Amine Oxidation. Part XII.¹ Reactions of Some NN-Dimethylbenzylamine N-Oxides with Acetic Anhydride and of Some N-Acetoxy-NNdimethylbenzylammonium Perchlorates with Acetate Ion. The Polonovski Reaction

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The reactions of acetic anhydride with NN-dimethylbenzylamine N-oxide and five of its substituted derivatives (the Polonovski reaction) to give NN-dimethylacetamide, an N-benzyl-N-methylacetamide, and a benzaldehyde have been studied by use of n.m.r. and g.l.c. The effect of the substituents on the relative proportions of debenzylation and demethylation is discussed in terms of a variable transition state in the product-determining step for debenzylation : with an electron-donating group, such as 4-OMe, it is iminium ion-like whereas with the electron-withdrawing 4-NO₂ it has carbanionic character. The preparations of N-acetoxy-NN-dimethylbenzylammonium perchlorate and its 4-Cl and 4-NO2 derivatives are described. The thermal stability of these salts and their reactions with acetate ion are reported. These data agree with an N-acetoxyammonium ion being the first intermediate in the Polonovski reaction, and with the overall conversion of this ion into acetamides being an ionic process induced by acetate ion. No evidence for any radical intermediates was obtained.

THE reactions of pyridine and alkylpyridine N-oxides with acetic anhydride have been thoroughly studied, and convincing evidence for both ionic and radical

reaction³) the generally accepted mechanism is the sequence of ionic processes [illustrated for an NNdimethylbenzylamine N-oxide in reactions (i)-(ix)]

TABLE 1

Yields (% based on N-oxide) of products from the reactions of some substituted NN-dimethylbenzylamine N-oxides with acetic anhydride

$\begin{array}{l} Substrate \\ C_6H_4 \cdot CH_2 \cdot N^+ (O^-)Me_2 \end{array}$	Products			Ratio of Me _s NAc to
	Me,NAc	XC ₆ H ₄ ·CH ₂ ·NMeAc	хс₅н₄∙сно	$XC_{6}H_{4} \cdot CH_{2} \cdot NMeAc$
x	-		• •	·
4-MeO *	73.7	17.6		4.2
4 -MeO †	49.4	24.4	58.7	2.0
4-Me *	66.7	13.4		5.0
H *	70.7	23.1		3.1
H†	82.4	28.4	82.4	2.9
4-C1 *	78.0	12.0		6.5
4-Cl †	76.1	11.2	74.2	6.8
3-CF's *	76.7	12.6		6.1
4-NO, *	45.7	7.1		6.4
4-NO ² †	32.8	4.8		6.8

* Yields measured by ¹H n.m.r. † Yields measured by g.l.c.

TABLE 2

Yields (% based on N-acetoxyammonium salt) of acetamides from the reactions of some substituted N-acetoxy-NNdimethylbenzylammonium perchlorates with acetate ion

Substrate XC ₆ H ₄ •CH ₂ •N+(OAc)Me ₂	Solvent	Products			Ratio of Me _s NAc to
		Me_2NAc	XC ₆ H ₄ ·CH ₂ ·NMeAc	Total	XC ₆ H ₄ ·CH ₂ ·NMeAc
X					
H *	HOAc	28.7	7.9	36.6	3.6
Н†	HOAc	33.3	11.9	45.2	2.8
Н¥	Ac ₂ O	76.1	25.0	101.1	3.1
4-Cl *	Ac ₂ O	72.9	19.2	92.1	3.8
4- NO ₂ *	Ac_2O	90.6	17.1	107.7	5.3
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* Yields measured by ¹H n.m.r. † Yields measured by g.l.c.

mechanisms has been obtained.² For the corresponding reaction of aliphatic tertiary amine N-oxides (Polonovski

¹ Part XI, J. R. Lindsay Smith and L. A. V. Mead, J.C.S.

¹ Part XI, J. R. Lindsay Smith and L. A. V. Meau, J.C.S. Perkin II, 1976, 1172. ² (a) T. Koenig, J. Amer. Chem. Soc., 1966, **88**, 4045; (b) V. J. Traynelis in, 'Mechanisms of Molecular Migrations,' vol. II, ed. B. S. Thyagarajan, Interscience, New York, 1969, p. 1; (c) H. Iwamura, M. Iwamura, T. Nishida, and S. Sato, J. Amer. Chem. Soc., 1970, **92**, 7474; (d) H. Iwamura, M. Iwamura, T. Nishida, and I. Miura, Tetrahedron Letters, 1970, 3117; (e) T. Cohen and

proposed by Huisgen and his co-workers,⁴ although this is less well established.

G. L. Deets, J. Amer. Chem. Soc., 1972, 94, 932; (f) V. J. Tray-nelis, K. Yamauchi, and J. P. Kimball, *ibid.*, 1974, 96, 7289; (g) V. J. Traynelis, J. P. Kimball, and K. Yamauchi, J. Org. Chem., 1975, 40, 1313.

⁸ M. Polonovski and M. Polonovski, Compt. rend., 1927, 184, 331; Bull. Soc. chim. France, 1927, 41, 1190.
 ⁴ R. Huisgen, F. Bayerlein, and W. Heydkamp, Chem. Ber.,

1959, **92**, 3223.

Alternative routes involving radical 5 and ylide 6 intermediates, such as (8) and (9), have also been proposed.

We report here, as an extension of our earlier studies,⁷ the reactions of some ring-substituted NN-dimethylbenzylamine N-oxides with acetic anhydride, and the treated with a large excess of acetic anhydride, and the yields of the products were estimated by ¹H n.m.r. spectroscopy (mesitylene as internal standard). With four of the reactions the yields were also measured by g.l.c (mesitylene, bibenzyl, or 4-nitrobiphenyl as standard). These yields and the ratio of debenzylation

(1) +
$$B^- \longrightarrow ArCH_2NMe + BH + AcO^-$$
 (iii)
(3) ||
CH₂

$$\begin{array}{cccc} (3) + AcO^{-} & & ArCH_2 \cdot NMe & (v) \\ (5) & & | \\ CH_2 \cdot OAc & \end{array}$$

$$(4) + Ac_2O \longrightarrow ArCH \longrightarrow NMe_2 + AcO^- (vi)$$

$$(5) OAc Ac$$

(5) +
$$Ac_2O$$
 \longrightarrow $ArCH_2 \cdot NMeAc + AcO^- (vii)
(7) $|$
 $CH_2 \cdot OAc$$

(6) +
$$AcO^ \rightarrow$$
 ArCHO + Me_2NAc + Ac_2O (viii)

synthesis and reactions of some N-acetoxy-NN-dimethylbenzylammonium perchlorates.

RESULTS

Reactions of Substituted NN-Dimethylbenzylamine N-Oxides.—Six NN-dimethylbenzylarnine N-oxides were

⁵ J. C. Craig, F. P. Dwyer, A. N. Glazer, and E. C. Horning, J. Amer. Chem. Soc., 1961, 83, 1871. to demethylation are recorded in Table 1. The total yield of the two amides in each reaction accounted for >89% of the N-oxide substrate, except in the reactions of 4,NN-trimethylbenzylamine N-oxide and NN-dimethyl-4-nitrobenzylamine N-oxide. In the last reaction, although the aromatic proton signals of the products account for 105% of the starting N-oxide and there are no unaccounted-for absorbances, the combined amide yield is ca. 50%.

¹H N.m.r. spectra recorded during the reactions all ⁶ Y. Hayashi, Y. Nagano, S. Hongyo, and K. Teramura, *Tetrahedron Letters*, 1974, 1299.

⁷ P. A. Bather, J. R. Lindsay Smith, and R. O. C. Norman, J. Chem. Soc. (C), 1971, 3060.

contained significant absorptions attributable to the intermediates (2)—(7). In the reaction of NN-dimethyl-4-nitrobenzylamine N-oxide the addition of water converted the intermediates, probably a mixture of (4) and (6), rapidly and quantitatively into 4-nitrobenzaldehyde and dimethylacetamide. The amount of intermediates in the reaction mixtures when the product yields were measured was always <5%, except in the reaction of 4,NN-trimethylbenzylamine N-oxide, where the intermediates accounted for *ca.* 10% of the product.

In none of the n.m.r. spectra recorded during these reactions was there any evidence of CIDNP-enhanced absorption or emission signals.

Synthesis and Reactions of Substituted N-Acetoxy-NN*dimethylbenzylammonium Perchlorates.*—Three crystalline N-acetoxy-NN-dimethylbenzylammonium perchlorates were prepared either by treatment of a solution of the corresponding N-oxide in saturated aqueous sodium perchlorate with acetic anhydride or by addition of silver perchlorate and acetyl chloride in acetonitrile to a solution of the N-oxide in acetonitrile. Solutions of these salts are stable in the absence of strong nucleophiles or bases. Thus the n.m.r. spectrum of N-acetoxy-NNdimethylbenzylammonium perchlorate in dry acetic acid, acetic anhydride, or acetonitrile remains almost unchanged after being heated at 80 °C, whereas the addition of water to a solution in acetonitrile rapidly converts it into the N-oxide hydroperchlorate and acetic acid. Acetate ion reacts with these salts in acetic acid to give the corresponding N-oxide and N-benzyl-Nmethylacetamide, NN-dimethylacetamide, and benzaldehyde, the Polonovski products; with acetic anhydride as solvent only the Polonovski products are obtained (Table 2). Absorptions attributable to intermediates were only observed in the n.m.r. spectra of the reactions in acetic anhydride.

G.l.c.-mass spectrometric analysis of the reaction of N-acetoxy-NN-dimethylbenzylammonium perchlorate with acetate ion in acetic [²H]acid showed that neither the benzaldehyde nor the N-benzyl-N-methylacetamide had incorporated any deuterium.

DISCUSSION

Our results are in general agreement with the scheme of ionic reactions (i)—(ix) and give no indication of any radical processes.

the NN-dimethylbenzylamine N-oxide, and that the Polonovski reaction with acetate ion acting as a base [reactions (ii) and (iii)] is in competition with this. The dual nature of acetate in these reactions was observed by Huisgen and Kolbeck,⁸ who examined the reactions of a selection of N-acyloxy-derivatives of bridgehead amines. Changing the solvent to acetic anhydride results in a quantitative conversion of the N-acetoxyammonium perchlorate into Polonovski reaction products; presumably any N-oxide formed by the reverse of reaction (i) is reconverted into the N-acetoxyderivative by the excess of acetic anhydride. With water in the absence of acetate ion the N-acetoxyammonium perchlorates are hydrolysed to the corresponding N-oxides by nucleophilic attack.

A comparison of the reactions of the N-acetoxy-NNdimethylbenzylammonium perchlorates with acetate ion in acetic acid or acetic anhydride with those of the parent N-oxides with acetic anhydride shows the great similarity of the distribution of Polonovski reaction products from the three systems. These results confirm, as is generally accepted, that N-acetoxyammonium ions are intermediates in the Polonovski reaction.⁸

The thermal stability of N-acetoxy-NN-dimethylbenzylammonium perchlorate in the absence of nucleophiles or bases is good evidence against the homolysis ⁹ of acetoxyammonium cations [reaction (x)] or the intramolecular *syn*-elimination [reaction (xi)] being part of the Polonovski reaction.

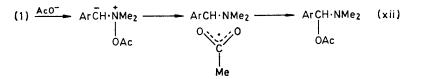
$$Ar CH_2 \cdot \dot{N}Me_2 \longrightarrow Ar CH_2 \cdot \dot{N}Me_2 + AcO \cdot (x)$$

$$OAc$$

$$Ar CH \longrightarrow \dot{N}Me_2 \longrightarrow Ar CH \Longrightarrow \dot{N}Me_2 + AcOH (xi)$$

$$H \longrightarrow O = C - CH_3$$

An alternative radical pathway, the rearrangement of an ylide to an α -amino-ester [reaction (xii)] seems unlikely for two reasons. First, the benzaldehyde obtained from the reaction of N-acetoxy-NN-dimethylbenzylammonium perchlorate with acetate ion in acetic [²H]acid contained no deuterium; some incorporation into the aldehyde would have been anticipated if an



The results of the reactions of acetate ion with the N-acetoxyammonium perchlorates in acetic acid reveal that the predominant process involves acetate ion acting as a nucleophile [reverse of reaction (i)] to give

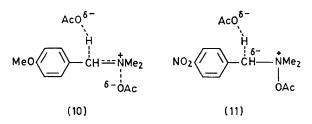
⁸ R. Huisgen and W. Kolbeck, Tetrahedron Letters, 1965, 783.

ylide is formed in this reaction. Secondly, no CIDNP signals were observed in the n.m.r. spectra recorded during the reactions. It is noteworthy that in the Meisenheimer and Stevens rearrangements the analogous radical-pair mechanism has been substantiated by the observation of emission signals in the ¹H n.m.r. spectra

⁹ T. Sato and T. Otsu, Chem. and Ind., 1970, 125.

of the reactions,^{10,11} and CIDNP signals have been observed in the reaction of 4-methylpyridine N-oxide with acetic anhydride.^{2c, g}

The product distributions from the Polonovski reactions of the NN-dimethylbenzylamine N-oxides throw light on the nature of the transition states for reactions (ii) and (iii), for whereas the rate of the former process should be influenced by substituents on the aromatic ring, the rate of the latter should be relatively unaffected. The results, which are qualitatively similar to those we reported previously,⁷ reveal that with all the reactants there is a marked preference for debenzylation over demethylation and that substituents, be they electronwithdrawing or -donating, increase this preference. By analogy with the variable transition-state concept in E2processes,¹² it is likely that the elimination step is concerted and that the transition-state changes from being iminium ion-like, with extensive C-H and N-O bond cleavage (10), with electron-donating substituents, through to being ylide-like, with extensive C-H cleavage and carbanionic character (11), with electron-withdrawing substituents. However, even in the reaction of NN-dimethyl-4-nitrobenzylamine N-oxide there is no evidence for a two-step elimination via an ylide. The intermediate we observed by n.m.r. spectroscopy in this reaction, which we initially suspected might be an ylide, on addition of water gave dimethylacetamide and not the substrate or parent N-oxide, suggesting that a likely structure for this species is (4), or that it is a mixture of (4) and (6).



EXPERIMENTAL

¹H N.m.r. spectra were measured with Varian A60 and Perkin-Elmer R10 (60 MHz) spectrometers. Mass spectra were measured with an A.E.I. MS12 spectrometer. G.l.c. analysis was carried out by use of a Pye Series 104 chromatograph with a flame ionisation detector.

Materials.-Acetic acid was dried by refluxing with acetic anhydride (10% v/v) and purified by fractional distillation. Acetic [2H]acid was prepared from acetic anhydride and deuterium oxide. Laboratory grade acetonitrile was purified by distillation from phosphorus(v) oxide. Sodium perchlorate was of AnalaR grade. Silver perchlorate, acetyl chloride, mesitylene, and bibenzyl were laboratory grade reagents. The NN-dimethylbenzylamine N-oxides were prepared from the parent NN-dimethylbenzylamines 13 by the procedure described previously for NN-dimethylphenethylamine N-oxides.7 Solutions of the N-oxides in acetonitrile were dried overnight over molecular

sieves (type 4A). Filtration and removal of solvent gave the materials which were used in this study. The substituted N-benzyl-N-methylacetamides (XC₆H₄·CH₂·NMeAc) which were prepared from the corresponding secondary amines with acetic anhydride had the following ¹H n.m.r. absorptions (τ values; solvent acetic anhydride): X = H, 2.73 (5 H, s), 5.44 (2 H, s), and 7.10 and 7.14 (3 H, 2s); X = 4-Me, 2.89 (4 H, s), 5.50 (2 H, s), 7.12 and 7.16 (3 H, 2s), and 7.70 (3 H, s); X = 4-MeO, 2.97 (4 H, m), 5.51 (3 H, s), 6.23 (3 H, s), and 7.11 and 7.15 (3 H, 2s); X =4-Cl, 2.71 (4 H, m), 5.44 (2 H, s), and 7.07 and 7.14 (3 H, 2s); $X = 4-NO_2$, 2.17 (4 H, m), 5.32 (2 H, s), and 6.99 and 7.10 (3 H, 2s); X = 3-CF₃, 2.44 (4 H, s), 5.33 (2 H, s), and 7.00 and 7.09 (3 H, 2s). N-Acetoxy-NN-dimethylbenzylammonium perchlorate was prepared by vigorously shaking a solution of the N-oxide (3 g) in saturated aqueous sodium perchlorate (50 cm³) at 0 °C for 1 h with acetic anhydride (5 cm³). The acetoxyammonium perchlorate (2.8 g) precipitated from this solution and had m.p. 103- 105° (from methanol), τ (CD_3CN) 2.40 (5 H, m), 4.87 (2 H, s), 6.20 (6 H, s), and 7.77 (3 H, s) (Found: C, 45.0; H, 5.5; N, 4.75. C₁₁H₁₆ClNO₆ requires C, 45.0; H, 5.5; N, 4.8%). N-Acetoxy-NN-dimethyl-4-chlorobenzylammonium and -4-nitrobenzylammonium perchlorates, which could not be prepared by the above procedure, were obtained in low yield by adding a solution of silver perchlorate (1 equiv.) and acetyl chloride (1.5 equiv.) in the minimum quantity of acetonitrile to a solution of the N-oxide (1 g) in the same solvent (20 cm³) at 0 °C. After 20 min the mixture was warmed to room temperature and filtered; the filtrate was concentrated under vacuum and the residual oil was washed with ether. The 4-nitrobenzylammonium salt (0.22 g) separated from the oil and had m.p. 150.5-152.5°, τ (CD₃CN) 1.88 (4 H, m), 4.72 (2 H, s), 6.10 (6 H, s), and 7.72 (3 H, s) (Found: C, 39.0; H, 4.3; N, 8.4. C₁₁H₁₅ClN₂O₈ requires C, 39.1; H, 4.5; N, 8.3%). The residual oil containing the 4-chlorobenzylammonium salt was dissolved in methanol and the product (0.52 g, 15%) was precipitated by slow addition of ether; m.p. 110-113°, τ (CD₃CN) 2.42br (4 H, s), 4.87 (2 H, s), 6.20 (6 H s), and 7.77 (3 H, s) (Found: C, 40.1; H, 4.5; N, 4.3. C₁₁H₁₅Cl₂NO₆ requires C, 40.3; H, 4.6; N, 4.3%).

Reactions of N-Oxides.--The N-oxide (ca. 0.1 g) and an internal standard [mesitylene (ca. 60 mg) or bibenzyl (ca. 25 mg)] were accurately weighed out and cooled to -78 °C before acetic anhydride (0.5 cm³) previously cooled to -78 °C was added. The mixture was allowed to warm to room temperature before its n.m.r. spectrum was recorded. It was then heated (100 °C) for ca. 1 h, and its n.m.r. spectrum was recorded again. The yields of products were calculated with reference to the internal standard. Some of the reaction mixtures were analysed by g.l.c. The small amounts (<1%) of tertiary amine detected in the g.l.c. analyses of some experiments were not estimated.

Reactions of N-Acetoxy-NN-dimethylbenzylammonium Perchlorates.-The acetoxyammonium perchlorate (80-100 mg) and mesitylene (35-50 mg) were accurately weighed out and dissolved in the solvent (0.5 cm³) (acetic

¹¹ (a) U. Schöllkopf, U. Ludwig, G. Ostermann, and M. Patsch, Tetrahedron Letters, 1969, 3415; (b) R. W. Jemison, S. Mages-waran, W. D. Ollis, S. E. Potter, A. J. Pretty, I. O. Sutherland, and Y. Thebtaranonth, Chem. Comm., 1970, 1201.

 R. A. More O'Ferrall, J. Chem. Soc. (B), 1970, 274.
 J. R. Lindsay Smith and D. Masheder, J.C.S. Perkin II, 1976, 47.

¹⁰ (a) A. R. Lepley, P. M. Cook, and G. F. Willard, J. Amer. Chem. Soc., 1970, 92, 1101; (b) G. Ostermann and U. Schöllkopf, Annalen, 1970, 737, 170.

acid, acetic [2 H]acid, acetic anhydride, or acetonitrile). The n.m.r. spectrum of the solution was recorded and shown to remain unchanged even after heating at 80 °C for 4 h (acetic anhydride solutions were only heated at 80 °C for *ca.* 10 min). The addition of water or sodium acetate followed by warming rapidly converted the salts into

products which were analysed by n.m.r. spectroscopy and g.l.c.

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