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

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IT has been suggested[1] 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 shown[2]

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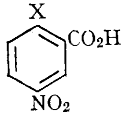
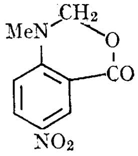
[1] O. Meth-Cohn and H. Suschitzky, *J. Chem. Soc.*, 1963, 4666.
[2] P. S. Bailey, *Chem. Rev.*, 1958, **58**, 977 and references cited therein.

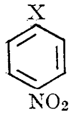
to give good yields of *N*-oxides when ozonised, we hoped to isolate the postulated intermediate (II) of the above reaction by ozonation of the tertiary amine (Ia).



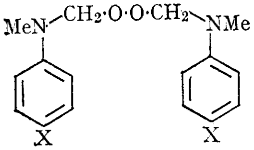
(I) a, X=NMe$_2$
b, X=NHMe
c, X=NMe$_2$·O



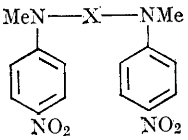
(II)



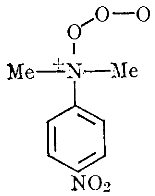
(III)
a, X=NMe$_2$
b, X=NHMe
c, X=NMeCHO
d, X=NMe$_2$·O
e, X=CONMe$_2$
f, X=NMeCH$_2$OH
g, X=NMeCH$_2$OOH



(IV)
a, X=NO$_2$
b, X=H



(V)
a, X=CH$_2$OCH$_2$
b, X=CH$_2$



(VI)

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°, $C_{16}H_{18}N_4O_6$ (37—46%), *N*-formyl-*N*-methyl-*p*-nitroaniline (IIIc) m.p. 116—117°, *N*-methyl-*p*-nitroaniline (IIIb) and some starting material (8—10%). Acid hydrolysis of the crude mixture gave after crystallisation from ethanol 80—85% yield of the demethylated product (IIIb). 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 $C_{16}H_{18}N_4O_6$ 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 Knapp[5] 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 Horner[5] 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

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* *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 reaction[7] to give a carbinolamine (IIIf). This view is supported by the work of Henbest and Stratford[8] who demonstrated the formation of a carbinolamine in the ozonation of tri-n-butylamine. A feasible route to the peroxide (IVa), following the well established method of Rieche,[9] is condensation of the hydroperoxide (IIIg) with the carbinolamine (IIIf). The possible formation of such a hydroperoxide from the initial adduct (VI) is under investigation. That the formation of the peroxide (IVa) is not a result of autoxidation[10] of the tertiary amine (IIIa) is indicated by the fact that we obtained essentially the same yields of ozonation products by use of oxygen-free ozone. The formyl derivative (IIIc) can then be formed by the known dehydration of the hydroperoxide (IIIg).

(*Received, August* 13*th*, 1965; *Com.* 508.)

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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.