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Aryl Migration in the Meisenheimer Rearrangement

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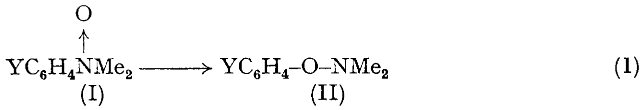
Summary Migration of the benzene ring from nitrogen to oxygen in tertiary amine oxides is reported, and the mechanism is proposed as a concerted intramolecular cyclic process.

THE Meisenheimer rearrangement involves the migration of a group from nitrogen to oxygen in tertiary amine oxides having no β-hydrogen atom[1,2] ($R^1R^2R^3N\rightarrow O$ to $R^2R^3NOR^1$). Allyl,[3] benzyl,[4–7] neopentyl,[8] and homoadamantyl[9] are the only groups known to migrate in this thermal rearrangement and to our knowledge the migration of an aryl group has not been reported. We now report the first example of aryl migration from N to O in substituted dimethylaniline oxides. Some dimethylaniline oxides substituted with electron-withdrawing groups undergo ready thermal rearrangement yielding trisubstituted hydroxylamines in high yields as indicated by n.m.r. and t.l.c. analyses and hydrolysis [equation (1)]. Unsubstituted dimethylaniline oxide does not undergo rearrangement even at elevated temperatures, and dimethylaniline oxides with electron-donating substituents on heating show no tendency to undergo rearrangement although small amounts (*ca.* 5—7%) of tertiary amines are formed owing to thermal deoxygenation.[10] Thus electron-withdrawing substituents have an important effect on the course of rearrangement.

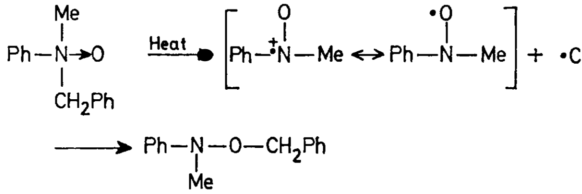


$$\underset{\text{(I)}}{YC_6H_4\overset{\overset{O}{\uparrow}}{N}Me_2} \longrightarrow \underset{\text{(II)}}{YC_6H_4\text{–}O\text{–}NMe_2} \qquad (1)$$

Y	% Yield[a] of (II)	Y	% Yield[a] of (II)
a; *p*-NO_2	96	d; *p*-PhCO	20
b; *p*-CN	75	e; *m*-NO_2	0
c; *o*-NO_2	55		

[a] Yields are for reaction for 1·5 h in refluxing dioxan.

Although the mechanism of the Meisenheimer rearrangement has been a subject of much controversy,[4–8] it is now generally accepted that migration of the benzyl group in the rearrangement of benzyldimethylamine oxide[5] and benzylmethylaniline oxide[4,6] occurs by homolytic C–N bond cleavage with the formation of free-radical intermediates [equation (2)]. Further, neopentyl[8] and homoadamantyl[9] groups also migrate *via* free radicals during thermolysis of their *N*-oxides. However, the migration of the aryl group from N to O in the thermal rearrangements reported now does not fit this radical mechanism.



(2)

The kinetics of the thermal isomerization of (Ia) in nitrobenzene have been studied, and the Arrhenius activation parameters have been calculated. The rate of rearrangement was followed by monitoring the intensity of the two singlets at δ 3·7 and 2·8 for the NMe_2 groups in the n.m.r. spectra of the *N*-oxide and the rearranged product respectively. The rate was followed (duplicate runs) up to 90% completion at 50, 60, and 70 °C. Good first-order kinetics were observed, giving rate constants at these temperatures of 2·89 ±

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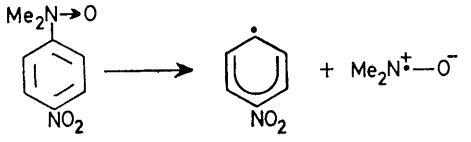
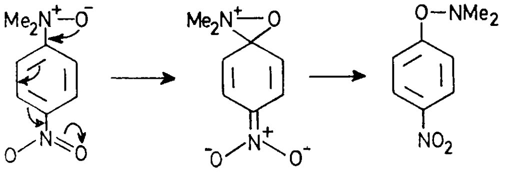
$0{\cdot}014 \times 10^{-4}$, $8{\cdot}80 \pm 0{\cdot}027 \times 10^{-4}$, and $22{\cdot}0 \pm 0{\cdot}57 \times 10^{-4}\,s^{-1}$, respectively. An Arrhenius plot gave a good straight line leading to the activation parameters E_a 22·39 kcal mol^{-1}, $\Delta H^{\ddagger}$ 21·72 kcal mol^{-1}, and $\Delta S^{\ddagger}$ $-7{\cdot}57$ cal K^{-1} mol^{-1}.

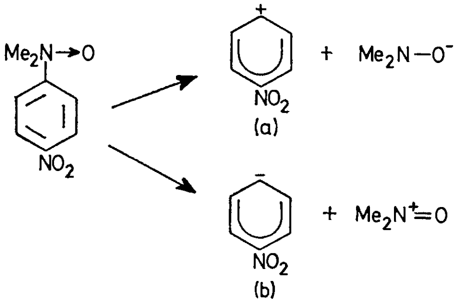
The negative value of the entropy of activation is strong evidence against dissociation into radicals [equation (3)]


(3)

since dissociation into neutral particles should show a positive $\Delta S^{\ddagger}$ value.[11] Indeed Schollkopf *et al.*[6] and Shulman *et al.*[5] have both taken a positive $\Delta S^{\ddagger}$ value to indicate a radical mechanism in the rearrangement of *N*-benzyl-*N*-methylaniline oxide and benzyldimethylamine oxide, respectively. Moreover, phenyl radicals are generally much less stable than benzyl radicals. From our present results we propose that the rearrangement of *p*-nitrodimethylaniline oxide proceeds by a concerted intramolecular cyclic mechanism (S_Ni) [equation (4)]. The negative entropy of activation indicates that the transition state has a rigid structure with far fewer degrees of freedom compared to the reactant, in agreement with the cyclic mechanism.


(4)

For the rearrangement to occur the electron-withdrawing group must be *ortho* or *para* relative to the N → O function. This is reasonable since only in these positions can the NO_2 group delocalize the incoming negative charge carried by the attacking oxygen. Another mechanistic possibility involves heterolytic dissociation into the charged species (a) or (b).



Dissociation into (a) can be ruled out since species (a) would be of extremely high energy, and dissociation into (b) can also be excluded since it cannot explain the lack of rearrangement of the *meta*-nitro-compound. The anion (b) can only be stabilized through inductive effects since conjugative effects are not possible, and so the *meta*-nitro group would be more effective than the *para*-nitro group in stabilizing the intermediate (b) through inductive effects.

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[1] J. Meisenheimer, *Ber.*, 1919, **52**, 1667.
[2] J. Meisenheimer, *Ber.*, 1922, **55**, 513.
[3] R. F. Kleinschmidt and A. C. Cope, *J. Amer. Chem. Soc.*, 1944, **66**, 1929.
[4] U. Schollkopf, M. Patsch, and H. Schafer, *Tetrahedron Letters*, 1964, **36**, 2515.
[5] G. P. Shulman, P. Ellgen, and M. Connor, *Canad. J. Chem.*, 1965, **43**, 3459.
[6] U. Schollkopf, U. Ludwing, M. Patsch, and W. Franken, *Ann. Chem.*, 1967, **77**, 703.
[7] J. P. Lorand, R. W. Grant, and R. W. Wallace, *J. Org. Chem.*, 1973, **38**, 1813.
[8] J. I. Brauman and W. A. Sanderson, *Tetrahedron*, 1967, **23**, 37.
[9] B. L. Adams, and P. Kovacic, *J. Amer. Chem. Soc.*, 1974, **96**, 7014.
[10] T. Y. Ahmed, M.Sc. Thesis, University of Mosul, 1975; L. I. Jallo, M.Sc. Thesis, University of Mosul, 1976.
[11] E. S. Gould, 'Mechanism and Structure in Organic Chemistry,' Holt, New York, 1959, p. 182.