

Ozonation of Tertiary Amines and Amides. An Ozone-induced Polonovski Reaction

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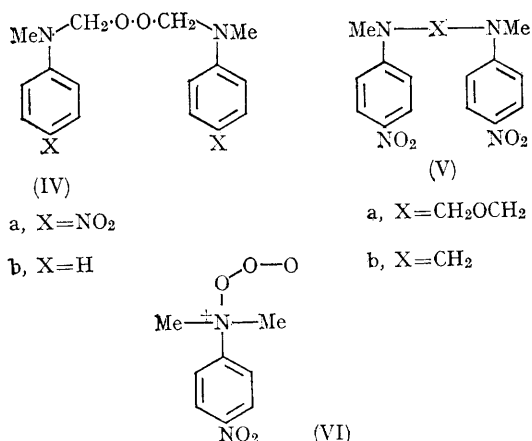
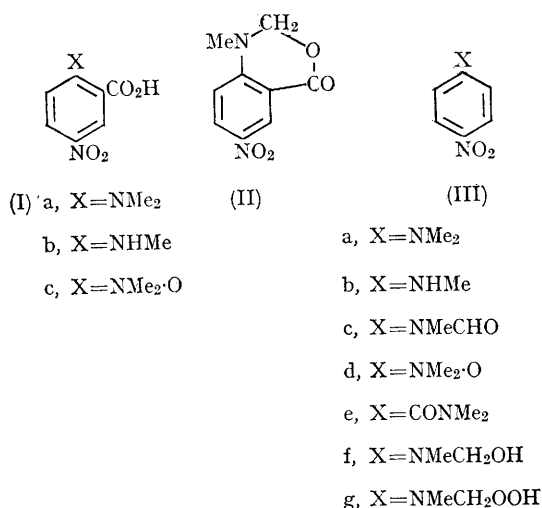
It has been suggested¹ that demethylation of the *NN*-dimethylanthranilic acid (Ia) by action of hot performic acid to give (Ib) occurred by way of an

intramolecular Polonovski reaction, through the *N*-oxide (Ic) and the hydrobenzoxazone (II). Since aliphatic tertiary amines have been shown²

¹ O. Meth-Cohn and H. Suschitzky, *J. Chem. Soc.*, 1963, 4666.

² P. S. Bailey, *Chem. Rev.*, 1958, 58, 977 and references cited therein.

to give good yields of *N*-oxides when ozonised, we hoped to isolate the postulated intermediate (II) of the above reaction by ozonation of the tertiary amine (Ia).



When the amine (Ia) was ozonised in ethyl acetate, methylene chloride, or methanol solution at 0°, one molar equivalent of ozone (in oxygen or nitrogen) was absorbed quantitatively and the hydrobenzoxazone (II) was isolated (20–25%) together with the demethylated product (Ib; 70–75%). The hydrobenzoxazone (II), m.p. 175–

176°, was identical with the product obtained by treatment of the amine (Ib) with hot formaldehyde solution (30%),³ or by action of active manganese dioxide on the tertiary amine (Ia) in refluxing chloroform.⁴ In order to find out if the *N*-oxide (Ic) could be an intermediate in the ozonation, we reacted *p*-nitrodimethylaniline (IIIa) with ozone under identical conditions to those above. Again one molar equivalent was absorbed quantitatively. However, instead of the expected *N*-oxide (IIId) we obtained a mixture of a yellow product, m.p. 176–177°, C₁₆H₁₈N₄O₈ (37–46%), *N*-formyl-*N*-methyl-*p*-nitroaniline (IIIc) m.p. 116–117°, *N*-methyl-*p*-nitroaniline (IIIf) and some starting material (8–10%). Acid hydrolysis of the crude mixture gave after crystallisation from ethanol 80–85% yield of the demethylated product (IIIf). On the other hand, treatment of the tertiary amine (IIIa) with hot performic acid gave only the *N*-oxide (IIId) m.p. 108–110°.

The insoluble yellow product C₁₆H₁₈N₄O₈ was shown to be the amino-peroxide (IVa). It contained one active oxygen per mole as shown iodometrically with sodium iodide/perchloric acid reagent and showed the characteristic absorption for peroxides in its infrared spectrum [ν_{\max} (KBr) 960 cm.⁻¹ (v.s.)]. Horner and Knapp⁵ have shown that treatment of *N*-methylaniline with formaldehyde and hydrogen peroxide yields the peroxide (IVb). We found that *p*-nitro-*N*-methylaniline (IIIb) gave the peroxide (IVa) in high yield when treated with the same reagents in hot ethanolic solution. Furthermore the properties that Horner⁵ described for the peroxide (IVb) are also shown by our ozonation product. Thus, refluxing the peroxide for one minute in triethyl phosphite^{5,6} gave the ether (Va), m.p. 177–178°. This ether decomposed at its m.p. to yield formaldehyde and the amine (Vb) m.p. 276–278°, which could be synthesised by action of formaldehyde on *p*-nitro-*N*-methylaniline (IIIb). Also, heating of the peroxide (IVa) at 150° caused decomposition to the formyl derivative (IIIc),⁵ while treatment with cold acid gave the amine (IIIb).⁵

The initial attack of ozone on aliphatic tertiary amines is considered to take place at the nitrogen atom.² We believe that this is also the case with (IIIa) since the ozonation of a comparable amide (IIIe) is much slower and not quantitative.* The primary adduct (VI) can then rearrange in the

* cf. D. H. R. Barton, L. D. S. Godinho, and J. K. Sutherland, *J. Chem. Soc.*, 1965, 1779.

³ V. Villiger, *Ber.*, 1909, **42**, 3534.

⁴ O. Meth-Cohn, unpublished results.

⁵ L. Horner and K. H. Knapp, *Annalen*, 1959, **622**, 79.

⁶ (a) L. Horner and W. Jurgeleit, *Annalen*, 1955, **591**, 138. (b) C. Walling and R. Rabinowitz, *J. Amer. Chem. Soc.*, 1959, **81**, 1243.

manner of a Polonovski reaction⁷ to give a carbinolamine (III_f). This view is supported by the work of Henbest and Stratford⁸ who demonstrated the formation of a carbinolamine in the ozonation of tri-*n*-butylamine. A feasible route to the peroxide (IV_a), following the well established method of Rieche,⁹ is condensation of the hydroperoxide (III_g) with the carbinolamine (III_f). The possible formation of such a hydroperoxide from the initial

adduct (VI) is under investigation. That the formation of the peroxide (IV_a) is not a result of autoxidation¹⁰ of the tertiary amine (III_a) is indicated by the fact that we obtained essentially the same yields of ozonation products by use of oxygen-free ozone. The formyl derivative (III_c) can then be formed by the known dehydration of the hydroperoxide (III_g).

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⁷ R. Huisgen, F. Bayerlein, and W. Heydkamp, *Chem., Ber.*, 1959, **92**, 3223.

⁸ H. B. Henbest and M. J. W. Stratford, *J. Chem. Soc.*, 1964, 711.

⁹ A. Rieche, E. Schmitz, and E. Beyer, *Chem. Ber.*, 1959, **92**, 1206.

¹⁰ L. Horner and H. Junkermann, *Annalen*, 1955, **591**, 53.