

Synthesis of 1-Diazo-2-(1*H*)-phenazinone.

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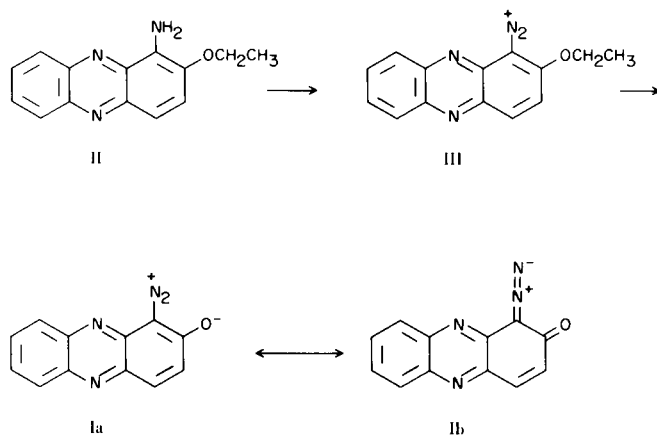
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Our study of phenazines with potential biological activity has led to consideration of the heterocyclic diazo-ketone (I), which would be expected to undergo interesting photochemical (2) and coupling (3), reactions.

Although diazotizations of phenazinium salts are used in the preparation of azosafranine dyes (4), no diazonium salts or azo compounds resulting from diazotization of phenazines have been reported. Because coupling reactions were not observed, diazotization of 1-aminophenazine was reported to fail (5). Hegedus reported failure of the diazotization reaction of 1-amino-2-hydroxyphenazine (6).

The phenazine-1-diazonium salt should be relatively unreactive toward S_N1 displacement because of the demonstrated electrophilicity of the phenazine system (7). Similarly bimolecular nucleophilic displacement at C-1 of unoxidized phenazine is very slow (8). The chemistry of aryl diazonium salts is not limited to consideration of reactions of the diazo group. A substituent *ortho* or *para* to a retained diazonium group is activated toward bimolecular nucleophilic substitution (9,10,11). Meldola has reported that in order for *p*-methoxy or *p*-nitro groups to be displaced from the diazonium salts an additional electrophilic group must be present (12). This condition is satisfied in the phenazine system, and the displacement of a substituted group by water might be expected.

The synthesis of 1-diazo-2-(1*H*)-phenazinone (I), the stable conjugate base of the corresponding phenazinol diazonium salt, has been accomplished by the diazotization of 1-amino-2-ethoxyphenazine (II) with nitrous acid.

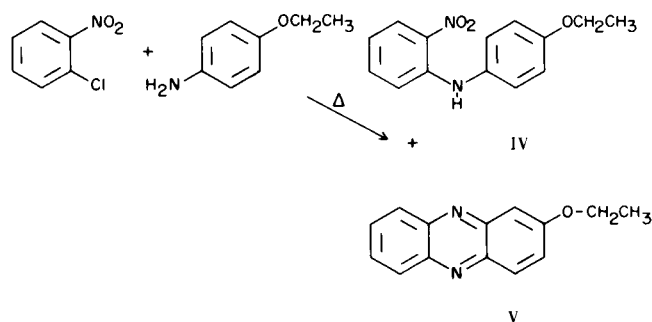


Displacement of the activated ethoxy group of the intermediate diazonium salt (III) by water occurred rapidly, and intermediate (III) could not be isolated under aqueous conditions.

The mass spectrum of the diazophenazine confirms the molecular weight (parent ion at m/e 222) and is consistent with an expected decomposition involving loss of nitrogen followed by loss of carbon monoxide which results in fragments with m/e 194 and 166 (base).

The diazophenazinone (I) is unusually stable to chemical reagents. It was not attacked by cyanide ion in an attempted Sandmeyer reaction. The diazophenazine was recovered unchanged from concentrated hydrochloric acid containing stannous chloride.

Coupling with 2-naphthol did not occur in basic aqueous or alcoholic solution nor in acetic acid. However the diazophenazinone did react with phloroglucinol in basic alcoholic solution to give a deep red azo dye, which formed a violet lake with cupric ions.



The predominant canonical form of diazo oxides has been usually ascertained by the infrared absorption frequency of the diazo group (13). The low frequency of the 1-diazo-2-ketophenazine (2115 cm^{-1}) and the ease with which it is eluted from an alumina column imply that the actual electronic configuration resembles Ib, the diazoketone form, rather than Ia, the diazonium oxide form.

The preparation of the 1-amino-2-ethoxyphenazine was straightforward. Interestingly, 2-ethoxyphenazine (V) was formed in the attempted preparation of its precursor, 2-nitro-4-ethoxydiphenylamine (IV), from phenetidine and *o*-chloronitrobenzene.

EXPERIMENTAL

2-Ethoxyphenazine.

A mixture of *p*-phenetidine (52.78 g.), sodium acetate (38.48 g.), and *o*-nitrochlorobenzene (38.48 g.) was heated under reflux in a 500 ml. flask for 20 hours. The black tar remaining was steam distilled to remove unreacted starting material. The residue was dissolved in benzene and chromatographed on alumina. A red band (2-nitro-4'-ethoxydiphenylamine) and a yellow band (2-ethoxyphenazine) were eluted with petroleum ether-benzene. From the yellow band were obtained, after recrystallization from methanol, 3.0 grams of 2-ethoxyphenazine, m.p. 114-115°. The mother liquor from the recrystallization was combined with the material eluted from the red band and the mixture was subjected to ring closure (14). Purification by sublimation and recrystallization from methanol gave 5.1 g. of 2-ethoxyphenazine, m.p. 114-115°, (15).

1-Amino-2-ethoxyphenazine.

2-Ethoxyphenazine (8.1 g.) was treated with concentrated sulfuric acid (80 ml.) and potassium nitrate (20 g.) at 0° for 2 hours (7). The mixture was poured into ice-water, and the orange precipitate was recrystallized from methanol giving 6.01 g. of yellow needles of 1-nitro-2-ethoxyphenazine, m.p. 199-201°. This was dissolved in benzene and catalytically reduced with hydrogen (palladium on charcoal), giving the dark purple 1-amino-2-ethoxyphenazine, m.p. 105-107°, in quantitative yield on crystallization from the benzene.

Anal. Calcd. for C₁₄H₁₃N₃O: C, 70.26; H, 5.48; N, 17.56. Found: C, 70.08; H, 5.55; N, 17.28.

1-Diazo-2-(1*H*)-phenazinone.

1-Amino-2-ethoxyphenazine (2.525 g.) was dissolved in 13.3 ml. of water and 12.0 ml. of concentrated hydrochloric acid. The dark brown solution was cooled to 0° and a solution of sodium nitrite (0.79 g.) in 2.1 ml. of water was added slowly, causing a yellow-brown precipitate to begin to form. The resulting mixture was neutralized with sodium carbonate at 0°. The solution was heated to boiling and filtered, giving a yellow-brown residue, which turned black in sunlight.

The brown solid was dissolved in chloroform and chromatographed on alumina rapidly. When the column was not protected from light, the product decomposed into a dark brown compound which was not eluted readily. Two small yellow bands (with bright yellow fluorescence) and one large dark yellow band (with dark red fluorescence) were eluted from the column with benzene. The two light yellow bands yielded small amounts of some non-

crystalline material. The material from the large dark yellow band was recrystallized from chloroform, giving 1.66 g. of yellow crystals, which decomposed from 152-170°.

I.R. (chloroform), 2115, 1625, 1535, 1410, 1355, 1315, 1227, 1150, 1124, 1020, 838 cm⁻¹.

U.V. (ethanol) 243 (log ε 4.09), 297 (log ε 3.89), 238 (log ε 3.90) nm.

M.S. 222, 194, 166, 139 m/e.

Anal. Calcd. for C₁₂H₆N₄O: C, 64.86; H, 2.72; N, 25.21. Found: C, 65.00; H, 2.74; N, 25.30.

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