amount of a black, insoluble substance), and finally recrystallized from methanol to give 2.3 g of **9f**, mp 315–318° dec.

Anal. Calcd for $C_{13}H_{10}BrNO_2$: C, 53.44; H, 3.46; Br, 27.36; N, 4.80. Found: C, 53.37; H, 3.50; Br, 27.30; N, 4.84.

3,4-Dimethoxy-2-methylbenzyl Bromide.—A mixture of 2,3-dimethoxytoluene (80 g), bromomethyl methyl ether (137 g), and glacial acetic acid (88 ml) was maintained at 30° for 8 hr. The reaction mixture was poured into ice–water and the solid was recrystallized from hexane to give 73 g of the benzyl bromide, mp 66–68°. Structural assignment was by analogy with the corresponding chloro compound.[14]

Anal. Calcd for $C_{10}H_{13}BrO_2$: C, 49.00; H, 5.35; Br, 32.39. Found: C, 48.97; H, 5.40; Br, 32.39.

Acknowledgments.—We thank Dr. V. Boekelheide for useful discussions, and the Analytical Research Department for analyses and spectral data.

Registry No.—**3a**, 42031-49-2; **3b**, 21852-33-5; **4b**, 24403-47-2; **5**, 21852-31-3; **8a**, 42031-53-8; **8b**, 21852-51-7; **8c**, 21831-11-8; **9a**, 42031-56-1; **9b**, 21852-49-3; **9c**, 21831-08-3; **9d**, 21852-24-4; **9e**, 42031-60-7; **9f**, 3919-24-2; 3,4-dimethoxy-2-methylbenzyl bromide, 21831-10-7; 2,3-dimethoxytoluene, 4463-33-6; bromomethyl methyl ether, 13057-17-5.

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[14] E. D. Hornbaker and A. Burger, *J. Amer. Chem. Soc.*, **77**, 5314 (1955).

Kinetics in the Thermolysis of 1-Arylethyldimethylamine Oxides in Aqueous Media[1]

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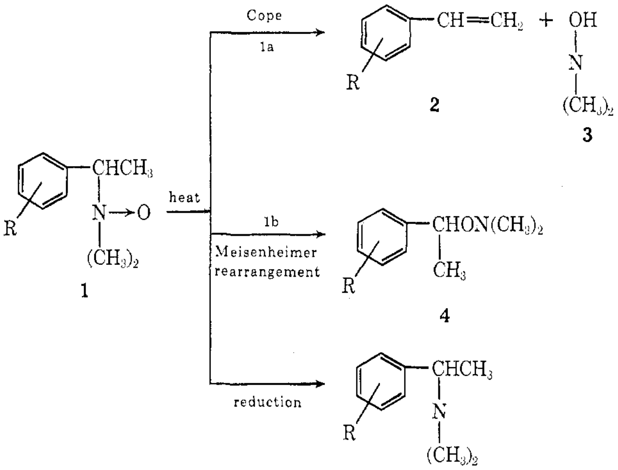
The kinetics of the thermolysis of unsubstituted and 1-(*p*-methoxy, *o*-methoxy, *p*-methyl, *o*-methyl, *p*-chloro, and *p*-nitro)phenylethyldimethylamine oxides, 1, at 94° in aqueous media have been determined by nuclear magnetic resonance spectroscopy. Essentially only the Cope elimination reaction occurred with all amine oxides except in the last two cases, those containing *p*-Cl and *p*-NO_2 substituents. With amine oxides possessing electron-withdrawing substituents, the Meisenheimer rearrangement and the formation of the free tertiary amine complicated the evaluation of the rate of the Cope elimination reaction. Good agreement was obtained between log k/k_0 with Hammett's σ constants for the amine oxides possessing electron-donating substituents which showed a ρ of -6.5. Activation parameters for the *p*-OMe derivative in the Cope thermolysis are $E_a = 39.6$ kcal/mol and $\Delta S^\dagger = 32$ eu. Mechanistic implications of the Cope reaction are discussed in light of these data.

Several studies have shown that during the thermolysis of benzyl tertiary amine oxides **1** there are at least three main competing reactions occurring (Scheme I), the Cope elimination, 1a, the Meisenheimer rearrangement, 1b, and reduction to the tertiary amine. In the Cope elimination the olefin **2** and dimethylhydroxylamine **3** are formed. The Meisenheimer rearrangement involves a migration of benzyl group from nitrogen to oxygen yielding **4**.[2a]

SCHEME I



The competition between these three reactions is markedly affected by the nature of the groups on the tertiary amine oxides. Essentially, only the Cope reaction occurs unless benzyl or allyl groups are involved. In cases where the Cope elimination reaction cannot occur, it has been shown that the electron-withdrawing groups on the benzyl group (*e.g.*, NO_2) enhance the Meisenheimer reaction.[2b] No reports, however, have appeared of a substituent effect study where the two reactions compete from the same starting material.

This study has been directed to the kinetics of the Cope reaction, a Hammett $\rho\sigma$ study, a determination of Arrhenius activation parameters, effects of water on the reaction rate constants, and proximity effects in the Cope reaction. These aspects of the Cope reaction have not been reported. Also reported is additional esr evidence for a radical intermediate in the Meisenheimer rearrangement.

Results

Aqueous Media.—The thermolysis of the tertiary amine oxides was carried out in aqueous media for various reasons. Amine oxides are difficult to obtain pure, since they readily form hydrates. The removal of the water from the hydrate is difficult without partial decomposition of the amine oxide, even at reduced pressure.[3] Lepley, Cook, and Willard[3b] attempted to remove all water from the oxide of *N,N*-dimethylbenzylamine by a freeze-drying process at 0.01 Torr. The hydroscopic, free-flowing white powder proved to be the monohydrate with an nmr ($CHCl_3$) peak at δ 5.03. This is also the position found for the water

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[1] This paper was presented in part at the 28th Annual Northwest Regional Meeting of the American Chemical Society, Pullman, Wash., June 1973, Abstract ORGN, 26.

[2] (a) A. C. Cope, T. T. Foster, and P. H. Towle, *J. Amer. Chem. Soc.*, **71**, 3929 (1949); (b) U. Schöllkopf, U. Ludwig, M. Patsch, and W. Franken, *Justus Liebigs Ann. Chem.*, **703**, 77 (1967).

[3] (a) G. P. Shulman, P. Ellgen, and M. Connor, *Can. J. Chem.*, **43**, 3459 (1965); (b) A. R. Lepley, P. M. Cook, and G. F. Willard, *J. Amer. Chem. Soc.*, **92**, 1101 (1970).

TABLE I

EFFECT OF VARYING THE WATER CONCENTRATIONS OF THE THERMOLYSIS OF TERTIARY AMINE OXIDES[a]

Registry no.	1-Arylethyldimethylamine oxide Substituent	$k \times 10^5$, sec^{-1} (94.5°) About 33% water[b]	65–70% water	75–80% water
42142-05-2	p-OCH$_3$	117, 115, 117[c]	86.6, 86.6[d]	79.0, 79.0[d,e]
42142-06-3	p-CH$_3$	31.0, 31.1[c]	17.2	14.6[e]
42142-07-4	H	6.0, 5.8[c]	1.5	1.47
42142-08-5	p-Cl	53.0, 62.2[c,f]	14.0, 12.2[c,f]	
42142-09-6	p-NO$_2$	6.93, 7.1[c,f]	10.0, 10.7[c,f]	
42142-10-9	o-OCH$_3$		12.7, 12.7[d]	
42142-11-0	o-CH$_3$			13.47, 13.88[c]

[a] Based on the loss of starting amine oxide as measured by nmr. The precision of the experiments was greater than 10%. [b] Attempts were made to remove all of the water *in vacuo* in a rotatory evaporator. However, not all of the water could be removed by this technique owing to decomposition. The final traces of water most likely could not be removed even by freeze drying.[3] [c] Multiple determinations. [d] The same value was obtained for the rate constant as measured by the loss of amine oxide or the formation of the dimethylhydroxyl amine. [e] 94.0°. [f] These values represent the sum of three rate constants: Cope elimination, Meisenheimer rearrangement, and the reduction of the amine oxide to the free amine by the hydroxylamine product. Therefore, it was not feasible to determine quantitatively the several reaction rates.

absorption in our experiments. The advantage of using water is that the amine oxides dissolve readily in water and yet decompose below 100°. Therefore, a study of their thermolysis is readily attainable in aqueous media. A driving force in the Cope elimination may be a basic attack by an unshared electron pair of the oxygen on the β hydrogens. This is supported by the fact that addition of water reduces the rate of reaction, as shown in Table I. However, when sufficient water is added, the rate is not so dependent on the water concentration. Hence, kinetic studies were made at water concentrations where small changes in concentration did not influence the rate. The water concentration appears also to reduce the rate of the Miesenheimer rearrangement. However, mechanistically these reactions are different.

Rate Measurements by Nmr.—The two methyl groups on the unpyrolyzed 1-arylethyldimethylamine oxide (~3.05) have different shifts than the same methyl groups which appear in the product, dimethylhydroxylamine (2.77 ppm). These strongly absorbing hydrogens provided an ideal means to follow the kinetics of the Cope elimination with nmr. [The nmr spectrum for a representive compound, 1-(p-methoxyphenyl)-ethyl-N,N-dimethylamine oxide, and a table listing the absorptions in the nmr spectra for the amine oxides are given in supplementary microfilm material.] Furthermore, measuring the rate of disappearance of the starting amine oxide and the appearance of the dimethylhydroxylamine considerably reinforced the precision of the rate measurement where the competing reactions, the Meisenheimer rearrangement and the reduction of the tertiary amine, were not important.

The kinetic results are shown in Table I. 1-p-Methoxyphenylethyldimethylamine oxide in aqueous solution pyrolyzes cleanly to two products, p-methoxystyrene and dimethylhydroxylamine. Nmr did not indicate any Meisenheimer rearrangement product from this compound. Therefore, Arrhenius measurements were obtainable for this compound (Table II). No Meisenheimer product resulted from the o-methoxy derivative as well. A first-order kinetics plot for the thermolysis of the p-methoxy derivative is given in the supplementary microfilm material.

Nmr showed that the o- and p-methoxy derivative proceeded exclusively to the Cope elimination product with no indication of the Meisenheimer product; the o- and p-methyl derivative gave 98–99% Cope product and the unsubstituted 1-phenylethyldimethylamine oxide pyrolyzed 95–97% *via* the Cope reaction and 3–5% *via* the Meisenheimer rearrangement. With the p-Cl and p-NO$_2$ derivatives, the extent of the Meisenheimer rearrangement and the reduction to the free tertiary amine increased appreciably and for these reasons, evaluation of the extent of the Cope reaction could not be suitably obtained.

TABLE II

RATE OF THERMOLYSIS OF 1-p-METHOXYPHENYLDIMETHYLAMINE OXIDE AS A FUNCTION OF TEMPERATURE[a]

Temp, °K	351.5	360.0	363.0	367.0	367.5
$k \times 10^5$, sec^{-1}	7.46	18.6	30.4	79.0	86.6

[a] These rate data were determined by nmr by noting the disappearance of the amine oxide and the rate of formation of the dimethylhydroxylamine. The decomposition followed excellent first-order kinetics at each temperature. The Arrhenius activation parameters calculated, using a computer, from these data are $E_a = 39.6$ kcal/mol and $\Delta S^\dagger = 32$ eu.

Electron spin resonance studies revealed that the free radical (CH$_3$)$_2$NO· was formed in all of the thermolyses even in the case where no nmr evidence of a Meisenheimer rearrangment was found, *e.g.*, with the o- and p-methoxybenzyl derivatives. This is a very stable free radical and one that is readily characterizable with esr. The splitting into 21 peaks is as theory predicts for this radical. The a_H splitting was determined to be 14.2 G and the a_N was 16.6 G. As the temperature was lowered the radical signal gradually disappeared. This very sensitive method of detecting free radicals (one part per 100 million) concurs that the Meisenheimer rearrangement occurs *via* a radical cleavage–recombination mechanism, and furthermore that, although nmr did not reveal a Meisenheimer reaction in the case of the o- and p-methoxy derivative, it was shown to occur to a very limited extent. (See paragraph at the end of paper about supplementary material.)

Hammett $\rho\sigma$ Plot.—The results in Table I clearly demonstrate that electron-releasing groups activate the Cope rearrangement in arylethyldimethylamine oxides. From the rate of loss of starting amine oxide and the rate of formation of dimethylhydroxylamine, it was evident that electron-withdrawing groups enhance the Meisenheimer rearrangement. A limited Hammett

$\rho\sigma$ plot of the Cope elimination using only data from those compounds in which the radical rearrangement occurred to less than 5% showed a ρ value of -6.5. The limits of error for this result are less than ± 2. A better plot was obtained with σ than with σ^+.

Arrhenius Parameters.—As stated, the 1-*p*-methoxyphenyldimethylamine oxide pyrolyzed almost exclusively *via* the Cope elimination reaction. Therefore, Arrhenius activation parameters for this reaction were attainable and were found to be $E_a = 39.6$ kcal/mol and $\Delta S^\dagger = 32$ eu. The data from which these activation parameters were calculated, using a computer, are shown in Table II.

Para to ortho ratio in the Cope elimination reaction rates showed (Table I) an appreciable proximity effect for the methoxy substituent (p-OCH_3/o-$OCH_3 = 6.8$) but no proximity effect was observed for the methyl substituent (p-CH_3/o-$CH_3 = 1.1$). This, very likely, is another example of steric inhibition of resonance.

Experimental Section

Materials.—The amine oxides were prepared through several steps starting from the corresponding acetophenones which were available from Aldrich Chemical Co. The purity was checked using melting points and refractive indices. They follow: *p*-Cl, n^{20}_{4} 1.544; *p*-CH_3, n^{20}_{4} 1.5334; *o*-CH_3, n^{20}_{4} 1.5322; *o*-OCH_3, n^{20}_{4} 1.5393; *p*-NO_2, mp 78–80°; *p*-OCH_3, mp 34–37°. Acetophenone (98.8%) was obtained from Baker Analyzed Reagent Co.

1-Arylethylamines were synthesized by following the procedure described by Ingersoll[4] starting with the acetophenone derivative and ammonium formate. Ammonium formate was prepared from ammonium carbonate and formic acid. The amines were also identified by ir spectroscopy and mass spectral analysis, and were shown to be pure. (*See paragraph at end of paper for* supplementary material on yields, nmr chemical shifts, boiling points, etc.)

1-Arylethyldimethylamines were formed from the primary amines by the action of formaldehyde in the presence of formic acid.[5] Yields, nmr chemical shifts, and boiling points are given in the supplementary material. The amines were also identified by ir spectroscopy and mass spectral analysis.

1-Arylethyldimethylamine Oxides.—The tertiary amines were dissolved in an equal volume of methanol. To this solution was added slowly four volumes of a 30% solution of hydrogen peroxide. The mixture was stirred magnetically at room temperature for 96 hr. After the oxidation was completed, 50 mg of platinum black (Fischer) was added to decompose the excess hydrogen peroxide and the mixture was stirred at room temperature for an additional 48 hr. Potassium iodide–starch test paper was used to confirm the complete absence of hydrogen peroxide. The black suspension was filtered over Whatman No. 1 filter paper (this grade proved to be necessary) and the filtrate was evaporated at room temperature in a rotary evaporator to $^1/_2$–$^1/_3$ volume. The concentration of amine oxide was shown by nmr to be about 33% (aqueous solution). Although the per cent yield could not be determined accurately, the tertiary amine in each case appeared to be converted quantitatively to its amine oxide, as no unreacted tertiary amine, or any other organic material, was detectable by nmr.

As stated, the nmr showed no sign of an organic impurity. Carbon, hydrogen, and nitrogen analyses were *not feasible* because the oxides were in their hydrate form. Mass spectrographic analyses showed a small molecular ion with a base peak of M − 61, the loss of dimethylhydroxylamine. These data clearly characterize the purity of the amine oxides.

Kinetic Experiments. Sample Preparation.—The hydrated amine oxides were further diluted with water (see Table I) before introduction into an nmr tube. The tube was filled to a height of 50 mm. The dilution and amount placed in the tube proved to be important. The olefin formed during the course of the reaction is water insoluble and does not dissolve in the aqueous phase. It is critical that the radiowave pass through the aqueous phase only containing the water-soluble tertiary amine oxide reactant and most of the dimethylhydroxylamine product as it is formed. The olefin formed (except in the case of the *p*-nitro derivative) was less dense than the aqueous medium and formed a thin layer at the top of the nmr tube.

Instrument Calibration.—Nmr spectra were taken on a Varian Associates A-60 analytical nmr spectrometer equipped with a V-6040 nmr variable-temperature controller. The instrument was tuned, the field homogeniety was checked, and the temperature and the integrator were calibrated *before* and *after* each kinetic run. *Field width calibration at 500 cycles were taken using the* Varian 943346-07 standard with a chemical shift of chloroform of 434.5 cycles with respects to an internal standard of TMS. Integration calibrations were made using Varian test integrator 943346-15 containing 5% ethylbenzene. High-temperature calibrations and tuning were done using ethylene glycol.

The temperature was controlled by a Varian V-6040 variable controller to within ±1° and measured using Varian 943346-05 ethylene glycol standard. The dial of the variable controller was calibrated prior to each kinetic run. Sufficient time (30–40 min) was used to allow the probe area to reach equilibrium temperature. After the ethylene glycol sample was placed in the probe, special care was taken to ensure the best temperature control possible by doubling the recommended stabilization time from 5 to 10 min. After 4 min the $\Delta\delta$ for the ethylene glycol standard held constant. Temperature measurements (using ethylene glycol) were taken immediately before and after each experiment and the results were discarded if the variation in temperature was greater than 1°.

Rate Measurements.—The nmr tubes were left open during the kinetic runs to avoid explosions in the nmr probe. No change in volumes was observed during the kinetic runs. After the sample was placed in the probe, sufficient time (>180 sec) was used to equilibrate the temperature to the operation temperature (94°) before kinetic readings were made. The rate of the disappearance of the reactant, the tertiary amine oxide, was followed by recording the change in intensity of the two singlets at just above 3 ppm with time.

Kinetic measurements (integration of the two singlets) was commenced after a sufficient temperature stabilization period (180 sec). As the peak height decreases, the new height was represented by a_t; therefore

$$\ln a_0/a_t = kt$$

which rearranges to

$$\ln a_t = -kt + \ln a_0$$

A plot of $\ln a_t$ *vs.* t resulted in the evaluation of k (Table I and II). It was not necessary to evaluate a_0.

Similarly, the rate of formation of dimethylhydroxylamine was measured by noting the change in the integration of the singlet at 2.7 ppm and noting its change with time. In the studies of *o*- and *p*-methoxy derivatives, where no measureable amount of Meisenheimer rearrangement occurred, the rate constants were the same by both analytical methods (Table I).

Esr Measurement.—The esr measurements were taken on a Varian Associates epr spectrometer No. V-4500 equipped with a 100 KC modulation. The esr spectrum of the free radical $(CH_3)_2$-$NO\cdot$ *formed in the thermolysis of* 1-aryldimethylamine oxide resulting from a Meisenheimer reaction is given in the supplementary material. The hyperfine splitting values ($a_H = 14.2$ G and $a_N = 16.6$ G) were readily measurable from the spectrum. The radical formation was detected at lower temperatures and after shorter times when a *p*-nitro or *p*-chloro substituent was present than with amine oxides bearing a methyl or methoxy substituent.

Discussion

The value of pyrolysis of tertiary amine oxides (the Cope elimination reaction) as a preparative method of alkenes has been reviewed by Cope and Trumbull.[6] In this review, Cope and Trumbull commented briefly

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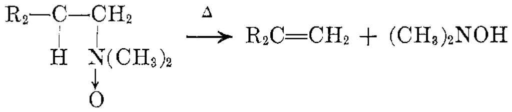
[4] A. W. Ingersoll in "Organic Syntheses," Collect. Vol. II, A. H. Blatt, Ed., Wiley, New York, N. Y., 1943, p 503.

[5] H. T. Clark, H. B. Gillespie, and S. Z. Weisshaus, *J. Amer. Chem. Soc.*, **55**, 4571 (1933).

[6] A. C. Cope and E. R. Trumbell in "Organic Reactions," Vol. 2, R. Adams, Ed., Wiley, New York, N. Y., 1960, p 317.

on the mechanism of this elimination reaction and stated that the stereochemical evidence presented by Cram and McCarty[7] (stereoselective cis elimination) "establishes an intramolecular mechanism (for this reaction) involving a planar five-membered cyclic transition state (which) resembles the Chugaev reaction and the pyrolysis of esters." There has been no additional evidence given to support or challenge this mechanism, although all references to the mechanism of this reaction quote Cope and Trumbull's mechanism.



$$\underset{H}{R_2-\overset{|}{C}}-\underset{\underset{O}{\downarrow}}{\underset{N(CH_3)_2}{\overset{|}{CH_2}}} \xrightarrow{\Delta} R_2C{=}CH_2 + (CH_3)_2NOH$$

The first-order kinetics reported in this paper supports the intramolecular nature of this reaction, but the large negative ρ (-6.5), the large positive $\Delta S^\dagger$ value (+32 eu), and the effect of solvent challenge the simplicity of the mechanism described by Cope and Trumbull for the pyrolysis of tertiary amine oxides in aqueous medium. The data is more in line with a heterolytic cleavage than a quasi-five-membered ring transition. The size and sign of the ρ value argues for a very polarized benzylic carbon in the course of pyrolysis of 1-arylethyldimethylamine oxides. The extent of this charge is appreciably more advanced at the transition state than in the pyrolysis of esters or xanthates.

Amine oxides are particularly polar. Therefore, protic solvents have a major influence on their rate of pyrolysis. The importance water has on the reaction rate is evidenced from the data shown in Table I but is perhaps even more dramatically shown by the work of Cram, *et al.*[8] They reported the ratio of the rate constants (k_{DMSO}/k_{H_2O}) in the pyrolysis of 2-*N*,*N*-dimethylamino-3-phenylbutane oxides as approximately 10^5 for the threo and 10^4 for the erythro isomer. Even larger ratios were reported when tetrahydrofuran was used as solvent.

There are several ways protic solvents can alter the reaction rate. Hydration reduces the nucleophilic attack of the oxygen at the β hydrogen. Furthermore, it reduces the magnitude of the positive charge at nitrogen, which in effect strengthens the $C-N^+$ bond which has the effect of raising the activation energy. The high positive entropy of activation (+32 eu) is associated with the loss of hydration in going from the ground state to the activated state. Heterolysis of the $C-N^+$ bond would also account for part of the large $+\Delta S^\dagger$. The high $+\Delta S^\dagger$ (32 eu) found for this reaction argues against the formation of a five-membered cyclic transition state as proposed by Cope and Trumbull. The cyclic mechanism is associated with a negative entropy of activation. If indeed a cyclic mechanism is involved, the increase in $\Delta S^\dagger$ resulting from the loss of solvation overshadows the small negative $\Delta S^\dagger$ brought about from the formation of a cyclic transition state.

As stated above, the significantly negative ρ value (-6.5) indicates that considerable charge develops on the benzylic carbon in the transition state. This is in line with the large $\Delta S^\dagger$ and can be interpreted to mean that ions are actually formed in the benzylic system. The large entropy of activation for this reaction when an excess of water is used is in marked contrast to that found by Cram, *et al.*,[8] who studied the effects of water on the Cope elimination reaction in THF and DMSO. Apparently the benzylic system, being capable of developing ions in the Cope reaction, orders the solvent in a different manner than the *N*,*N*-dimethyl-3-phenyl-2-butylamine oxide, which Cram, *et al.*, studied. Although the value of ρ is not so precise as it would have been had more points on the Hammett plot been obtainable, the data are sufficient to set the ρ value between -4.5 and -8.5. Because the medium stabilized the developed charge on carbon, it is not necessary for there to be *enhanced* stabilization by methoxy substituents on the ring; therefore, σ gives a better plot than σ^+.

Further evidence for a highly developed charge in the transition state comes from a proximity effect study. A careful study was made of the para/ortho ratio for OCH_3 and CH_3 in the pyrolysis of 1-arlethyldimethylamine oxides. The para/ortho ratio for OCH_3 was 6.8 and for CH_3 was 1.1. This demonstrates that the reaction is sensitive to the conformation of the methoxy substituent. When a methoxy substituent is placed ortho to the reacting site, it cannot rotate into its most favorable conformer for charge delocatization. The conformation is not critical for methyl. As stated, this reinforces the concept of a highly developed charge in the transition state. A similar study in gas-phase pyrolysis of esters where the ρ value is only -0.67 revealed the para/ortho ratio for methoxy to be 1.67.[9]

Based on these data, the following mechanism for the Cope elimination is proposed. Heating causes a less ordered transition state by the loss of water, which is the major cause for the large positive $\Delta S^\dagger$. As water is lost, the $C-N^+$ bond is weakened and the carbon atoms develops a positive charge. The extent of this charge must be sufficient to account for the large negative ρ value, and if ions are formed this would help account for the positive $\Delta S^\dagger$. The stereochemistry (cis elimination) that Cram, *et al.*, observed may not persist in cases such as studied here where heterolysis occurs at the benzylic carbon. If it is determined by further investigation that the reaction is stereoselective with systems containing a benzylic carbon attached to nitrogen, then, in some way (perhaps by a solvent cage), stereoselective loss of a β hydrogen must occur. In the Stevens rearrangement, it has been suggested that a solvent cage has been invoked to explain the retention of configuration.[10a] By removing water molecules, the oxygen becomes sufficiently basic to abstract a β hydrogen. If a quasi-five-membered ring transition state is formed, the polarity around the C–N bond must be sufficient to account for the large negative ρ value. The entropy loss in going through a confined five-membered ring would be overshadowed by the entropy gained due to the loss of water molecules of hydration. The difference between amine oxide pyrolyses and the pyrolyses of esters centers around the extent of charge build-up on the benzylic carbon atom

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[7] (a) D. J. Cram and J. E. McCarty, *J. Amer. Chem. Soc.*, **76**, 5740 (1954); (b) A. C. Cope and C. L. Bumgardner, *ibid.*, **79**, 960 (1957).

[8] D. J. Cram, M. R. V. Sahyum, and G. R. Knox, *J. Amer. Chem. Soc.*, **84**, 1734 (1962); M. R. V. Sahyum and D. J. Cram, *ibid.*, **85**, 1263 (1963).

[9] R. Taylor, G. G. Smith, and W. H. Wetzel, *J. Amer. Chem. Soc.*, **84**, 4817 (1962).

[10] (a) R. A. W. Johnstone, *Mech. Mol. Migr.*, **2**, 249 (1969); (b) R. D. Bach, D. Andrzejewski, and L. R. Dusold, *J. Org. Chem.*, **38**, 1742 (1973); (c) A. R. Lepley and A. G. Giumanni, *Mech. Mol. Migr.*, **3**, 297 (1971); (d) W. K. Musker, *Fortschr. Chem. Forsch.*, **14**, 295 (1970).

and also the effects brought upon by the solvent. Further studies using other solvents such as DMSO and THF will assist in substantiating or challenging these conclusions.

Bach, *et al.*,[10b] have recently discussed the mechanism of the Cope reaction in cyclooctyldimethylamine oxide. With such systems polarization of the C–N bond in the transition state would not be so likely as with the systems discussed in this paper.

The Meisenheimer Rearrangement.—The mechanism of the Meisenheimer rearrangement and similar reactions, which has been debated for many years, has recently been reviewed,[10] and will only be discussed briefly here. However, since the Meisenheimer reaction accompanies the Cope reaction in several cases, it is appropriate that a few comments be made. For many years the Meisenheimer reaction has been linked to the Wittig rearrangement of ethers[11] and the Stevens rearrangement of quaternary ammonium salts.[12] An SNi mechanism has been seriously considered for all three of these reactions, but the present thinking is that they all occur *via* a cleavage–recombination process. The Meisenheimer reaction most likely follows a radical cleavage–recombination mechanism. The detection by esr of the dimethylamine oxide radical found in this study is further evidence that a radical is formed in the Meisenheimer isomerization. This is the first detection by esr of a radical in the *thermally* induced Meisenheimer reaction.

Wragg, *et al.*,[13] reported first-order kinetics for this reaction. Schöllkopf, *et al.*,[2b] reported activation energies between 33 and 40 kcal for the isomerization of benzylmethylaniline oxides in the aqueous alcohol and activation entropies between 19 and 41 eu. Shulman, *et al.*,[3a] have reported an E_a value of 34.2 ± 1 kcal and an entropy of activation of +7.9 ± 2.5 eu for the rearrangement of benzyldimethylamine oxide. In itself, this strongly implies that a cleavage–recombination mechanism operates and that no cyclic transition state (SNi or SNi′) is involved. It was reported, however, that the amount of water present altered the $\Delta S^\dagger$ in this reaction (the higher the concentration of water, the larger the $\Delta S^\dagger$). Therefore, the significance of the large $\Delta S^\dagger$ as evidence for a cleavage mechanism should be attenuated. In addition to these data, Schöllkopf and coworkers have shown that extensive racemization occurs during isomerization of α-deuteriobenzyldimethylamine oxide[14,15] and that a radical intermediate $CH_3N(O\cdot)C_6H_5$ has been detected by esr during the course of this reaction when initiated photochemically.[16] It is significant, as shown in this work, that this same radical can be thermally induced and that it forms appreciably more readily with amine oxides bearing electron-withdrawing substituents, *e.g.*, NO_2 and Cl. Schöllkopf, *et al.*, reported a ρ value of 0.9 in the isomerization of substituted benzylmethylaniline oxides[13] and a ρ of 1.3 in the thermal isomerization of benzylmethylaniline oxides substituted in the aniline ring.[17] They have submitted these results in support of a cleavage–recombination mechanism.

Schöllkopf and coworkers stated that these ρ values are too small for a carbanion mechanism. Lorand and coworkers[18] have presented additional evidence for a radical cage mechanism. They studied the effect of oxygen on the isomerization of *N*-benzyl-*N*-methylaniline *N*-oxide in ethanol–water solution and found that oxygen greatly reduced the yield of the Meisenheimer product (a drop from 89% to 33%); yet the rate constant stayed the same with or without oxygen. Lorand and O'Connell[19] have attempted to generate a 1-adamantyl radical *via* a Meisenheimer rearrangement reaction of 1-dimethylaminoadamantane *N*-oxide without success. Tabushi and associates[20] have provided additional evidence for a radical mechanism by showing that BuSH prohibited the reaction effectively. Allyl groups isomerize in the radical form before recombination.

It is important to realize that radical detection in itself does not establish that the thermally induced Meisenheimer isomerization takes place by a radical-recombination mechanism, since its formation could occur through a side reaction, the oxidation of a dialkylhydroxyl amine, a product of the Cope reaction.

Perhaps the most convincing evidence for an intramolecular rearrangement mechanism in the Meisenheimer reaction comes from the observations by Lepley, *et al.*,[3b] and Ostermann and Schöllkopf,[21] who have observed proton magnetic resonance emission spectra for the nitroxyl and benzyl radicals. Pine[22] has discussed the value and also the cautions to be applied to these results. Craig, *et al.*,[23] supplied evidence for an intermolecular mechanism for the Meisenheimer reaction. Taken as a whole, the evidence for a radical cleavage–recombination mechanism is convincing.

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Registry No.—*p*-Chloroacetophenone, 99-91-2; *p*-methylacetophenone, 122-00-9; *o*-methylacetophenone, 577-16-2; *o*-methoxyacetophenone, 579-74-8; *p*-nitroacetophenone, 100-19-6; *p*-methoxyacetophenone, 100-06-1; acetophenone, 98-86-2.

Supplementary Material Available.—The nmr data for the amine oxides and the primary and tertiary amines are tabulated in three tables and will appear following these pages in the microfilm

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edition of this volume of the journal. Also included in the supplement are the nmr spectrum of a representative amine oxide, 1-(*p*-methoxyphenyl)ethyldimethylamine oxide, the first-order kinetics plot for the Cope elimination reaction for this compound, and the esr for the free radical, $(CH_3)_2NO\cdot$. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., Washington, D.C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JOC-73-4172.

Phosphorus-Containing Products from the Reaction of Propargyl Alcohols with Phosphorus Trihalides. II. The Crystal and Molecular Structure of 2-Hydroxy-3,5-di-*tert*-butyl-1,2-oxaphosphol-3-ene 2-Oxide[1,2]

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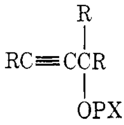
The reactions of 1,3-di-*tert*-butylpropargyl alcohol (**2**) with PBr_3 in chloroform or carbon tetrachloride gave the expected propargyl and allenic halides plus a 10–20% yield of 2-bromo-3,5-di-*tert*-butyl-1,2-oxaphosphol-3-ene 2-oxide (**3**-Br). In dioxane or hexane the product was 2,2,6,6-tetramethyl-3,4-heptadiene-3-phosphonic acid (**5**-OH). Mild hydrolysis of **3**-Br led to the title compound, **3**-OH, an isomer of **5**-OH. Attempts to interconvert **3**-OH and **5**-OH gave phosphonic anhydride **6**. The intermediate, dibromophosphite **4**, was observed by nmr. The reaction of **2** with PCl_3 in chloroform afforded **3**-Cl in 6% yield. The crystal structure of **3**-OH was determined by X-ray crystallography. The constraint inherent in the essentially planar unsaturated five-membered ring distorts the atoms bonded to phosphorus away from their normal tetrahedral positions. The P–O bond lengths for the two exocyclic oxygen atoms are identical (1.51 Å), suggesting that the acid proton is intramolecularly hydrogen bonded equally to both atoms.

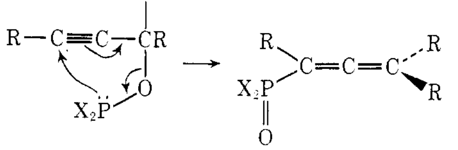
The reaction of propargyl alcohols with phosphorus trihalides has long been recognized as a general source of propargyl and allenic halides.[3] These transformations are believed to involve preliminary formation of the corresponding dihalophosphite ester (**1**). This



$$\begin{array}{c} R \\ | \\ RC{\equiv}CCR \\ | \\ OPX_2 \end{array}$$

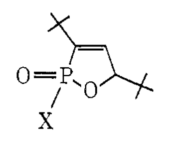
1

normally reacts with two additional alcohol molecules to give a trialkyl phosphite, which is then partitioned to allenic and propargyl products through nucleophilic attack by external halide ion. The possibility exists, however, that the phosphorus atom, with its nonbonding pair of electrons, might function as a competitive *internal* nucleophile. Precedents for such processes include the rearrangement, upon standing, of dialkyl propargyl phosphites to allenic phosphonates,[4] and similar rearrangements during the reaction of phosphorus trichloride (PTC) with propargyl alcohols in the presence of amines.[5,6] Mechanistic data about such transposition has been interpreted in two ways. The fact that the rate of rearrangment seemed to parallel the expected carbonium ion stability of the propargyl fragment led to the postulation of an SNi′ (ion-pair) mechanism.[4] However, absence of the isomeric propargyl phosphonate has been taken as evidence for a concerted mechanism.[5]



(1)

There are three mechanistic extremes for such a rearrangement: stepwise with preliminary C–O heterolysis (SNi′ ion pair), concerted [3,2] sigmatropic shift (thermally allowed in the all-suprafacial mode), or stepwise with preliminary P–C bond formation *via* nucleophilic attack by phosphorus on the triple bond. We recently reported[2] that the reaction of 1,3-di-*tert*-butylpropargyl alcohol (**2**) with phosphorus tribromide (PTB), either neat or in chloroform, afforded a 10–20% yield of a crystalline, phosphorus-containing compound, in addition to the expected propargyl and allenic bromides. Based on its spectral and chemical properties, this compound was believed to be the novel five-membered oxaphospholene **3**-Br. Clearly, the



(**3**-Br, X = Br, etc.)

occurrence of such a product argues strongly for P–C bond formation preceding C–O bond rupture, even though the 1,3-di-*tert*-butylpropargyl system is quite solvolytically reactive under SN1 conditions.[7] We present here further details of these and related reactions as regards their mechanisms and synthetic utility. In addition we report the results of an X-ray crystallographic study on a derivative of **3**-Br, which fully confirms previous and present structural assignments.

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