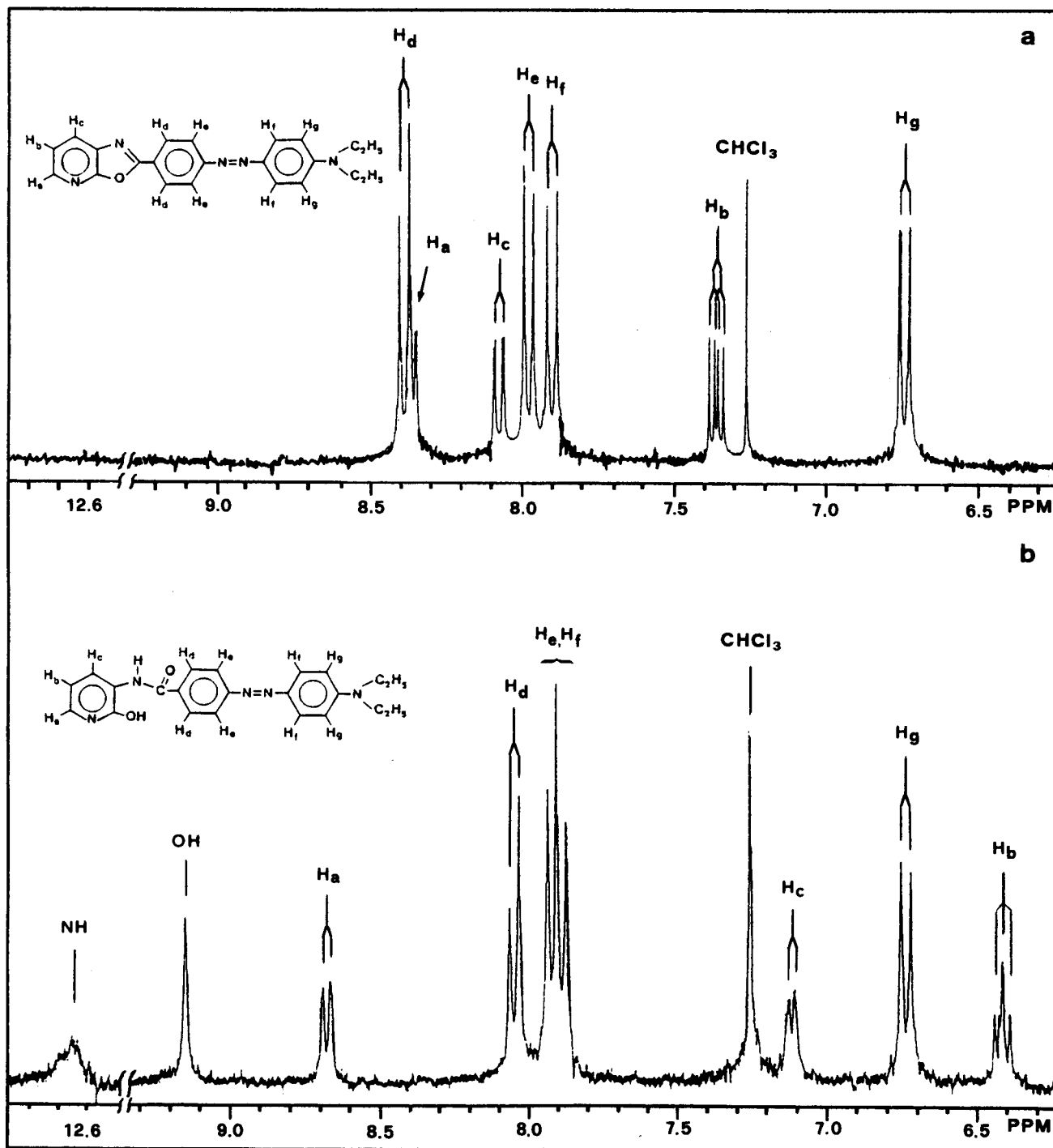

Figure 1. The ^{1}H-nmr Spectra of Dyes **5** (a) and **6** (b).

|	H_a	H_b	H_c	H_d	H_e	H_f	H_g
Dye 5	8.35	7.36	8.08	8.39	7.98	7.90	6.74
Dye 6	8.68	6.42	7.12	8.05	7.91	7.91	6.74
$\Delta\delta$ (6 -5)	0.33	-0.94	-0.96	-0.34	-0.07	0.01	0.00

[a] Formulas and symbols in Figure 1.

6 compared to 5. The following remarks can be made: (i) The nearer the protons are to the oxazole ring, the greater is their downfield shift due to the electron attracting power of the pentatomic ring; (ii) when the oxazole ring is cleaved, the failure of its deshielding effect is evidenced by negative $\Delta\delta$ values; (iii) in dye 6, the H_a proton is strongly deshielded and this apparent anomaly can be attributed to the variation of charge density on the pyridine nitrogen atom which in turn, influences by magnetic anisotropy of the α-pyridine position. A ring current variation can also play an important role.

Infrared Spectra.

As a consequence of the opening of the oxazole ring, dye 6 is expected to show additional bands due to the presence of an amido group and an hydroxyl group. In fact, further bands at 1640 cm^{-1} and 3360 cm^{-1} appear. The position of the latter is consistent with the formation of an intramolecular hydrogen bond between the hydroxyl functionality and the carbonyl of the amido group.

Mass Spectra.

A complete analysis of the spectra lies outside the aim of this work, however the most significative fragmentations
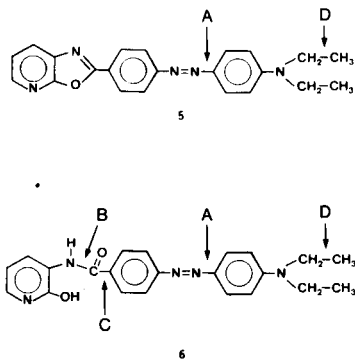
confirm the proposed structures. In the 'closed' dye 5 the molecular peak (m/e 371) is also the base peak, the weak point under electron impact being indicated by arrow A. The loss of a methyl, D, is also a fragmentation pathway. In the 'opened' dye 6 (molecular peak m/e 389) the base peak is represented by the fragmentation at B (m/e 280) accompanied by cleavages C, A, and D.

As a final remark, it is also worth mentioning that

amines 1 and 2 and their precursors 9 and 10 (if the synthetic pathway depicted in the Scheme 2 is followed) have

Scheme 2
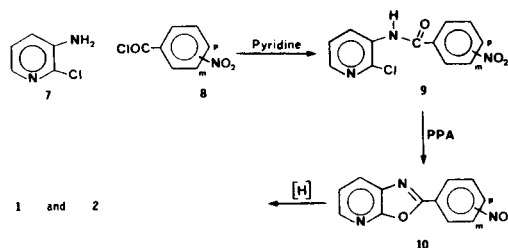
not been so far described in spite of their simplicity. Only the para-isomer 10 was directly obtained by reacting 2-hydroxy-3-aminopyridine with p-nitrobenzoyl chloride in PPA [4].

The dyes of the present series, including a comparison of dyes 5 and 6, are being tested as disperse dyes for polyamide and polyester fabrics and the results obtained will appear in the colour-textile literature.

EXPERIMENTAL

The R_f values were determined on (i) RP-18 F$_{254}$ tlc plates (Merck), using methanol:water 9:1 as eluent and (ii) silica gel 60 F$_{254}$ tlc plates (Merck), using as eluent B-A-W (butanol:acetic acid:water) 4:1:5. Electronic spectra were recorded on a Pye Unicam SP 8-100 spectrophotometer in ethanol. The nmr spectra were obtained with a Jeol GX 270 spectrometer in deuteriochloroform solution (3%). Infrared spectra were detected in potassium bromide with a Perkin-Elmer 781 infrared spectrophotometer. Mass spectra were obtained with a Kratos MS 80 mass spectrometer.

Amides 9 were prepared following the general procedure indicated in [5]. Nitrobenzoyl chloride 8 (15.2 g, 8.2 x 10^{-2} mole) dissolved in pyridine (200 ml) was added at 12-14° to a solution of 3-amino-2-chloropyridine 7 (10.5 g, 8.2 x 10^{-2} mole) in pyridine (30 ml) and the mixture was kept overnight at the same temperature. Glacial acetic acid was added and the amides, after washing with 10% acetic acid, were crystallized from ethanol/water to yield 22.5 g (99%) of product. Data for para-isomer and, in parenthesis, for meta-isomer, mp, 177-178° (145-146°).

Anal. Calcd. for C$_{12}$H$_8$ClN$_3$O$_3$: C, 51.90; H, 2.90; N, 15.13. Found: C, 52.06 (52.00); H, 2.97 (3.01); N, 15.04 (15.15).

Nitro derivatives 10 were prepared following the general procedure indicated in [5]. Amides 9 were treated for six hours at 180° in polyphosphoric acid (85% phosphorus pentoxide). The reaction mixture was poured into distilled water and basified with sodium hydroxide. The precipitate was collected and washed with water. Data for the para-isomer and, in parenthesis, for the meta-isomer are: Crystallization solvent, ethanol/water (acetonitrile); Yield, 75% (44%), mp, 242-243° [4] (208-209°).

Anal. Calcd. for C$_{12}$H$_7$N$_3$O$_3$: C, 59.76; H, 2.93; N, 17.42. Found: C, 59.75 (59.68); H, 2.98 (3.04); N, 17.37 (17.37).

Amine 1 was prepared following the general procedure indicated in [6]. Sodium borohydride-sulphur 1:3 (Aldrich) (1.5 g) were suspended in anhydrous tetrahydrofuran (5 ml). After the evolution of hydrogen, a suspension of 10 (*meta* isomer) (1 g, 4.15 x 10^{-3} mole) in anhydrous tetrahydrofuran (25 ml) was added, refluxing the mixture for ten hours. After filtration at room temperature, the solvent was removed and the residue was crystallized from ligroin to yield 0.50 g (54%) of 1, mp 225-226°.

Anal. Calcd. for $C_{12}H_9N_3O$: C, 68.24; H, 4.30; N, 18.86. Found: C, 68.18; H, 4.33; N, 18.74.

Amine 2 was prepared by refluxing for six hours 1 g of 10 (*para*-isomer) (4.15 x 10^{-3} mole) and sodium hydrogen sulfide 2 g (2.7 x 10^{-2} mole) dissolved in 80% aqueous methanol (25 ml). After cooling, the product was collected by filtration, washed with water and crystallized from methanol/water to yield 0.33 g (35%) of 2, mp 246-247°.

Anal. Calcd. for $C_{12}H_9N_3O$: C, 68.24; H, 4.30; N, 18.86. Found: C, 68.29; H, 4.41; N, 18.75.

Dye 5 and its *meta*-counterpart were prepared by addition of concentrated hydrochloric acid (0.23 ml) and isoamyl nitrite (0.68 ml, 5 x 10^{-3} mole) to a solution of 0.5 g of 2 (2.5 x 10^{-3} mole) in ethanol (15 ml) at 0° with stirring. The solution of the diazonium salt thus obtained, was added to *N,N*-diethylaniline (0.38 g, 2.5 x 10^{-3} mole) dissolved in acetic acid (5 ml) at 10-12° with stirring. After three hours, a saturated solution of sodium acetate was added and the crude dye was collected and washed with water. A specimen was also purified on a Kieselgel 60 column, using ethyl acetate as eluent. Data for the *para*-isomer and, in parenthesis, for the *meta*-isomer; crystallization solvent, methanol/water (ethanol/water), yield, 46% (35%), mp, 195-197° (163-165°).

Anal. Calcd. for $C_{22}H_{21}N_5O$: C, 71.14; H, 5.70; N, 18.86. Found: C, 71.26 (71.29); H, 5.88 (5.73); N, 18.73 (18.88).

Dye 6 was prepared treating, near the boiling point, a mixture of 0.5 g of 2 (2.5 x 10^{-3} mole) and concentrated hydrochloric acid (5 ml). After cooling, a solution of sodium nitrite (0.18 g, 2.5 x 10^{-3} moles) in water (4 ml) was added dropwise at 0°. The solution of the diazonium salt thus obtained, was added to *N,N*-diethylaniline (0.38 g, 2.5 x 10^{-3} mole) dissolved in acetic acid (5 ml) at 10-12° under stirring. After three hours, a saturated solution of sodium acetate was added and the crude dye was collected and washed with water. The dye was purified on a Kieselgel 60 column, using ethyl acetate as eluent, to yield 0.29 g (31%) of 6, mp 247-249°.

Anal. Calcd. for $C_{22}H_{23}N_5O_2$: C, 67.85; H, 5.95; N, 17.98. Found: C, 67.69; H, 6.07; N, 17.90.

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