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SYNTHESIS AND SOME REACTIONS OF o-NITROSOANILINE

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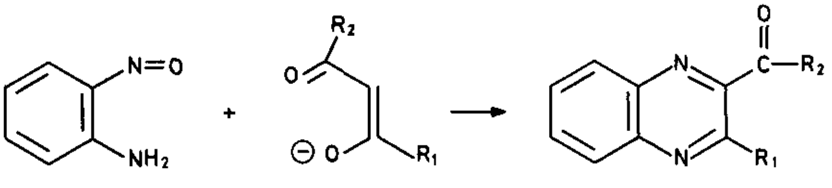
A simple synthesis of o-nitrosoaniline is reported. This compound reacts with some enolate anions, glyoxals, and substituted phenolate anions to give quinoxalines, 1-hydroxy-2-quinoxalinones, and phenazines respectively.

o-Nitrosoaniline was first isolated by Bailey and coworkers(1) in minute amounts sufficient for its identification. Recently, a rather tedious, low-yield (3%) method for the preparation of o-nitrosoaniline (1) was reported from this laboratory(2). Since the chemistry of o-nitrosoaniline has not been explored, it was of interest to find a simpler method for the preparation of o-nitrosoaniline (1) and to study its reactions. We found that dropwise addition of peracetic acid(3) (25 ml) to o-phenylenediamine (9 mM) in chloroform (12 ml) at -20° was attended with the development of a dark brown color. The solution was neutralized with sodium bicarbonate (40%, 30 ml) and extracted further with chloroform. The concentrated chloroform solution was chromatographed on alumina (70 g, grade III) and eluted with petroleum ether-benzene (1:2) to give dark green 1 in 17% (180 mg) yield. Other oxidizing agents, such as Caro's acid and m-chloroperbenzoic acid, at a range of temperatures, gave lower yields of 1. In all these oxidations, o-nitroaniline was formed along with 1. The former emerged first from the chromatography column.

In a previous paper we reported that o-nitrosoaniline (1) reacts with benzofuran-3(2H)-one and with benzoin to give quinoxaline derivatives(2). In this paper we report the preparation of quinoxalines from the reactions of 1 and enolate anions derived from β-diketones, β-ketoesters, and α-methylene ketones. Acetyl acetone (2a), benzoylacetone (2b) and ethylacetoacetate (2c) reacted smoothly with 1, in 5% methanolic potassium hydroxide at reflux temperature, to give quinoxalines 3a,b,c in 74%, 47%, and 70% yields respectively. The identity of these products was established by comparison with authentic samples$^{(4)}$.



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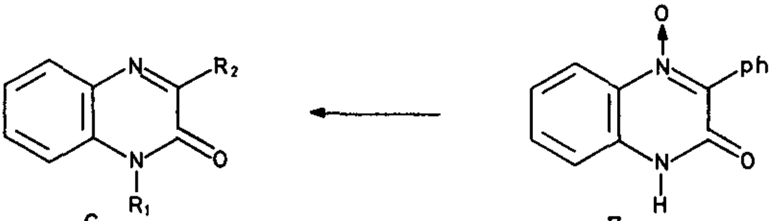
a, $R_1 = R_2 = CH_3$
b, $R_1 = CH_3$, $R_2 = C_6H_5$
c, $R_1 = CH_3$, $R_2 = OC_2H_5$

Furthermore, 1 reacted with deoxybenzoin under basic conditions to give 2,3-diphenylquinoxaline (4) and 2,3-diphenylquinoxaline-1-oxide (5). The latter is presumed to have arisen from the reaction of 1 with benzoin which resulted from the oxidation of deoxybenzoin$^{(2)}$. Similarly, methyl phenylacetate reacted with 1 to give 3-phenyl-2(1H)-quinoxalinone (6a, 23% yield), the identity of which was confirmed by comparison with an authentic sample prepared by reduction of 3-phenylquinoxaline-2(1H)-one-4-oxide$^{(5)}$ (7) with sodium dithionite. Phenylglyoxal, glyoxal or pyruvaldehyde, upon brief heating in neutral media, reacted with 1 to give the quinoxalinones 6b (45% yield), 6c (18% yield), and 6d (7% yield) respectively. The structure of 6c was confirmed by comparison with an authentic sample prepared by heating quinoxaline-1,4-dioxide in acetic anhydride$^{(6)}$. Quinoxalinones 6b, 6c, and 6d, which showed infrared bands at 3360-3320 and 1655 cm^{-1}, gave a dark red color with ferric chloride.

Because benzofurazan oxide is known to react with phenolate anions to give phenazine-5,10-dioxides, it was of interest to find out whether o-nitrosoaniline, being at two oxidation levels below benzofurazan oxide, would react with phenolate anions to



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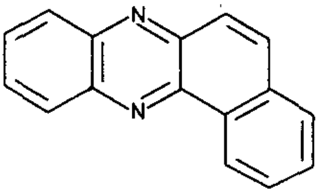
a, $R_1 = H$, $R_2 = C_6H_5$
b, $R_1 = OH$, $R_2 = C_6H_5$
c, $R_1 = OH$, $R_2 = H$
d, $R_1 = OH$, $R_2 = CH_3$

give phenazines. Indeed, benzo[a]phenazine (8, 54%)(7) and naphtho-[1,2-b, 3,4-b']diquinoxaline (11, 27%)(8) were obtained from the reactions of 1, in alcoholic base, with 2-naphthol and 1-naphthol respectively. Product 11 could arise through the intermediacy of 10 which, in turn, might have resulted from the oxidation of intermediate 9. An analogous behavior has been observed in the reaction of benzofurazan oxide with 1-naphthol(9). Similarly, phenol or hydroquinone yielded quinoxalo[2,3-a]phenazine (12, 23%)(10).



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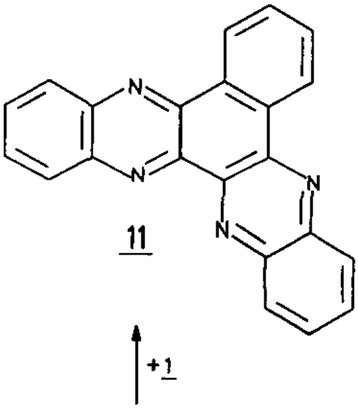

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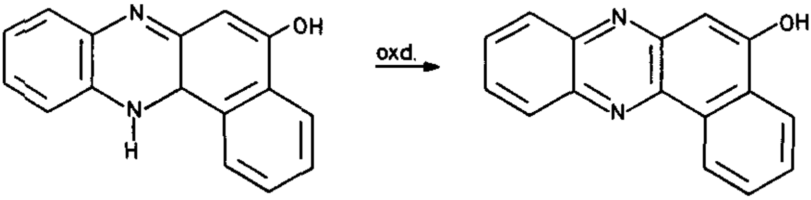

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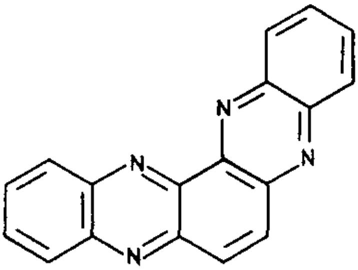

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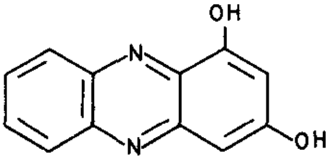

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A methanolic potassium hydroxide solution of phloroglucinol and 1 was heated gently on a steam bath for a few seconds. Acidification of the reaction mixture with hydrochloric acid gave 1,3-dihydroxyphenazine (13)(11) in 22% yield. The identity of phenazines 8, 11, 12 and 13 was established by infrared spectra and comparison with literature melting points.

The present method of preparing phenazines 8, 11, 12, and 13 is simple and superior to known methods. For example, the preparation of 11 requires the availability of 1,2,3,4-tetrahydronaphthalene-1,2,3,4-tetrone. Moreover, the use of 1,3-diketones rather than 1,2-diketones, in the preparation of quinoxalines, is an advantage since 1,3-diketones are relatively easier to prepare.

References and Notes

1. A.S. Bailey, J.M. Peach, C.K. Prout, and T.S. Cameron, J. Chem. Soc. (C), 1969, 2277.
2. M.Z. Nazer, M.J. Haddadin, J.P. Petridou, and C.H. Issidorides, Heterocycles, 1977, 6, 541.
3. L.F. Fieser and M. Fieser, 'Reagents For Organic Synthesis', John Wiley, New York, 1967, Vol. 1, p. 459.
4. a) M.J. Haddadin, G.E. Zahr, T.N. Rawdah, N.C. Chelhot, and C.H. Issidorides, Tetrahedron, 1974, 30, 659; b) M.J. Haddadin and M.A. Atfah, unpublished results.
5. G. Tennant, J. Chem. Soc., 1964, 2666.

6. R.T. Coutts, D. Noble, and D.G. Wibberley, J. Pharm. Pharmacol., 1964, 16, 773.

7. O. Fischer and E. Hepp, Ber., 1887, 20, 2471.

8. T. Zincke and A. Ossenbeck, Ann., 1899, 307, 1

9. M.J. Abu El-Haj, B.W. Dominy, J.D. Johnston, M.J. Haddadin, and C.H. Issidorides, J. Org. Chem., 1972, 37, 589.

10. G.H. Cookson, J. Chem. Soc., 1953, 1328.

11. G.R. Clemo and A.F. Daglish, Ibid., 1948, 2318.

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