Tetrahedron. 1967. Vol. 23. pp. 37 to 44. Pergamon Press Ltd. Printed in Northern Ireland

REARRANGEMENT OF A NEOPENTYLAMINE OXIDE[1]

J. I. BRAUMAN and W. A. SANDERSON
Department of Chemistry, Stanford University, Stanford, California 94305

(*Received in U.S.A.* 19 *March* 1966; *accepted for publication* 7 *July* 1966)

Abstract—Dimethylneopentylamine oxide when pyrolyzed produces neopentane and dimethylneopentoxyamine. The product ratios and amounts provide evidence regarding the nature of the reaction; the rates of decomposition allow an estimate of ca. 32 kcal/mole for the energy of the primary carbon-nitrogen bond in aliphatic amine oxide.

INTRODUCTION

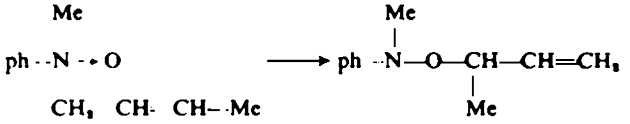
THE thermal decomposition of tertiary amine oxides (I) has been extensively studied.[2] For amine oxides when R_1 is allylic or benzylic, the Meisenheimer rearrangement

$$\underset{\mathrm{I}}{R_1R_2R_3N \rightarrow O}$$

occurs, yielding an alkoxyamine, Eq 1.[3] This N to O migration is achieved readily,

$$R_1R_2R_3N \rightarrow O \longrightarrow R_2R_3N{-}O{-}R_1 \qquad (1)$$

and has been studied, for example, as a device for ring expansion.[4] In the case where R_1 is allylic, the reaction has been shown to be intramolecular, presumably with a five-center transition state,[5] Eq 2



$$\begin{array}{c}\mathrm{Me}\\ \mathrm{ph{-}N{\to}O}\\ \mathrm{CH_2\ \ CH{-}\ CH{-}Me}\end{array} \longrightarrow \mathrm{ph{-}\overset{\displaystyle Me}{N}{-}O{-}\underset{\displaystyle Me}{CH}{-}CH{=}CH_2} \qquad (2)$$

Although such a mechanism is not possible when R_1 is benzylic, the reaction nevertheless is still intramolecular and proceeds at a reasonable rate.[6] The relative rates of rearrangement of a number of substituted benzyldimethylamine oxides have been measured and $\rho \sim 1{\cdot}6$ was found for this reaction.[7] These authors also found that the optically active α-*d*-benzyl group racemizes to an extent of about 70% during rearrangement,[7] which they interpreted as being consistent with a radical reaction.

The present study of the pyrolysis of *dimethylneopentylamine oxide* (I, R_1 = neopentyl, $R_2 = R_3$ = methyl) was undertaken for two reasons. First, it was

---

[1] We gratefully acknowledge support in part by the National Science Foundation (NSF-GP-3888) and the National Institutes of Health of the U.S. Public Health Service (GM-5248).

[2] A. C. Cope and E. R. Trumbull, *Org. Reactions* **11**, 317 (1960).

[3] J. Meisenheimer, *Chem. Ber.* **52**, 1667 (1919); J. Meisenheimer, H. Greeske and A. Willmersdorf, *Ibid.* **55**, 513 (1922).

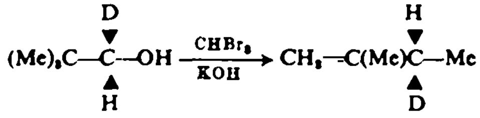
[4] L. D. Quin and F. A. Shelburne, *J. Org. Chem.* **30**, 3135 (1965).

[5] R. F. Kleinschmidt and A. C. Cope, *J. Amer. Chem. Soc.* **66**, 1929 (1944).

[6] A. H. Wragg, T. S. Stevens and D. M. Ostle, *J. Soc. Chem.* 4057 (1958).

[7] U. Schöllkopf, M. Patsch and H. Schäfer, *Tetrahedron Letters* 2515 (1964).

anticipated that this decomposition might shed some light on the observation[8] of the extraordinary stereospecific production of optically active 2-methyl-1-butene-3-*d* from active neopentyl-1-*d* alcohol with bromoform and aqueous potassium hydroxide, Eq 3. An "anomalous" amine oxide pyrolysis rearrangement apparently involving a



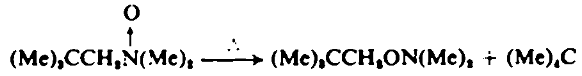
$$(Me)_3C{-}\overset{D}{\underset{H}{C}}{-}OH \xrightarrow[KOH]{CHBr_3} CH_2{=}C(Me)\overset{H}{\underset{D}{C}}{-}Me \qquad (3)$$

concerted abstraction of a γ-hydrogen and β-α hydride migration has been observed,[9] and it seemed possible that such a reaction might serve as a model for the neopentyl alcohol reaction. Second, the decomposition of purely aliphatic amine oxides which cannot produce olefins directly by β-hydrogen abstraction has not been studied.[10] Thus, it was also anticipated that the pathway and products of the decomposition of dimethylneopentylamine oxide would prove helpful in elucidating further the nature of amine oxides and their pyrolytic behavior.

RESULTS

Decompositions were accomplished in two ways: first, as usual, by heating a sample under reduced pressure and trapping the volatile products, and, second, by direct pyrolysis in a Pyrex glass lined inlet of a gas chromatograph.[11,12] With both techniques, the product mixture as analyzed by VPC was the same.

The three major products of the pyrolysis were isolated by preparative VPC and characterized. The first, dimethylneopentylamine, was identical with the precursor of the N-oxide. The second was neopentane as revealed by its NMR and IR spectra. The third was shown to be *dimethylneopentoxyamine* (II) by its NMR,[13] mass spectrum (see later), and elemental analysis. Only a trace of 2-methyl-1-butene was detected.



$$(Me)_3CCH_2\overset{O}{\overset{\uparrow}{N}}(Me)_2 \xrightarrow{\Delta} (Me)_3CCH_2ON(Me)_2 + (Me)_4C$$

II

The decomposition in the VPC inlet was carried out at inlet temperatures varying from 160–350°. When the Pyrex glass insert was treated with silicone oil to minimize surface reactions,[14] no change was observed in the composition or amounts of the products. The ratios of the major products to a standard, 1,2-dimethoxyethane, were measured as a function of the inlet temperature. At the higher temperatures the ratios were constant, falling to zero at the lower temperatures. At the same time, however, the ratio (ca. 6:1) of alkoxyamine to neopentane remained essentially constant over the entire temperature range.

---

[8] W. A. Sanderson and H. S. Mosher, *J. Amer. Chem. Soc.* **83**, 5033 (1961); and, to be published.

[9] A. C. Cope, N. A. LeBel, H. H. Lee and W. R. Moore, *J. Amer. Chem. Soc.* **79**, 4720 (1957).

[10] Y. Hattori, *J. Pharm. Soc. Japan* **60**, 24 (1940); *Chem. Abstr.* **34**, 3387 (1940) has reported that trimethylamine oxide when pyrolyzed gives O,N,N-trimethylhydroxylamine.

[11] J. C. Craig, N. Y. Mary and S. K. Roy, *Analyt. Chem.* **36**, 1142 (1964).

[12] We have also established that, for example, cyclohexene is produced when dimethylcyclohexylamine oxide is subjected to identical treatment.

[13] Starting material and major products showed only zero-order NMR spectra, no spin–spin coupling.

[14] This technique has been demonstrated to inhibit reactions known to occur on glass surfaces, Dr. David M. Golden personal communication.

DISCUSSION

The results of the thermal decomposition experiments are revealing with regard to the pathway of the reaction and consequently to the strength of the C—N bond in amine oxides. The work of Schöllkopf[6] provides evidence that, at least in the case of benzyl compounds, the Meisenheimer rearrangement is a radical process. This is indicated not only by the substituent effects ($\rho \sim 1{\cdot}6$) but also by the production, in some cases, of a stable nitroxide radical.[7] Further, it has previously been demonstrated[6] that the rearrangement is intramolecular since in the mixed decomposition of two amine oxides crossed-over products were not observed.

That the reaction should proceed by a radical pathway is eminently reasonable in view of the known stability of nitroxide radicals. Thus, a number of nitroxide radicals have been synthesized,[15] and it has been demonstrated that such radical moieties are often sufficiently inert not to interfere with chemical reactions carried out on other functional groups in the same molecule.[16] The stability of the nitroxide radical manifests itself in a lowering of the bond dissociation energy of the C—N bond. This, coupled with the additional stabilization of the benzyl radical accounts for the great ease with which the reaction occurs.

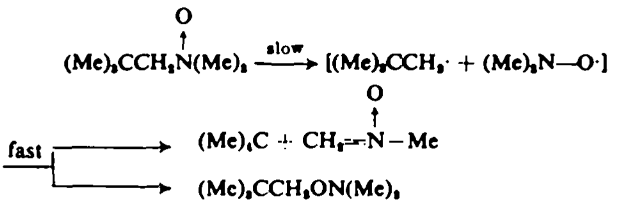
The pyrolysis of dimethylneopentylamine oxide provides significant added information. Since the rearrangement proceeds relatively easily, the added benzylic resonance is not required for the reaction to occur. Thus, when β-hydrogen atoms are present in the molecule, the favored reaction is olefin formation. In the absence of β-hydrogens, the Meisenheimer rearrangement takes place, and this reaction is facile even without benzylic or allylic groups. Consequently, the important factor in the Meisenheimer decomposition is the nitroxide radical stabilization, and the benzylic resonance energy[17] of ca. 12·5 kcal/mole is not of overriding importance. The appearance of neopentane as a major product is also highly suggestive of a radical reaction—the neopentyl radical presumably abstracts a hydrogen atom from some other species. Most important, however, is the constant product ratio of alkoxyamine to neopentane independent of temperature and reaction conditions. This indicates that both these products are formed after the rate determining step and from a common intermediate. Further, it might be expected that if neopentane were formed from neopentyl radicals which had escaped from a cage in solution, the extent of this escape should be greatly dependent upon the reaction conditions. However, the relative amount of neopentane is *not* dependent on the conditions, since the gas phase and solution reactions give the same product ratios. Therefore, it seems reasonable that there are at least two competing radical reactions, Eq 4, and that most of the neopentane is produced from them. Added evidence is the observation that treating the glass surface in order to reduce possible wall reactions has essentially no effect on the rate and products of the reaction. This too, indicates that the products may be formed from a radical pair. Also in support of this pathway is the predominance of N-neopentyl as opposed to N-methyl cleavage. The N-methyl bond is expected to

---

[15] A. K. Hoffmann and A. T. Henderson, *J. Amer. Chem. Soc.* **83**, 4671 (1961); A. K. Hoffmann, W. G. Hodgson and W. H. Jura, *ibid.* **83**, 4675 (1961); A. K. Hoffmann, A. M. Feldman, E. Gelblum and W. G. Hodgson, *ibid.* **86**, 639 (1964); A. K. Hoffman, A. M. Feldman and E. Gelblum, *ibid.* **86**, 646 (1964).

[16] E. G. Rozantzev and L. A. Krinitzkaya, *Tetrahedron* **21**, 491 (1965).

[17] R. Walsh, D. M. Golden and S. W. Benson, *J. Amer. Chem. Soc.* **88**, 650 (1966).



$$(Me)_3CCH_2\overset{O}{\overset{\uparrow}{N}}(Me)_2 \xrightarrow{slow} [(Me)_3CCH_2\cdot + (Me)_2N{-}O\cdot]$$

$$\xrightarrow{fast} (Me)_4C + CH_2{=}\overset{O}{\overset{\uparrow}{N}}{-}Me \qquad (4)$$

$$\xrightarrow{fast} (Me)_3CCH_2ON(Me)_2$$

be somewhat stronger, and this accounts largely for the products observed. However, methoxymethylneopentylamine may well be among the uncharacterized minor products. It is probable that the other expected major product, $CH_2{=}N(Me)O$, is undetected because of its decomposition or long retention on the VPC column.

The lack of a significant amount of olefin in the products of this reaction makes it clear that the pathway involving γ-hydrogen abstraction is not a particularly favorable one. Thus, the amine oxide pyrolysis as a model for the neopentyl alcohol-bromoform-potassium hydroxide reaction is poor.

If the slow step is that postulated in Eq 4, it is possible to estimate the bond strength of the C—N bond in tertiary amine oxides from the decomposition data. We assume that the reaction which takes place in the VPC inlet is a true gas phase pyrolysis. Further, we assume that the materials are vaporized and reach thermal equilibrium immediately. That these assumptions are essentially correct is borne out by the internal consistency of the results obtained. The time during which reaction occurs in the inlet can be estimated. At a constant flow rate of 60 ml/min measured at the outlet (ca. 25°, 1 atm.) a constant mass flow of gas is maintained throughout the column. The velocity of gas passing through the inlet, and thus the residence time in the inlet then depends on the pressure (ca. 4 atm) and temperature (160–350°) there. With an inlet volume of 0·35 ml, the sample remains in the inlet for approximately 0·85 sec at 200°. At lower temperatures the time is slightly longer, and conversely.[18] By making use of an unreactive, co-injected, internal standard, it is possible to measure the relative amount of products formed as a function of the inlet temperature. It was observed that when a mixture of dimethylneopentylamine oxide and dimethoxyethane was injected under varying inlet temperature conditions, the relative areas of alkoxyamine to dimethoxyethane varied from zero below 160° to about 0·8 at 300° and above.[19] The ratios correspond to 0 and 100% reaction respectively. Since the time and extent of reaction are known, an integrated rate constant at each temperature can be determined assuming first-order kinetics:

$$\ln \frac{R_\infty}{R_\infty - R} = kt \tag{5a}$$

$$k = \frac{1}{t} \ln \frac{R_\infty}{R_\infty - R} \tag{5b}$$

where R_∞ is the constant ratio obtained at high temperature and R is the ratio at any given temperature. An Arrhenius plot of log k *vs.* $1/T$ gives the activation energy

---

[18] The authors thank a referee for calling attention to some of the effects of temp and press on residence times. Assuming a constant residence time for all temperatures results in an estimate of E_a about 0·9 kcal/mole lower.

[19] The absolute area of the dimethoxyethane was also roughly constant because the sample size was fairly reproducible, showing that the dimethoxyethane itself was not reacting.

E_a for reaction (4). A least-squares plot (Fig. 1) shows $E_a = 31{\cdot}7 \pm 1{\cdot}8$ kcal/mole, $A = 10^{13{\cdot}6 \pm 0{\cdot}8}\ \mathrm{sec}^{-1}$ (correlation coefficient = 0·994). By analogy with many other radical reactions, this activation energy may be taken as the bond dissociation energy of the C—N bond. The A factor is consistent with such a reaction,[20] particularly considering that the nitroxide radical is highly stabilized and therefore has a relatively constrained geometry.

Although an exact model for such a reaction is not available, it is instructive to compare it with a gas phase rearrangement of a molecule with formal charge to a formally neutral isomer. Schneider and Rabinovitch[21] have studied the rearrangement of methyl isocyanide to acetonitrile, Eq (6).

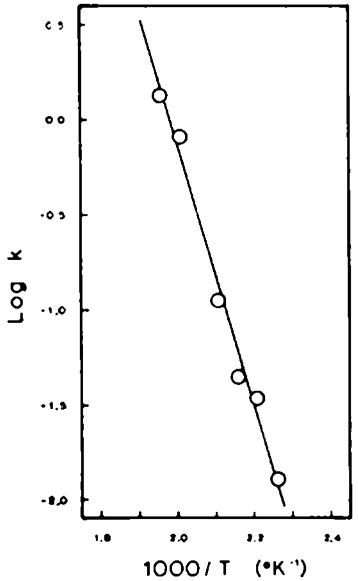


FIG. 1. Arrhenius plot for the thermal decomposition of dimethylneopentylamine oxide.

$$\mathrm{Me}\overset{+}{\mathrm{N}}{\equiv}\overset{-}{\mathrm{C}} \rightarrow \mathrm{MeCN} \tag{6}$$

This reaction has $E_a = 38$ kcal/mole, $A = 10^{13{\cdot}6}\ \mathrm{sec}^{-1}$. Thus, the preexponential factors are similar for the two reactions. The very reasonable value obtained for the A factor in the amine oxide pyrolysis lends support to the value of the activation energy.

It should also be possible to determine the resonance energy of the nitroxide radical. However, it is necessary to know the heats of formation of amine oxides, and these are not readily available. Finally, it must be emphasized that the bond energy in amine oxides estimated by this technique is subject to error and should be used accordingly.

EXPERIMENTAL

Capillary m.ps are uncorrected. IR spectra: Perkin-Elmer 237-B grating spectrophotometer; NMR spectra: by Dr. L. Durham with Varian A-60 and HR-100 spectrometers; Mass spectra: by Mr. R. G. Ross on an A.E.I. MS-9 instrument with both direct and heated inlets; Microanalyses:

---

[20] S. W. Benson and W. B. De More, *Ann. Rev. Phys. Chem.* **16**, 397 (1965).

[21] F. W. Schneider and B. S. Rabinovitch, *J. Amer. Chem. Soc.* **84**, 4215 (1962); **85**, 2365 (1963).

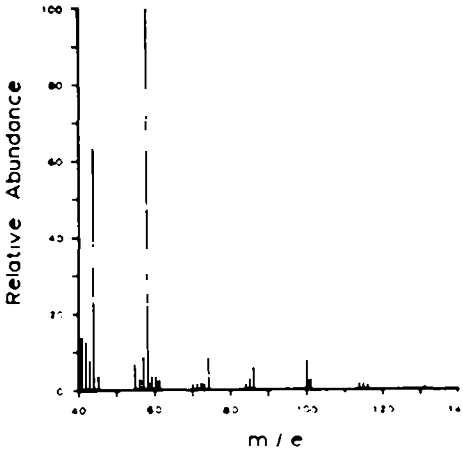


FIG. 2. Mass spectrum of dimethylneopentylamine oxide.

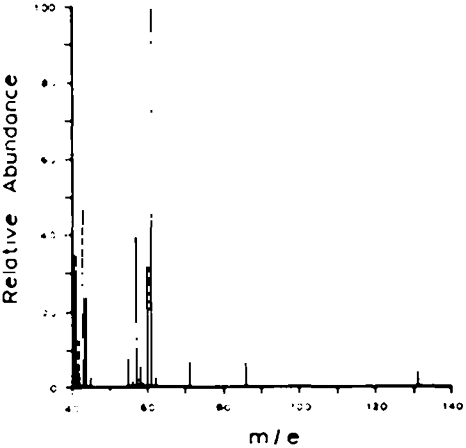


FIG. 3. Mass spectrum of dimethylneopentoxyamine.

by Messrs. E. Meier and J. Consul at the Stanford Microanalytical Laboratory; Gas chromatography: a Wilkens Aerograph A-90-P3 whose injection block was fitted with a Pyrex glass insert; analysis with 20 ft, ¼ in Carbowax 20 M column; preparative work with a 20 ft, ⅜ in FFAP column.

Dimethylneopentylamine oxide. This was prepared[8] by treatment of a methanolic soln of dimethylneopentylamine[12] with 35% H_2O_2 followed by concentration at red. press. The dimethylneopentylamine oxide had IR ν_{max} 960 cm^{-1} (liquid film) characteristic ν_{max} 970–950 cm^{-1}.[13] The NMR (CCl_4) showed τ 8·82 (9 protons), τ 6·90 (2) and τ 6·83 (6) all singlets. For the *picrate* (Found: C, 43·09; H, 5·79; N, 15·83. $C_{13}H_{20}N_4O_8$ requires: C, 43·33; H, 5·60; N, 15·55%.)

Pyrolyses. These were carried out neat in a flask heated under red. press. and connected to Dry-Ice traps. The volatile materials collected in the traps were separated and isolated by preparative VPC. The same products were produced when the amine oxide was injected directly into a heated glass lined inlet of the VPC.[10,11] The three major components were characterized.

A. *Dimethylneopentylamine*. This was identical with the starting material from which the N-oxide was made.

B. *Neopentane*. The structure was confirmed by its NMR (CCl_4) τ 9·08 (singlet) and IR in CCl_4 which was identical with that in the literature.[14]

---

[12] H. C. Brown and W. H. Bonner, *J. Amer. Chem. Soc.*, 75, 14 (1953).

[13] L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*, p. 308. Wiley, New York (1958).

[14] E. R. Shull, T. S. Oakwood and D. H. Rauk, *J. Chem. Phys.* 21, 2024 (1953).

C. *Dimethylneopentoxyamine.* The third major component was shown to be dimethylneopentoxyamine by its NMR (CCl_4) τ 9·13 (9 protons), τ 7·53 (6), τ 6·73 (2), all singlets; mass spectrum mol wt M^+ m/e 131. (Found: C, 63·87; H, 12·95; N, 10·46. $C_7H_{17}NO$ requires: C, 64·07; H, 13·06; N, 10·68%.)

Kinetic studies. The extent of decomposition was followed by VPC by injecting 5 μl. samples of a solution of ca. equal amounts of 1,2-dimethoxyethane and dimethylneopentylamine oxide into the glass lined VPC inlet. The relative areas of neopentane, dimethylneopentoxyamine, and dimethoxyethane were then measured. The absolute area of the dimethoxyethane peak was constant, as were the retention times. This technique was used at different temps, and the results were reproducible. When the glass liner was heated to 200°, quenched in silicone oil, allowed to cool, rinsed with CCl_4 and then replaced in the VPC, no effect was observed on the product composition or amounts.

Mass spectra. The fragmentation behaviour of the isomeric amine oxide and alkoxyamine under electron impact is enlightening with regard to their chemical structures. The amine oxide was introduced directly into the ion source because of its lack of volatility and thermal instability; the thermally stable alkoxyamine was introduced *via* a heated inlet. It might have been expected that the isomeric compounds would fragment to identical products since cleavage to two radicals would appear to be the thermal, non-ionic path of lowest energy. In fact, the products were almost entirely different (Figs 2 and 3), indicating that for the ionized molecules different breakdown occurs. The different mass spectra also indicate that thermal isomerization of the amine oxide did not occur prior to ionization. The products are in complete accord with the parent structures, and application of straightforward electron impact rules for predicting products[15] allows rationalization of the major ions from both isomers.

Table 1 indicates likely structures for some of the amine oxide fragments; Table 2 indicates likely structures for the alkoxyamine fragments.

TABLE 1. AMINE OXIDE FRAGMENTS

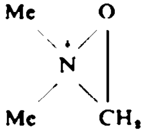
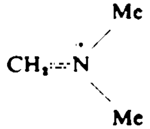
Formula	m/e
$(Me)_3CCH\text{--}\overset{\cdot}{N}\text{--}O$	100
	74
	58

TABLE 2. ALKOXYAMINE FRAGMENTS

Formula	m/e
$(Me)_3CCH\text{—}\dot{O}$	86
$(Me)_2\overset{+}{C}CH_2CH_3$	71
$(Me)_2\overset{+\cdot}{N}OH$	61
$(Me)_2\overset{+}{N}\text{--}O$	60

---

[15] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds*, Holden-Day, San Francisco, Calif. (1964).

Thus, it is clear that the fragments reflect the structures of their precursors. C—N bond cleavage is not a favorable process in the ionized amine oxide. The mass spectra, in conjunction with the elemental analysis and NMR, serve as conclusive structure proofs.

It has been reported[34] that the mass spectra of amine oxides show strong parent and *M*-16 ions (loss of oxygen). We have observed both of these peaks, but their intensities are relatively low. Consequently, these peaks cannot be used specifically as diagnostic for amine oxides.

Acknowledgment—We are indebted to Professor Harry S. Mosher for advice and encouragement and to Professor C. Djerassi and Dr. A. M. Duffield for the mass spectra.

Added in proof—The rearrangement of benzyldimethylamine oxide has recently been studied [G. P. Shulman, P. E. Ellgen and M. Connor, *Can. J. Chem.* **43**, 3459 (1965)]. They found $E_a = 34{\cdot}2$ kcal/mole. Since their compound was benzylic, a lower activation energy would have been expected. The discrepancy may be due to the method of decomposition of the amine oxide. Shulman's reaction was carried out in solution, which would probably make the activation energy higher.

---

[34] T. A. Bryce and J. R. Maxwell, *Chem. Comm.* 206 (1965).