The Reaction of 3-Aminoisoquinoline With Nitrous Acid

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The product of the reaction of 3-aminoisoquinoline and nitrous acid has been identified as the previously unreported 3,4-isoquinolinedione 4-oxime hydrate.

In 1956, Boyer and Wolford, in preparing 3-isoquinolinol (1) by the diazotization of 3-aminoisoquinoline (2) with a three-fold excess of nitrous acid, isolated an unidentified by-product as well as 1. Elemental analysis and infrared spectral data were presented for this material which was also prepared by treatment of 1 with nitrous acid (1).

Five years later, Baumgarten *et al.* (2) pointed out that yields of 1 in the diazotization sequence could be increased appreciably by employing equimolar quantities of 2 and nitrous acid. These workers also reported that 1 reacted further with nitrous acid to provide an unknown substance; attempts to confirm the earlier workers' elemental analysis on the substance were unsuccessful (2).

The reaction of 2 with three-fold excess of nitrous acid has been repeated in these laboratories and the product, isolated in 88% yield, has been identified as 3,4-isoquinolinedione 4-oxime hydrate (3) (Figure 1). The structure

Figure 1
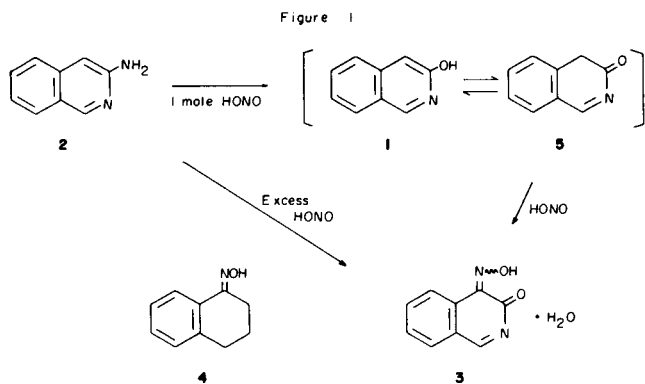
assignment for 3 rests on the following considerations: elemental and water analysis, infrared and nuclear magnetic resonance spectral data as well as low and high resolution mass spectral data.

The aromatic region of the nmr spectrum of 3 was characterized by a multiplet centered at δ 7.58 integrating for three protons and a multiplet at δ 8.50 integrating for one proton. To test the hypothesis that the downfield signal represents the 5-proton (peri to the oximino function), the model oxime 4 (3) was prepared for nmr comparison purposes.

The aromatic region of 4 was characterized by a three

proton multiplet at δ 7.18 and a one proton multiplet at δ 7.88. As expected, the protons of 3 appeared downfield in relation to those of model oxime 4. Nonetheless, the similarities in splitting patterns of the two compounds varifies the assignment of the downfield signal of 3 to the 5-proton.

That the heterocyclic ring remained intact during the diazotization is indicated by a singlet at δ 5.63 which is ascribed to the 1-proton.

Further evidence for structure 3 is derived from its electron impact and chemical ionization mass spectra. Figure 2 summarizes the proposed mass spectral fragmentation

Figure 2

Mass Spectral Fragmentation of 3
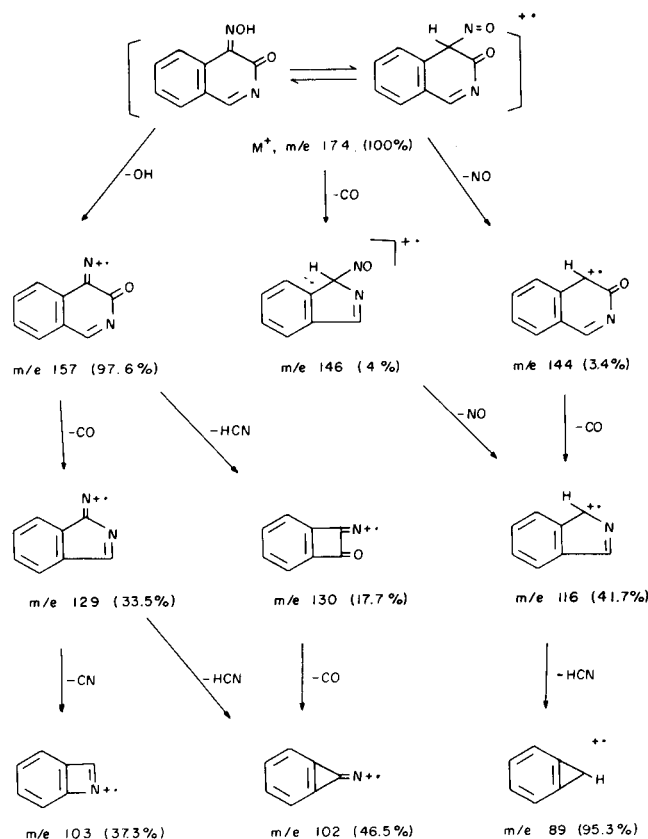
pattern observed at masses greater than m/e 80. The numbers shown in parentheses refer to the relative abundance of the ions. The molecular formulas corresponding to each of the structures representing ions greater than m/e 100 were verified by high resolution electron-impact mass spectrometry. That the ion observed at m/e 174 was indeed the molecular ion (M^+) was confirmed by the observance of M + 1, M + 29 and M + 41 ions in the chemical ionization spectrum when CH_4 was used as the carrier gas. The only fragment ion observed on chemical ionization corresponded to m/e 157.

The formation of oxime **3** from **2** is envisioned as proceeding thru **5**, a tautomer of 3-isoquinolinol **1**. Reaction of **5** with nitrous acid at the position adjacent to the carbonyl function gave **3**.

EXPERIMENTAL

Melting points were taken in a Mel Temp apparatus and are uncorrected. The nuclear magnetic resonance spectra were taken on a Bruker WP-80 instrument and were compared with TMS as an internal standard. Infrared spectra were determined as Nujol mulls on a Perkin-Elmer 137B spectrophotometer. The mass spectra were determined on a Finnigan Model 3300 gc/ms with Industries System 150 data system and on an AEI MS-902 high resolution mass spectrometer.

3,4-Isoquinolinedione 4-oxime hydrate (3).

To a solution of 47.1 g (0.48 mole) of concentrated sulfuric acid in 390 ml of water stirred at 30° was added quickly 17.3 g (0.12 mole) of 3-aminoisoquinoline (**2**) (4). The solution was cooled to 5° and a solution of 24.8 g (0.36 mole) of sodium nitrite in 60 ml of water was added over 45 minutes at 5-10°. The mixture was stirred at 3-7° for 2.5 hours and the solid was filtered, washed with 2 × 75 ml of water, and dried at 60° to give 20.2 g (88%) of the product. Recrystallization from water gave an analytical sample, mp 198-200° dec; nmr (DMSO-d_6): δ 5.63 (s, 1, 1-H), 7.58 (m, 3, 6-H, 7-H, 8-H), 8.50 (m, 1, 5-H); ir: (μ) 3.17 (O-H), 6.02 (C=O), 6.21 (C=N).

Anal. Calcd. for $C_9H_6N_2O_2 \cdot H_2O$: C, 56.25; H, 4.19; N, 14.58; H_2O, 9.37. Found: C, 56.02; H, 4.25; N, 14.44; H_2O, 10.1.

3,4-Dihydro-1(2H)-naphthalenone Oxime (4).

To a solution of 1.40 g (0.02 mole) of hydroxylamine hydrochloride in 50 ml of water was added 1.64 g (0.02 mole) of sodium acetate followed by 2.92 g (0.02 mole) of 3,4-dihydro-1(2H)-naphthalenone in 50 ml of methanol. After a 1.25 hour reflux period, the solution was concentrated to a volume of 60 ml and allowed to stand at room temperature overnight. The solid was recrystallized from 10 ml of methanol to give 1.95 g (61%) of **4**, mp 102-104°, lit mp 102-103°(3); nmr (DMSO-d_6): δ 1.75 (m, 2, 3-CH_2), 2.80 (m, 4, 2-CH_2 and 4-CH_2), 7.18 (m, 3, 5-H, 6-H, 7-H); 7.88 (m, 1, 8-H); ir: (μ) 3.05-3.25 (O-H), 6.11, 6.29 (C=C, C=N).

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.29; H, 6.95; N, 8.57.

REFERENCES AND NOTES

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