The precipitate was collected and crystallized from 95% ethanol, giving 5.70 g of long, hexagonal crystals (41.5%).

***trans*-2-Aminocyclohexyl Sulfate.**—To a suspension of *trans*-2-aminocyclohexanol (1.15 g) in dry $CHCl_3$, chlorosulfonic acid (0.67 ml) in CCl_4 (2 ml) was added dropwise below 0° during 1 hr. After stirring for 2 hr at room temperature, the reaction mixture was evaporated to dryness and freed from HCl *in vacuo* over KOH pellets. The residue was dissolved in ice water, and the solution was neutralized with solid $BaCO_3$ and then with $Ba(OH)_2$ solution. The precipitate was filtered off, and the filtrate was concentrated to a small volume and passed through a column of Dowex 50W X8 (H^+ form, 20–50 mesh) to remove the starting material. The eluate was neutralized with Dowex 1 X2 (OH^- form, 100–200 mesh) and concentrated, and the residue was crystallized from water, giving 0.53 g (27.2%) of prismatic crystals.

Disodium *trans*-2-Sulfoaminocyclohexyl Sulfate.—(±)-*trans*-2-Aminocyclohexanol (1.52 g) was sulfated by a method virtually identical with that described for disodium 2-sulfatoethylsulfamate, giving 0.82 g (19.5%) of needle crystals.

All the sulfated *cis*-2-aminocyclohexanols were prepared by the method used to prepare the corresponding trans derivatives described above.

Sodium 2-Deoxy-2-sulfoamino-D-glucose.—2-Deoxy-2-amino-D-glucose (12.9 g) was dissolved in water (180 ml) and the pH of the solution was adjusted to 9.6 by the addition of 10% NaOH. Pyridine–SO_3 (11.5 g) was added to the well-stirred solution over a period of 9.5 hr at room temperature. During this addition, the pH of the mixture was maintained between 9.6 and 10 by the addition of 10% NaOH. After stirring overnight at room temperature, the solution was concentrated to *ca.* 40 ml and added to 10% barium acetate solution. Precipitated $BaSO_4$ was filtered off through Radiolite 100 and the filtrate was adjusted to pH 4.6 by the addition of acetic acid and passed slowly through a column of Dowex 50W X8 (Na^+ form, 20–50 mesh). The eluate was immediately neutralized with NaOH and concentrated to *ca.* 20 ml. The product was precipitated by the addition of ethanol (400 ml), and the precipitate was collected by centrifugation and washed with ethanol. Solid Ag_2CO_3 was added to the solution of the product dissolved in water (50 ml). Precipitated AgCl and excess Ag_2CO_3 were centrifuged off and the supernatant was neutralized with Dowex 50W X8 (H^+ form, 20–50 mesh). The solution was concentrated to *ca.* 10 ml and the product was precipitated by the addition of ethanol (200 ml). The crude product, a white powder (6.47 g, 34.1%), was twice crystallized from methanol and water after treatment with activated charcoal, giving colorless crystals (3.70 g, 19.5%), $[\alpha]^{25}D + 48°$ (c 1, H_2O), mp 235° dec.

Registry No.—SO_3, 7446-11-9; 2-acetaminophenol, 614-80-2; (±)-*cis*-2-aminocyclohexanol hydrochloride, 38898-68-9; (±)-*trans*-2-aminocyclohexanol hydrochloride, 33092-83-0; (±)-*cis*-2-aminocyclohexanol, 38898-70-3; (±)-*trans*-2-aminocyclohexanol, 33092-82-9; 2-aminoethanol, 141-43-5; 3-amino-1-propanol, 156-87-6; 2-deoxy-2-amino-D-glucose, 3416-24-8.

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Radicals and Scavengers. II. Scavengers, Viscosity, and the Cage Effect in a Meisenheimer Rearrangement[1,2]

JOHN P. LORAND,*[3] RUSSELL W. GRANT, PATRICIA A. SAMUEL, ELIZABETH M. O'CONNELL, JOHN ZARO, JAMES PILOTTE, AND ROBERT W. WALLACE

Department of Chemistry, Boston University, Boston, Massachusetts 02215

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Radical scavengers have been used to study the thermal Meisenheimer rearrangement of *N*-benzyl-*N*-methylaniline *N*-oxide (I) in alkaline 80% aqueous ethanol at 70°. Oxygen at ≥1 atm reduces the yield of *N*-benzyloxy-*N*-methylaniline (II) to a minimum of 36%, while the yield under pure N_2 is 89%. A thiol and CCl_4, at higher concentrations, also reduce the yield of II. The three scavengers lead to benzaldehyde, toluene, and chloroform, not found in their absence. In the viscous solvent cyclohexanol at 70°, the "minimum" yield of II under O_2 is 69% of that under N_2. Rearrangement in chloroform at 60° gives CIDNP. These results support operation of a 40% cage effect as an important component of the homolytic dissociation–recombination mechanism previously proposed.

Many cases of inefficiency in the production of free radicals have been convincingly interpreted in terms of the "cage effect,"[4] and this phenomenon is now well enough understood to possess predictive value. The organic systems studied have but rarely involved either (a) a stable radical,[2,5,6] or (b) dissociation of only one bond,[2,7-9] the geminate radicals thus being in contact.

The thermal "Meisenheimer" rearrangement of tertiary amine oxides,[10] exemplified by that of *N*-benzyl-*N*-methylaniline *N*-oxide (I) (eq 1), must have both these characteristics if, as proposed by Schöllkopf,[11,12] it proceeds *via* a homolytic dissociation–recombination mechanism (eq 2, 3).

We have recently demonstrated[2] that the rearrangement of I in 80% ethanol–20% water at 70° proceeds with a 37% cage effect. Our evidence was that molecular oxygen at 1 atm, a scavenger of carbon radicals, reduced the yield from 89% (observed under nitrogen) to 33%. Oxygen did not, however, prevent the formation of II altogether; such behavior is diagnostic of a cage effect.

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[1] Taken in part from the A.M. theses of R. W. G. (1968), P. A. S. (1969), and E. M. C. (1971), and from the Ph.D. thesis of R. W. W. (1973, in preparation) at Boston University.

[2] Part I: J. P. Lorand, R. W. Grant, P. A. Samuel, E. M. O'Connell, and J. Zaro, *Tetrahedron Lett.*, 4087 (1969).

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[5] W. A. Pryor and K. Smith, *J. Amer. Chem. Soc.*, **89**, 1741 (1967); **92**, 5403 (1970).

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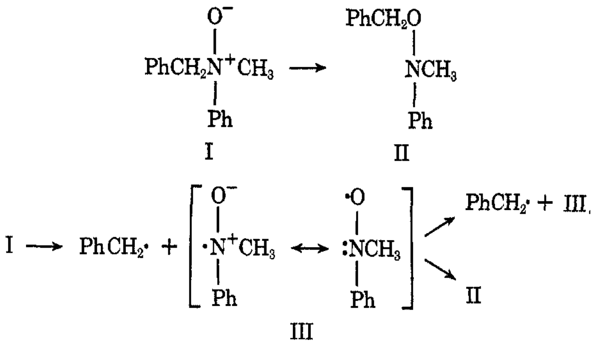
[9] H. Kiefer and T. G. Traylor, *ibid.*, **89**, 6667 (1967).

[10] (a) J. Meisenheimer, *Ber.*, **52**, 1667 (1919); (b) J. Meisenheimer, H. Greeske, and A. Willmersdorf, *ibid.*, **55**, 513 (1922); (c) R. F. Kleinschmidt and A. C. Cope, *J. Amer. Chem. Soc.*, **66**, 1929 (1944); (d) R. A. W. Johnstone in "Mechanisms of Molecular Migrations," Vol. 2, B. S. Thyagaragan, Ed., Interscience, New York, N. Y., 1969, pp 257–265.

[11] U. Schöllkopf and H. Schäfer, *Justus Liebigs Ann. Chem.*, **683**, 42 (1965).

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



$$PhCH_2\overset{O^-}{\underset{Ph}{N^+}}CH_3 \longrightarrow \overset{PhCH_2O}{\underset{Ph}{NCH_3}} \quad (1)$$

$$I \longrightarrow PhCH_2\cdot + \left[\overset{O^-}{\underset{Ph}{\cdot N^+CH_3}} \longleftrightarrow \overset{\cdot O}{\underset{Ph}{:NCH_3}}\right] \rightarrow PhCH_2\cdot + III,\ II \quad (2)$$

$$PhCH_2\cdot + III \longrightarrow II \quad (3)$$

We were at that time unaware of a series of "crossover" experiments by Schöllkopf, *et al.*,[13] implying a cage effect of 75–95% in water or aqueous methanol at 40–80°, markedly incompatible with our estimate. We have now extended our investigation to a much higher pressure of oxygen, to other scavengers, to aqueous methanol at 40° (the conditions used by Schöllkopf, *et al.*), and finally to the viscous solvent cyclohexanol. We now present these results, which support our earlier estimate of the cage effect. We shall explain the disagreement between our estimate and that from the crossover experiment, relate the cage effect to the mechanism of rearrangement, and comment on some puzzling observations.

Results

Reaction Products.—The rearrangement of I, prepared and stored as its hydrochloride, I HCl, was originally conducted in aqueous ethanol in the presence of a variety of bases, most frequently sodium hydroxide and the primary amine, tris(hydroxymethyl)aminomethane (Tris). Whenever Tris was used, the product II was accompanied by a basic by-product, IV, at first thought to be an isomer, which showed nmr absorption characteristic of a methyl and a benzyl group, as well as aromatic absorption not resolved from that of II. Much to our embarrassment, IV proved to be the reduction product, *N*-benzyl-*N*-methylaniline, from which the oxide had originally been prepared. This was shown by extracting IV from the mixture with mineral acid and converting it to the picrate, which was identical by melting point and mixture melting point with a sample prepared from our starting material. Although IV had also arisen in runs using sodium hydroxide, it subsequently became clear that, in the presence of a slight excess of base, no detectable amount of IV was produced. We thus abruptly abandoned the use of Tris in favor of NaOH. Although thermal reactions of amine oxides have invariably produced the corresponding amine, the mechanism of this reduction appears not to be understood. We found that *ca.* 50% reduction product arose from I HCl in concentrated aqueous pyridine, but a careful search for pyridine *N*-oxide as the oxidation product netted only a 5% yield.

A search was made for bibenzyl and toluene as reaction products. Both compounds were detected by glpc analysis of the crude reaction products: bibenzyl in *ca.* 0.1% yield from rearrangement of 0.028 *M* I HCl in 80% aqueous ethanol at 70°; toluene was found only when I HCl was initially 0.007 *M* (*cf.* Table II). Schöllkopf has reported the identification of bibenzyl by tlc.[13] No other products were identified under these reaction conditions, although the maximum yield of II under nitrogen was only 89%.

A few observations were made using chloroform as the reaction solvent, with the thought that its low polarity might accelerate the reaction, which involves the dissipation of opposite charges. Addition of DABCO (1,4-diazabicyclo[2.2.2]octane), or triethylenediamine, to a chloroform solution of I HCl led to precipitation of some DABCO hydrochloride and shifts in the nmr spectrum of the solution attributable to formation of at least some free oxide. The solution seemed stable enough at room temperature, but rearrangement took place at slightly higher temperatures, so that, even at 60°, CIDNP[14] was observed for both methyl and benzyl protons of II. The half-time at this temperature must not have exceeded a few minutes, while that in 80% ethanol at 70° is about 2 hr. Further work has not been done using chloroform, but we conclude that the rate in chloroform is at least ten times, and possibly more than one hundred times, greater than in ethanol.

Kinetics.—The rate of rearrangement of I under nitrogen and under oxygen was measured at 70.3° with the same techniques used to determine products (*cf.* Experimental Section). Because of the small size of aliquots, the yields probably entail larger errors than the "one-point" runs conducted with 200 ml or more of solution. Table I shows typical series of yields of II at various times. Plots of log $[II_f/(II_f - II_t)]$ against time were linear, and data for both N_2 and O_2 fit the same plot. The first-order rate constant was found to be $1.0 \pm 0.1 \times 10^{-4}$ sec^{-1}, corresponding to a half-life of 110 min.

TABLE I

KINETICS OF REARRANGEMENT OF I[a] AT 70.3° UNDER N_2 AND O_2

Time, min	Yield of II, *M* under N_2	Time, min	Yield of II, *M* under O_2
0	0	0	0
20	0.00294	20	0.00064
30	0.00434	70	0.00408
60	0.00844	170	0.00552
90	0.00969	220	0.00774
185	0.01196	280	(0.00968)
435	0.01786	400	0.00896
715	0.01932	1355	0.00976
755	0.02032		

[a] Initial concentration of I HCl = 0.02804 *M;* of NaOH, 0.0282 *M*, in 80% aqueous ethanol.

Oxygen as Scavenger.—Rearrangement of I HCl in the presence of excess sodium hydroxide in 80% aqueous ethanol at 70° was conducted while bubbling into the solution nitrogen, air, or pure oxygen, as previously reported.[2] The reaction has subsequently been conducted in a Parr bottle under 5 atm of pure oxygen, using vigorous magnetic stirring. The results are collected in Table II. The high-pressure run, performed, like the others, in duplicate, gave the same yield of II as the run under 1 atm of oxygen. Thus,

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[13] U. Schöllkopf, U. Ludwig, M. Patsch, and W. Franken, *Justus Liebigs Ann. Chem.*, **703**, 77 (1967).

[14] (a) H. R. Ward and R. G. Lawler, *J. Amer. Chem. Soc.*, **89**, 5518 (1967); (b) H. Fischer and J. Bargon, *Z. Naturforsch.*, **229**, 1556 (1967).

TABLE II

PRODUCT YIELDS IN REARRANGEMENT OF I AT 70.3° IN 80% ETHANOL

Scavenger	$(I)_0$, *M*	Yield,[a] % II	 Toluene	 PhCHO	 Bibenzyl, $PhCH_2$-CH_2Ph
None	0.007	67.3	0.66	*b*	
None	0.028	88.6	*b*	*b*	0.08
None	0.112	41.9[c]	*b*	8	
Air	0.028	41.2	*b*	Trace	
O_2 (1 atm)	0.028	36.0	*b*	17	
O_2 (5 atm)	0.028	35.3		43	

[a] After 13 hr (*ca.* 6 half-lives); averages of duplicate results. [b] None detected. [c] Also 23% IV and some tar.

oxygen at 1 atm has in fact reduced the yield of II to a minimum.

We originally reported[2] that benzaldehyde was produced in 4% yield in the oxygen experiments (and a trace amount under air). However, using a milder means of evaporating the pentane used to extract the product, we found benzaldehyde in 17% yield and at 5 atm, 37 and 49%, by integrating the formyl proton resonance relative to those of the product, II. The formation of benzaldehyde supports the notion of scavenging of benzyl radicals by oxygen, according to eq 4 and 5. It is puzzling, however, that a compound

$$PhCH_2\cdot + O_2 \longrightarrow PhCH_2OO\cdot \xrightarrow{SH} PhCH_2OOH \qquad (4)$$

$$PhCH_2OOH \xrightarrow{OH^-} PhCHO + H_2O \qquad (5)$$

so sensitive to autoxidation survives in the presence of peroxy radicals, and that attempts to detect its oxidation product, benzoic acid, were negative.

***tert*-Dodecanethiol as Scavenger.**—The rearrangement was conducted under N_2 under the same conditions, except with the addition of various amounts of *tert*-dodecanethiol, a good scavenger of carbon radicals, but expected to be less effective than oxygen.[15] The yields of II appear in Table III, and indeed a rather high concentration of the thiol was required to reduce the yield of II to the level attained by the very small

$$PhCH_2\cdot + RSH \longrightarrow PhCH_3 + RS\cdot \qquad (6)$$

concentration of dissolved oxygen in equilibrium with the gas at 1 atm. No attempt was made to ascertain whether higher thiol concentrations would further reduce the yield of II. The yields of toluene determined by glpc are also included in Table III, and roughly account for the deficit in the yield of rearrangement product. Control experiments showed substantial losses of toluene during work-up, and the correction factor which is included in the data of Table III is undoubtedly not constant, in reality.

A possible complication in these experiments would be hydrogen-bond formation between I and the thiol. Amine oxides are known to be strong acceptors;[16] thiols will form hydrogen bonds to strong acceptors such as sulfoxides, but S–H stretching frequency shifts in the infrared are only one-fourth those for the corresponding O–H analogs,[17] and formation constants are not reported. The presence of a thiol molecule at the birth of the geminate radical pair might cause some scavenging of caged nitroxyl radicals as in reaction 7;

TABLE III

YIELDS OF PRODUCTS IN REARRANGEMENT OF I WITH OTHER SCAVENGERS

Scavenger	Scavenger concn, *M*	Yield, % II	 Toluene[a]	 II + toluene
RSH	0.00	86.4		86.4
RSH	0.021	84.5	*b*	84.5
RSH	0.042	75.4	4.3	79.7
RSH	0.084	69.9	12.2	82.1
RSH	0.105	66.1	21.8	87.9
RSH	0.525	33.9	(95)[c]	(129)
CCl_4	0.040	82.3		
CCl_4	0.124	76.9		
CCl_4	1.30	59.0		

[a] Corrected on basis of 31% recovery in control work-ups. [b] Trace only. [c] Estimate must be high; recovery during work-up probably >31%.

$$RSH + \cdot ONR_2 \longrightarrow RS\cdot + HONR_2 \qquad (7)$$

reaction 6, however, is too slow to allow this possibility, the reported rate constant for α-toluenethiol and benzyl radical being $5 \times 10^4\ M^{-1}\ sec^{-1}$.[18] Were reaction 7 able to compete with diffusion, then bulk scavenging should have diminished the yield of II at much lower thiol concentrations than actually observed. Therefore, hydrogen bond formation between I and thiol is probably without consequence in this system.

Tetrahalomethanes as Scavengers.—Carbon tetrabromide, bromotrichloromethane, and carbon tetrachloride were expected to be fair to excellent scavengers for the benzyl radical, as per reaction 8. The tetrabromide

$$PhCH_2\cdot + CX_4 \longrightarrow PhCH_2X + CX_3\cdot \qquad (8)$$

in particular is known to be as good a chain transfer agent as *n*-butanethiol in styrene polymerization,[15] and bromotrichloromethane is an excellent reagent for chain bromination of alkanes and aralkanes.[19] Unfortunately, CBr_4 and $BrCCl_3$ could not be used as scavengers, since they caused the pH of reaction mixtures to decrease markedly, in accord with literature reports that they undergo chain reactions with ethanol, producing acid, haloforms, and acetaldehyde.[20] In the presence of CBr_4 or $BrCCl_3$, considerable IV appeared, even if base was in moderate excess; $BrCCl_3$ in ethanol was even found to consume dilute alkali rapidly. It is, of course, possible that CBr_4 and $BrCCl_3$ might be used in chloroform as solvent.

Only CCl_4, a relatively poor chain-transfer agent in styrene polymerization, could be used as a scavenger in the rearrangement of I, and the results at various CCl_4 concentrations are presented in Table III. Even at 1.3 *M* CCl_4, the yield of II decreased only to 59%; a small amount of chloroform was detected by glpc in this run, but not the others, arising presumably from reaction 9. It may be doubted that attack on CCl_4

$$CCl_3\cdot + CH_3CH_2OH \longrightarrow HCCl_3 + CH_3\dot{C}HOH \qquad (9)$$

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(15) C. Walling, "Free Radicals in Solution," Wiley, New York, N. Y., 1957, pp 152, 153.

(16) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman, San Francisco, Calif., 1960.

(17) A. Wagner, H. J. Becher, and K. G. Kottenhahn, *Ber.*, **89**, 1708 (1956).

(18) R. D. Burkhart, *J. Amer. Chem. Soc.*, **90**, 273 (1968).

(19) (a) E. S. Huyser, *ibid.*, **82**, 391 (1960); (b) G. J. Gleicher, *J. Org. Chem.*, **33**, 332 (1968).

(20) J. W. Heberling, Jr., and W. B. McCormack, *J. Amer. Chem. Soc.*, **78**, 5433 (1956).

actually took place, in view of Walling and Lepley's detection[21] of less than 1% of benzyl chloride in thermolysis of phenylacetyl peroxide in CCl_4 at 40°. In the latter study, however, the concentration of benzyl radicals was probably many times greater than in the present work, a factor which favors coupling.

Methanol as Solvent.—In order to eliminate the solvent as a variable and reconcile our results with those of the Schöllkopf group,[13] we performed two experiments in 97% methanol–3% water at 45°, one under nitrogen and one under oxygen. The yield of II under nitrogen was 68%; under oxygen, 34%. Since a rough estimate of the uncertainty of these yields is ±4%, the cage effect might range from 40 to 60%, *i.e.*, 50 ± 10%.

Cyclohexanol as Solvent.—Cage effects in homolytic dissociation reactions are well known to increase with viscosity, as the separation by diffusion of geminate radical pairs becomes more difficult.[4,5,9,22] In search of a strong operational test[23] of a cage effect, we conducted the rearrangement of I in the viscous solvent cyclohexanol, which even at 70° is *ca.* ten times more viscous than ethanol.[24] It was at first hoped that product yields could be determined by the uv spectrophotometric method previously used for measuring rates of appearance of II and its substituted analogs.[13] In this way, we obtained the rate constant $4.7 \pm 0.1 \times 10^{-4}$ sec^{-1} under either nitrogen or oxygen. This technique could not, however, be used to measure yields, because the absorbance after several half-lives was the same under oxygen as under nitrogen. Since the yield was expected to be less under oxygen, this result was ambiguous and indicated that the byproducts, which must also have contained trigonal nitrogen bonded to phenyl, had essentially the same absorbance as II. The yield of II was measured instead using the *nmr* technique previously employed, with the results shown in Table IV, which also gives the yield in aqueous ethanol under oxygen as determined by the same worker during the same period, with the same sample of I HCl. The yield of II under oxygen in cyclohexanol is thus evidently doubled compared to the yield in ethanol.

TABLE IV

YIELD OF REARRANGEMENT OF I IN ETHANOL AND CYCLOHEXANOL

Solvent	% yield of II under N_2	O_2 (1 atm)	Cage effect, %
78% ethanol		29.5[a]	40[b]
97% cyclohexanol	84	58	69

[a] Average of duplicate runs; all runs used the same batch of of I HCl and were performed by the same worker. [b] *Cf.* text.

Discussion

The Meisenheimer rearrangement presents several intriguing mechanistic problems, which have been discussed by Johnstone[10d] and by Schöllkopf.[13] That of the operation of a cage effect and its magnitude under certain conditions has, we believe, been solved through the experiments described herein. It is best to discuss the evidence for the cage effect in the context of existing evidence for mechanism.

Dissociation mechanisms are supported by a variety of data, despite the early thought[25] that an S$_N$i mechanism might operate.

(1) The entropy of activation for rearrangement of I in 97% methanol is +33 eu,[13] consistent with formation of two particles, but highly inconsistent with an intramolecular migration, which must involve decrease of rotational entropy. A complication is the probably concomitant loss of water hydrogen bonded to the oxygen.

(2) Optically active N-benzyl-α-d_1-dimethylamine oxide, in which the benzyl α carbon is asymmetric, produces the dimethyl analog of II with 61–78% racemization, *i.e.*, 22–39% retention of configuration.[12] A dissociation mechanism explains this result, but a concerted, intramolecular mechanism is expected to be completely stereospecific. In the cage part of the rearrangement, one expects coupling to compete with rotation[4] of the benzyl radical; some net retention of configuration should result.

Additional data are consistent with dissociation mechanisms in general and support or require a radical mechanism in particular.

(3) CIDNP[14] (chemically induced dynamic nuclear polarization, now more correctly called chemically induced nuclear spin sorting) has been observed in at least two examples of the Meisenheimer rearrangement, that of I[26a] and that of benzyldimethylamine oxide hydrate (neat).[26b] That is, when the rearrangement has been conducted in an nmr spectrometer at a temperature such that it is rapid, the products have shown emission with greatly enhanced intensity, rather than absorption of normal intensity. This is compelling evidence that a major part of the reaction follows a radical cleavage–recombination mechanism. That both methyl and benzyl protons of I and the dimethyl analog have shown emission is in accord with prediction for geminate radicals.[27] The kinetics observed under both O_2 and N_2 (*cf.* discussion, *vide infra*) are consistent with a single cleavage mechanism, only part of which produces trappable radicals.

(4) Methylphenyl nitroxide radical has been detected during rearrangement of I in methanol, *via* esr spectroscopy.[13] The amount of radical produced was very small, however, and it might arise from a minor competing process. We believe otherwise, but the mere observation of the radical by no means proves that all the rearrangement involves it.

(5) The yield of toluene from rearrangement of I in aqueous ethanol is vanishingly small. A carbanion mechanism should produce a large quantity of toluene by diffusion-controlled proton transfer from the protic solvent (eq 10).

$$PhCH_2^- + ROH \longrightarrow PhCH_3 + RO^- \qquad (10)$$

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[21] C. Walling and A. R. Lepley, *J. Amer. Chem. Soc.*, **94**, 2007 (1972).

[22] W. Braun, L. Rajbenbach, and F. R. Eirich, *J. Phys. Chem.*, **66**, 1591 (1962).

[23] F. E. Herkes, J. Friedman, and P. D. Bartlett, *Int. J. Chem. Kinet.*, **1**, 193 (1969).

[24] "Chemical Engineers' Handbook," J. H. Perry, Ed., McGraw-Hill, New York, N. Y., 1950, pp 372, 373; the viscosities of cyclohexanol and 70% ethanol at 70° are, respectively, 6.2 and 0.59 cP (the latter interpolated between values for 40 and 100% ethanol).

[25] (a) G. M. Bennett and A. W. Chapman, *Ann. Rep.*, 122 (1930); (b) C. R. Hauser and S. W. Kantor, *J. Amer. Chem. Soc.*, **73**, 1437 (1951).

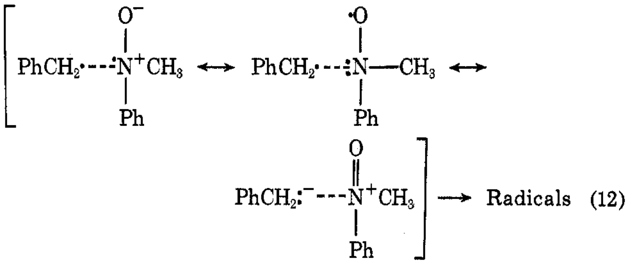
[26] (a) G. Ostermann and U. Schöllkopf, *Justus Liebigs Ann. Chem.*, **737**, 170 (1970); (b) A. R. Lepley, *J. Amer. Chem. Soc.*, **92**, 1101 (1970).

[27] R. Kaptein, *Chem. Commun.*, 732 (1971); we assume the α-proton hfc for benzyl radical to be negative, for the β (CH_3) protons of the nitroxyl radical, positive, and the latter has the larger g value.

(6) Polar substituents affect the rate of rearrangement of I much less than expected if dissociation produced a carbanion. Thus, substitution in the migrating benzyl group gives ρ +0.9,[13a] while substitution in *N*-phenyl gives ρ +0.9 also.[13b] In contrast, the base-catalyzed hydrogen isotope exchange of substituted toluenes has ρ +4.0.[28] The sign of ρ for the rearrangement is inconsistent with formation of benzyl cation; benzyl radical is therefore implicated.

The sign of ρ is the opposite of that usually found for radical reactions, *e.g.*, radical chain halogenations of substituted toluenes; bromination by Br_2 or NBS has ρ −1.4.[29] The usual explanation has been contribution of charge-transfer resonance structures to the transition state, as depicted for bromination and Meisenheimer rearrangement in eq 11 and 12. Zavitsas has recently questioned this idea,[30] and shown that substituent effects in certain systems correlate remarkably closely with differences in bond energies. Either interpretation of substituent effects focuses attention on the covalent bond scission. Schöllkopf, however, has neglected this approach in attributing the ρ values to dissolution of the oxide–water hydrogen bond. In support, he notes that the dissociation constants of the conjugate acids of the amine oxides give ρ +1.3. While this factor may contribute in the proper direction, it is unlikely that dissociation of hydrogen bonds, in which the proton is less than 20% transferred to the basic atom,[31] can have a ρ value as large as that for Brønsted acidity and, even less likely, a $\Delta H^{\ddagger}$ value in excess of 30 kcal/mol.

$$[PhCH_2\cdot{-}{-}{-}\dot{H}{-}{-}\cdot Br \longleftrightarrow PhCH_2^+{-}{-}{-}\dot{H}{-}{-}{-}Br^-] \longrightarrow PhCH_2\cdot + HBr \quad (11)$$



$$\left[PhCH_2\cdot{-}{-}{-}\dot{N}^+(O^-)(Ph)CH_3 \longleftrightarrow PhCH_2\cdot{-}{-}{-}\colon\!N(\cdot O)(Ph){-}CH_3 \longleftrightarrow PhCH_2\colon^-{-}{-}{-}N^+(=O)(Ph)CH_3\right] \longrightarrow \text{Radicals} \quad (12)$$

The charge-transfer hypothesis is supported by published rate data[32] (Table V). Most striking is the 40-fold acceleration due to two *p*-nitro groups in diphenylmethyldimethylamine oxide. The failure of the 9-fluorenyl analogs to rearrange significantly faster than diphenylmethyl must be due to compensation by an opposing effect, the absence of steric strain in the 9-fluorenyl oxide. The 2.5-fold greater rate of the *o*-tolyl compound suggests that relief of steric strain is important. Alternatively, the data of Table V could be explained according to Zavitsas, that is, in terms of the ability of substituents to decrease bond energies by delocalizing the unpaired electron.

TABLE V

EFFECT ON MIGRATING GROUP STRUCTURE ON REARRANGEMENT RATE

	—$10^3 k$, sec^{-1}, for stationary groups—		
Migrating group	$(CH_3)_2$	$-(CH_2)_5-$	$-(CH_2)_2-O(CH_2)_2-$
Diphenylmethyl	4.4	3.5	1.8
9-Fluorenyl	5.3	5.1	3.5
Phenyl-*o*-tolylmethyl	11.8	10.0	5.2
p,p'-Dinitrodiphenylmethyl	200		

Reversibility of Radical Cleavage.—The initial cleavage, 2, is probably irreversible, because optically active I in which the chiral center is nitrogen does not racemize during rearrangement.[18] Reversibility should lead to a detectable, if small, degree of racemization.

The fact that the rate of rearrangement of I is the same under oxygen as under nitrogen further supports this conclusion. If the scission were reversible, bulk radicals should also couple to regenerate I, as well as to form II. Oxygen would eliminate this and raise the observed rearrangement rate. A classic case in which this occurs is the thermal rearrangement of *N*-(1-cyanocyclohexyl)pentamethyleneketenimine to 1,1′-dicyanobicyclohexyl, which proceeds by dissociation into pairs of 1-cyanocyclohexyl radicals.[33]

Effect of Solvent on Rate.—The Meisenheimer rearrangement appears to be accelerated by decreases in solvent polarity, although the available data are limited. The rate for I increases by over two orders of magnitude when the solvent is changed from 97% methanol to 3% water–97% tetrahydrofuran.[13] We have concluded (*vide supra*) that the reaction is some two orders of magnitude more rapid in chloroform than in aqueous ethanol. These observations deserve further investigation, in order to determine whether the rate variations are due to (a) favoring of the dissipation of charge at the transition state by less polar solvents, or (b) weakening of hydrogen bonding, *i.e.*, solvation, of the oxide, raising its energy and increasing its rate of dissociation.

The Cage Effect.—The effect of radical scavengers on the outcome of the Meisenheimer rearrangement has not previously been taken into account. We have found the scavenger oxygen, known to react very rapidly with carbon radicals,[15] to reduce the yield of II from I to a limiting value which is 40% of that in its absence. In addition, *tert*-dodecanethiol and possibly carbon tetrachloride also diminished the yield of II, although limiting yields were not established in these cases. The role of all three of these must be to react with free benzyl radicals according to eq 4, 6, and 8, preventing them from reacting with free nitroxide radicals; the products benzaldehyde, toluene, and chloroform are indicative of these reactions. Operation of a cage effect explains the existence of a limiting yield, the inability of the scavenger to react with 100% of the radicals which form. Previous studies of cage effects have shown that, even when the radical–scavenger reaction is diffusion controlled, more than 0.1 *M* scavenger concentration is required to interfere with a cage effect.[34] In our experiments the

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[28] D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, p 29.

[29] R. E. Pearson and J. C. Martin, *J. Amer. Chem. Soc.*, **85**, 3142 (1963).

[30] A. A. Zavitsas, *ibid.*, **94**, 7390 (1972).

[31] D. Gurka, R. W. Taft, L. Joris, and P. v. R. Schleyer, *ibid.*, **89**, 5957 (1967).

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

[33] C-H. S. Wu, G. S. Hammond, and J. M. Wright, *J. Amer. Chem. Soc.*, **82**, 5386 (1960).

[34] H. P. Waits and G. S. Hammond, *ibid.*, **86**, 1911 (1964).

concentration of oxygen in solution never exceeded 0.01 *M*, and was usually much less. The thiol used and CCl_4 were expected to be less reactive than oxygen toward benzyl radicals, and accordingly much higher concentrations were required to depress the yield of II. Thus, even at the concentrations of 0.5 and 1.3 *M*, respectively, these compounds could not have suppressed the cage effect itself. CCl_4 at 1.3 *M* decreased the yield only to 59%. The cage effect in 80% ethanol at 70° is thus regarded as being 40%, and that in 97% methanol at 45°, *ca.* 50%. If the latter is significantly greater than the former, it is consistent with the known tendency of cage effects to increase at lower temperatures, as viscosity increases.[4]

It might be argued that a different mechanism is responsible for the 36% yield of II not eliminated by oxygen. This is the Achilles' heel of the cage effect hypothesis, which may be defended in the following four ways.

(1) The phase of the CIDNP effect (in the case of I and its dimethyl analog, emission) agrees with theory for geminate radicals. Existing theory[35] is powerful and has succeeded in accounting for enhancement factors, phase, the multiplet effect, and other aspects of CIDNP. The most convincing experiment in the present context would be observation of CIDNP in the presence of an efficient scavenger to prevent coupling of any but geminate radicals. This might be done using CBr_4 or $BrCCl_3$ in chloroform solution.[35a]

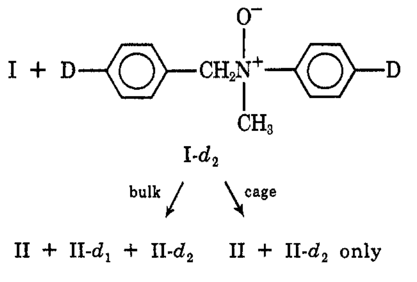
(2) If the rearrangement could be conducted in the vapor phase, in the presence of a scavenger, the yield should fall to zero, since at low pressures there are no cages. Although this experiment has provided elegant support for other cage effects, *e.g.*, that which forms methyl acetate in the thermal decomposition of acetyl peroxide,[36] it is probably not applicable here because of the low or nil volatility of amine oxides.

(3) The rate constant for the rearrangement of I is the same under oxygen as under nitrogen. Were another mechanism involved, a different rate constant should apply to the nonscavengeable part of the reaction. The rate constant under nitrogen would be the sum of that rate constant and the rate constant characteristic of the production of free radicals. Since the cage effect is roughly one-third of the total, the rate should be one-third under oxygen what it is under nitrogen, if two mechanisms were involved. For the cage-effect mechanism, the rate-limiting step, cleavage of I into two radicals, is the same whether caged or free radicals are considered. Following, as we have done, the formation of product, one in effect neglects two-thirds of the reaction, but, since the kinetics are first order, the rate constant is the same. We are not aware of the application of this criterion in any previous case, nor, more important, are we aware of any case which *does* involve two mechanisms, one nonradical, the other producing radicals with almost no cage effect, and both producing the same product.

(4) The limiting yield of rearrangement product is greater in a more viscous solvent. This criterion has been applied often, like no. 2; it depends on the anticipated decrease in rate of diffusion of radicals from their cage as the viscosity increases. We find the limiting yield in cyclohexanol to be 58%, which is 69% of the yield under nitrogen. A cage effect of 69% is nearly double that found in ethanol, an increase which is consistent with increases observed in other systems. It is noteworthy that viscous alcohols, including also glycerol and other glycols, have been used only twice previously[37,38] for investigating cage effects. Although this has provided us some anxious moments, the burden of proof is on the one who dares to suggest that a viscous solvent will not increase a cage effect. We prefer the thought that this observation and the previous ones extend the range of viscous solvents useful for investigating cage effects.

It might be argued that the alleged increase in cage effect in cyclohexanol is an illusion, actually due to decreased efficiency of oxygen as scavenger. That is, if the scavenging reaction is diffusion controlled, its rate must decrease considerably with a tenfold increase in viscosity, and a significant amount of coupling of bulk radicals to II might compete with scavenging. While an experiment conducted at 5 atm would settle the matter, we can present two additional observations which strongly refute this objection. First, the solubility of oxygen must be greater in cyclohexanol than in aqueous ethanol, both at 70°, by Henry's law, since the former is much less volatile; *i.e.*, the partial pressure of oxygen over cyclohexanol is more nearly 1 atm. Second, the decrease in rate of scavenging due to viscosity increase would be comparable to that due to decreasing the partial pressure of oxygen, as by changing from pure oxygen to air. In the ethanol experiments, this increased the yield of II from 36% to only 41%, an increase of less than one-fifth.

Discrepancy between the Present Results and Those of Schöllkopf, *et al.*—The Schöllkopf group has argued[13] that the rearrangement in methanol or water is intramolecular, *i.e.*, has a cage effect, to the extent of 75–95%, depending on solvent and temperature, in serious conflict with our estimate using the scavenger method. Their crossover experiment, decomposition of equal mixtures of I and I-d_2, and mass spectrometric analysis of the product for II, II-d_1, and II-d_2, is capable of affording an accurate estimate of cage effect. An analogous experiment[39] with the thermal decomposition of azo-1-phenylethane at 105° gave a result in excellent agreement with that of a scavenger experiment.[40] Evidently, however, the amine oxide solutions were not degassed; so most of the product isolated, in unstated yield, must have been cage product. This



(13)

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[35] G. L. Closs, *J. Amer. Chem. Soc.*, **91**, 4552 (1969); R. Kaptein and L. J. Oosterhoff, *Chem. Phys. Lett.*, **4**, 195, 214 (1969).

[35a] NOTE ADDED IN PROOF.—A. R. Lepley has recently reported to the senior author very strong emission from II in a mull of IHCl, DABCO, and $BrCCl_3$.

[36] L. Herk, M. Feld, and M. Szwarc, *J. Amer. Chem. Soc.*, **83**, 2998 (1961).

[37] W. N. White, H. S. White, and A. Fentiman, *ibid.*, **92**, 4477 (1970).

[38] W. K. Robbins and R. H. Eastman, *ibid.*, **92**, 6076, 6077 (1970).

[39] S. Seltzer and E. J. Hamilton, *ibid.*, **88**, 3775 (1966).

[40] F. D. Greene, M. A. Berwick, and J. C. Stowell, *ibid.*, **92**, 867 (1970).

explains the fact that the product was predominantly II and II-d_2, with very little II-d_1. Our experiments with methanol underscore this interpretation.

Stereochemistry of the Rearrangement of I.—We have noted in our communication[2] that the cage effect of I and the extent of retention of configuration in migrating benzyl-α-d_1 in the dimethyl analog of I are similar, although, owing to low rotation values, the latter value is not accurately known. Nevertheless, since the bulk reaction must lead to quantitative racemization, the retention occurs entirely in the cage process, and is very high, 62–100%. A second case, also involving the cleavage of only one bond, has been studied by Porter, *et al.*,[7] the photodissociation of optically active phenylazo-2-phenylbutane. In hexadecane, only about 10% racemization of azo compound took place, while about 50% of the remaining azo compound had undergone dissociation (inferred from the dependence of the quantum yield on viscosity in a series of paraffins).

The behavior of a typical two-bond initiator, azo-1-phenylethane, contrasts strongly with the pattern set by the Meisenheimer rearrangement and Porter's azo compound. Thermal decomposition of the optically active azoethane gave 2,3-diphenylbutane which was nearly a statistical mixture of *d*, *l*, and meso forms, even for the cage process (in the presence of the scavenger 2-methyl-2-nitrosopropane).[40] In this case a nitrogen molecule intervenes between the geminate radicals, and this may increase the probability that a 1-phenylethyl radical will rotate by 180° from its original orientation. Since, however, these experiments were performed at 105°, one should await a study of the photolysis at ambient temperature before pinning the blame on the nitrogen molecule.

Why is the yield of the Meisenheimer rearrangement nearly quantitative? In other words, why isn't more bibenzyl formed, if part of the reaction involves free radicals? Those radicals which diffuse into the bulk would normally give three coupling products in ratio 1:2:1, one of which should be bibenzyl. The clue is that one radical, methylphenyl nitroxide, is observable,[13] while the other, benzyl, is not. The nitroxide cannot couple with itself, but it can scavenge benzyl radicals. A similar situation obtains in the thermal decomposition of *tert*-butyl triphenylperacetate, $Ph_3CCO_3C(CH_3)_3$, in cumene, in that triphenylmethyl radical builds up and scavenges *tert*-butoxy and cumyl radicals; dicumyl cannot be detected.[6]

The way in which the nitroxide radical attains its high concentration has already been suggested by Schöllkopf: dimerization early in the reaction destroys benzyl radicals, converting them to bibenzyl. Formation of 0.05% bibenzyl from 0.01 *M* I allows the formation of 10^{-5} *M* nitroxide, easily detected by esr. The rapid rate of scavenging of benzyl radicals by nitroxide—inferred from the existence of a cage effect involving both—keeps the concentration of benzyl below observable limits. Schöllkopf did not believe that the detectable nitroxide radicals played a major role in the reaction, while our postulated cage effect of *ca.* 40% indicates that they produce more than half the product. Johnstone[10d] considered the kinetic and esr results to conflict, in that intermolecularity implied to him a departure from first-order kinetics. If, however, bond scission is rate determining, no amount of complications after this step can affect the kinetics, provided that there is no attack of radicals on amine oxide.

Experimental Section

General.—Nmr spectra were recorded and integrated on a Varian A-60 instrument; for later work a Jeolco C-60HL was utilized. For quantitative analyses of II, benzaldehyde, and toluene, the sample was dissolved in a known volume of CCl_4 containing a known concentration of anisole (δ for methyl protons, 3.55 ppm, remote from peaks of any products), and the methyl and/or methylene or formyl singlets integrated. Synthetic mixtures of II, toluene, and anisole were likewise integrated, and corrections applied.

Glpc analyses were performed with an F & M Model 700 chromatograph, the recorder equipped with a disc integrator. Quantitative analysis of toluene and bibenzyl was achieved with reference to synthetic mixtures.

Monoperphthalic Acid.—The method of Payne[41] was used with slight modification. A solution of sodium carbonate monohydrate (62 g, 0.5 mol) in 250 ml of water in a 1-l. beaker was cooled to −3 to −5° in brine, stirred magnetically, and chilled 30% hydrogen peroxide (68 ml, 0.6 mol) was added; the temperature remained below 0°. Phthalic anhydride, well pulverized (75 g, 0.5 mol), was added and the solution was stirred vigorously for 30 min, when all the anhydride had usually dissolved. Ether (350 ml) was added, then slowly 30 ml of concentrated sulfuric acid in 150 ml of water; gas was evolved; and a slushy white precipitate of phthalic acid formed. After filtration through glass wool into a 2-l. separatory funnel, the aqueous layer was further extracted with three 250-ml portions of ether. The combined ether extracts were washed with cold 40% ammonium sulfate solution and dried over magnesium sulfate in the refrigerator. Analysis by iodimetry, treatment of 2 ml of ethereal solution with 15 ml of 20% aqueous potassium iodide, followed by titration with 0.100 *N* sodium thiosulfate solution, indicated a yield of 88%; yields ranged from 69 to 99% in other runs.

***N*-Benzyl-*N*-methylaniline *N*-Oxide Hydrochloride (I HCl).**—A modification of the method of Stevens, *et al.*,[32] was used. A chilled solution of *N*-benzyl-*N*-methylaniline (Eastman) (70 g, 0.35 mol) in anhydrous ether was treated with ethereal monoperphthalic acid solution in 10% excess, at 0°, in a resin kettle equipped with a thermometer and stirring bar, immersed in an ice–salt bath. After stirring for 16–20 hr at −2 to 0°, the ether was decanted, the pale yellow-green cake on the kettle walls was dissolved in methylene chloride, and dry hydrogen chloride was bubbled through for 0.5 hr. The solution turned deep rose and phthalic acid precipitated. This was filtered off and the solvent was stripped under vacuum. The clear brown, viscous syrup which remained was dissolved in 100 ml of warm acetone, when a copious crop of white crystals appeared, which were collected under suction and dried. The material was stable indefinitely if stored under hydrogen chloride gas. The yield was 44.0 g (50.6% of theory); mp 126–127° with slow heating, 134–135° with rapid heating (lit. mp 124–126°,[42] 131°,[32] or 135°[43]); nmr δ 4.22 (3 H, singlet, methyl) and 5.46 ppm (2 H, AB quartet, methylene), in chloroform; aromatic absorption hidden by solvent. *Anal.* Calcd for $C_{14}H_{16}NOCl$ (mol wt, 249.7): C, 67.20; H, 6.44; N, 5.60; Cl, 14.20. Found: C, 67.32; H, 6.48; N, 6.09; Cl, 14.34.

Oxygen Scrubber.—Prepurified nitrogen was passed through a scrubber, prepared as follows, on its way to the reaction vessel. Zinc amalgam was prepared by adding mossy zinc to mercury in a beaker. To this was added 3 *N* hydrochloric acid to clean the zinc and hasten its amalgamation. The amalgam, washed several times with distilled water, was transferred to a 0.5-l. gas washing bottle. An aqueous solution of 60 ml of perchloric acid and 20.5 g of chromic perchlorate hydrate in 500 ml of water was added to the bottle. The resulting blue-black solution turned bright peacock blue as nitrogen passed through it for several hours. When the amalgam becomes exhausted, the green color of chromic ion appears.

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[41] M. Payne, *J. Org. Chem.*, **24**, 1354 (1959).

[42] J. Meisenheimer and J. Hoffheinz, *Justus Liebigs Ann. Chem.*, **385**, 117 (1919).

[43] J. Meisenheimer, *ibid.*, **449**, 188 (1926).

General Procedure for Rearrangement of I.—The reaction vessel was typically a 1-l., three-necked, round-bottomed flask fitted with two 1.5-ft condensers in series, a calibrated thermometer graduated in 0.1°, and a glass tube for bubbling oxygen or nitrogen through the solution. For runs conducted under nitrogen, a four-necked flask was used, the fourth neck being attached *via* flexible tubing (latex or Tygon) to a second, two-necked flask in which a solution of base was purged of air before being poured under slight nitrogen pressure into the solution of I HCl. Both flasks were thermally equilibrated in a large constant-temperature water bath for *ca.* 1 hr or more before mixing.

For a typical run under nitrogen, I HCl (0.495 g, 1.99 mmol), in 200 ml of 80% ethanol in the four-necked flask, and NaOH, (0.150 g, *ca.* 3.7 mmol) in 200 ml of 80% ethanol in the two-necked flask, were purged with scrubbed nitrogen and equilibrated at 70.3°. The base solution was poured into the I solution through the tubing and the mixture was allowed to stand under a slow nitrogen stream for 20 hr. The reaction mixture was poured into 800 ml of ice-cold saturated salt solution and extracted with five 150-ml portions of pentane. The pentane was stripped through a 1-ft glass helices packed column by means of a warm water bath. The residue, 2.5 ml, was analyzed by nmr (*vide supra*) after addition of 1.0 ml of 1.98 *M* anisole in CCl_4. The yield of II was 67%; no IV was detected.

Runs under air or oxygen were carried out similarly, except that purging prior to mixing was usually omitted.

The two runs at 5 atm oxygen employed a 500-ml Parr pressure bottle connected by copper tubing and compression fittings to the outlet of a reducing valve on an oxygen cylinder. Stirring was done with an oval Teflon-covered stirring bar and a magnet, attached to a speedometer cable, immersed in the water bath and driven by a stirring motor. The reducing valve was set at 60 psig after the vapor space had been purged briefly with oxygen, the flask was immersed in the bath, and stirring was begun. After *ca.* 13 hr, more than 6 half-lives, the pressure was released and the solution was worked up as described above. In these and 1 atm oxygen or air runs, benzaldehyde was detected and determined by nmr (formyl resonance at 10.0 ppm), as well as by odor. The yield of benzaldehyde was high only if the stripping of pentane was done with tepid water; use of hot water or steam resulted in low yields.

When *tert*-dodecanethiol was used as scavenger, it was added *via* a disposable syringe after mixing of the amine oxide and base solutions. CCl_4 when used as scavenger was added to the base solution before mixing.

Kinetics of the Rearrangement of I HCl.—Kinetic runs were carried out with slight modifications of the above techniques. In place of the thermometer there was a long Teflon syringe needle, to withdraw aliquots, 100 ml at first, decreasing to 50 ml at the end, as the concentration of product increased. The aliquots were quenched in ice water and worked up and analyzed for II as above. Rate constants were calculated from slopes of plots of $\log [II_f/(II_f - II_t)]$ *vs.* time. The length of time required for one-point experiments was chosen according to the results (*cf.* text).

Recovery of Toluene.—Synthetic mixtures containing *ca.* 0.5 mmol of toluene and some II in 80% ethanol were prepared and subjected to the standard work-up procedure. The recovery of toluene averaged 31% while that of II was quantitative. The observed yields of toluene were corrected by dividing by 0.31. No control was run for the largest amount of toluene observed, 1.13 mmol; in this case the correction factor should probably be smaller than 1/0.31.

Reaction of Tetrahalomethanes with Ethanolic Base.—A 0.10 *M* solution of bromotrichloromethane in 80% ethanol was allowed to stand overnight at room temperature. The apparent pH as measured with a meter was 1.8; a 5-ml aliquot diluted to 45 ml had pH 2.5. Standard aqueous 0.1 *N* NaOH was added; 5.0 ml brought the pH to 3.00, 6.5 ml to 4.70, and 10.0 ml to 11.80. Ten minutes later, the pH had drifted to 3.4.

A 0.10 *M* solution of carbon tetrabromide in 80% ethanol had pH 1.3 after standing overnight. Standard aqueous 0.1 *N* base, 3.0 ml, brought the pH to 11.60; 10 min later the pH was 10.0.

A 0.10 *M* solution of carbon tetrachloride in 80% ethanol, after standing for 40 min, had pH 7.3; dilution with 40 ml of ethanol brought the pH to 5.4. Only 0.5 ml of 0.1 *N* base was required to bring the pH to 12.3, where it remained for at least 10 min.

Rearrangement of I in Chloroform.—I HCl (3.0 g, 12 mmol) was dissolved in 200 ml of chloroform, and ammonia was bubbled in for 0.5 hr at 0°. The white precipitate of ammonium chloride was removed by filtration, and the chloroform was stripped on a rotary evaporator over a steam bath. CCl_4 (25 ml) was added and evaporated to remove traces of chloroform. The residue, a golden yellow liquid, bp 90° (0.1 mm), weighed 2.28 g (10.7 mmol) (maximum), 89% of theory: nmr δ 2.90 (3 H, singlet, methyl) and 4.76 ppm (2 H, singlet, methylene), in the aliphatic region, identical with the spectrum of the product from rearrangements in 80% aqueous ethanol. There was no absorption due to IV, which absorbs at δ 2.84 (3 H, methyl) and 4.35 (2 H, methylene) ppm, both singlets. *Anal.* Calcd for $C_{14}H_{15}NO$ (mol wt, 213.27): C, 78.84; H, 7.08; N, 6.56. Found: C, 78.42; H, 6.88; N, 6.74.

CIDNP from Rearrangement of I in Chloroform.—I HCl (*ca.* 125 mg, 0.5 mmol) was dissolved in 1 ml of chloroform in an nmr tube. The spectrum showed a methyl singlet at δ 4.22 and a methylene AB quartet at 5.46 ppm. After addition of DABCO (1,4-diazabicyclo[2.2.2]octane), *ca.* 100 mg (0.9 mmol), stoppering, and shaking, some precipitate remained. It was previously shown that DABCO hydrochloride is insoluble in chloroform. The nmr spectrum now showed, besides the singlet at 3.0 ppm due to DABCO, both methyl and methylene signals of I at higher field by *ca.* 0.3 ppm. Addition of more DABCO caused slight further shifts to higher field. The solvent shifted simultaneously to lower field by *ca.* 0.3 ppm, attributed to hydrogen bonding to both DABCO and the free amine oxide. (A solution of pyridine *N*-oxide in chloroform showed a similar low-field shift of the solvent resonance.)

The probe of the A-56-60 spectrometer was heated to 60° and the tube containing the chloroform solution of I and DABCO was reinserted. Scans of the spectrum within the first 2 min showed negative emission singlets at 2.9 and 4.7 ppm, characteristic chemical shifts of the methyl and methylene protons of II. Within 10 min, these became positive absorption peaks.

***N*-Benzyl-*N*-methylaniline.**—I HCl (12.1 g, 0.0485 mol) was allowed to rearrange for 19 hr at 72° in 350 ml of 80% ethanol in the presence of tris(hydroxymethyl)aminomethane (Tris) (29.0 g, 0.24 mol) under nitrogen. The work-up proceeded as above, affording 7.7 g of orange-yellow oil, the nmr spectrum of which showed singlets in the aliphatic region characteristic of both II and IV. The product was partitioned between pentane and aqueous 0.1 *N* HCl, the aqueous phase was made basic with dilute NaOH solution, and the oil which separated was extracted into pentane, which was stripped, leaving IV (3.2 g, 0.015 mol) (31%), bp 85° (0.15 mm), nmr as given above for IV. Addition of authentic IV (Eastman) enhanced existing nmr peaks. For picrates, the reaction product (from MeOH) had mp 101–102°; authentic IV (from MeOH) had mp 101–102°; the mixture had mp 101–102°; authentic material (from EtOH) had mp 101–104°; the mixture of picrates of an authentic sample (from MeOH and EtOH) had mp 101–104° (lit. mp 103°,[44] 128°[10b]; the latter melting point reported for material from EtOH, combustion analysis reported to agree with formula $C_{20}H_{18}N_4O_7$).

Anal. (of authentic material from EtOH). Calcd for $C_{20}H_{18}N_4O_7$ (mol wt, 426.37): C, 56.47; H, 4.03; N, 13.17. Found: C, 56.20; H, 4.21; N, 13.30.

We conclude that the report[10b] of mp 128° for IV picrate is in error.

Reactions of Amines with Amine Oxides. A. I HCl and Triethylamine.—I HCl (1.0 g) and triethylamine (4.1 g) in 50 ml of 90% ethanol were heated at 70° for 4 hr, and the standard work-up was applied. The products showed no evidence of IV in the nmr. Repetition of the experiment at 80° for 10 hr with the same, and then threefold, amount of triethylamine gave traces of IV.

B. Trimethylamine Oxide and *N*-Benzyl-*N*-methylaniline.—A solution of these compounds, 4.0 and 1.8 g, respectively, in 50 ml of 90% ethanol was refluxed for 19 hr. Following standard work-up, the nmr of the product showed no evidence of II.

C. I HCl and Pyridine.—A solution of these compounds (1.0 and 5 g, respectively) in 50 ml of 90% ethanol was refluxed for 4 hr under nitrogen. Standard work-up gave a product consisting of IV and II in approximate ratio 2:1. Pilot experiments were undertaken to develop a method of determining pyridine *N*-oxide: the reaction mixture was to be diluted with several hundred milliters of water and the pyridine removed by distillation; pyridine *N*-oxide would remain in the residue and be determined

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[44] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds, A Laboratory Manual," 5th ed, Wiley, New York, N. Y., 1964, p 336.

by uv absorption. Pyridine has λ_{max} 256 nm (log ϵ 3.5); pyridine *N*-oxide has λ_{max} 255 nm (log ϵ 4.1). Distillation of a dilute solution of pyridine caused eventual disappearance of the 256-nm maximum, but end absorption persisted off scale at low wavelength; evidently an impurity had been concentrated. Distillation had no effect on the absorbance of dilute pyridine *N*-oxide solution [*N*-oxide from Aldrich was recrystallized from CCl_4; colorless plates, mp 68–69° (lit.[45] mp 65–66°), were used]. Distillation of a solution of pyridine and pyridine *N*-oxide gave a uv spectrum lacking the fine structure characteristic of pyridine, but with λ_{max} 255 nm, and going off scale as characteristic of the impurity in pyridine. The reaction mixture, after pentane extraction of II and IV, gave after distillation a residue with the uv maximum typical of pyridine *N*-oxide and the impurity; absorbance of 2.1 l. of solution was 0.60; concentration of oxide was therefore 4.3×10^{-5} *M*, total 9.1×10^{-5} mol; theoretical yield of oxide assuming 65% yield of IV was 2.7×10^{-3} mol; actual yield was 3.3% of theory.

Registry No.—I HCl, 16547-17-4; II, 6880-03-1; IV, 614-30-2; IV picrate, 38734-75-7; monoperthalic acid, 2311-91-3; O_2, 7782-44-7; *tert*-dodecanethiol, 25103-58-6; CCl_4, 56-25-3.

Acknowledgments.—We are grateful to the Department of Chemistry at Rice University for permission to use the Varian A-56-60 nmr spectrometer while J. P. L. was attending the 159th National Meeting of the American Chemical Society in Houston, and to Professor Arthur R. Lepley for assistance in performing the CIDNP experiment. We thank Mr. David G. Jelinek (Central Michigan University) for reinvestigating the picrate of *N*-benzyl-*N*-methylaniline. This work was supported by grants from the U. S. Army Research Office, Durham, and the Graduate School of Boston University.

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[45] H. S. Mosher, L. Turner, and A. Carlsmith, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 828.

Mechanism of the Base-Induced Decomposition of *N*-Nitroso-*N*-methylurea

SIDNEY M. HECHT* AND JOHN W. KOZARICH

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

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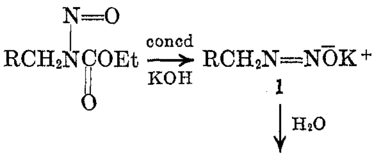
The mechanism corresponding to the base-induced decomposition of *N*-nitroso-*N*-methylurea is discussed. Evidence is presented for the decomposition which is consistent with initial abstraction of a urea proton, but not with a mechanism involving initial nucleophilic addition to the nitroso or carbonyl groups.

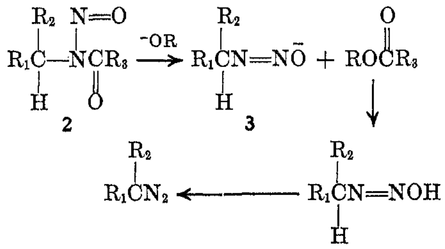
The base-induced decomposition of *N*-nitrosoamides, -carbamates, and -ureas to diazoalkanes has been the subject of many synthetic and mechanistic investigations. The mechanistic considerations, in particular, have stimulated considerable debate. In 1894, von Pechmann established that the hydroxide-induced decomposition of nitrosocarbamates afforded diazoalkanes.[1] Hantzsch and Lehmann[2] isolated the methyl and benzyl diazotates (**1**) and demonstrated that treatment of **1** with water afforded the corresponding diazoalkanes.



R = H, C_6H_5

An investigation by Gutsche and Johnson[3] of the methoxide-induced decomposition of several *N*-nitroso-*N*-benzylcarbamates expanded this scheme (Scheme I) and the subsequent isolation of methyl ethyl carbonate[4] from the base-induced conversion of *N*-nitroso-*N*-cyclohexylurethane (**2a**) provided convincing evidence for a mechanism initiated by methoxide attack on the carbonyl carbon. This scheme has also been established as operative for the decomposition of *N*-nitrosoamides.[5–7] Similarly, by indicating the formation of alkyl carbamate, Applequist and McGreer[8] implied that the alkoxide-induced decomposition of *N*-nitroso-*N*-cyclobutylurea (**2b**) to diazocyclobutane was initiated by attack on the carbonyl moiety.

SCHEME I



a, $R_1 = H$; $R_2 = C_6H_{11}$; $R_3 = OEt$
b, $R_1R_2 = (CH_2)_3$; $R_3 = NH_2$

In 1966, however, Jones, Muck, and Tandy[9] described experiments which appeared to exclude the Applequist and McGreer scheme as a possible mechanism for the conversion of *N*-nitroso-*N*-(2,2-diphenylcyclopropyl)urea to 2,2-diphenyldiazocyclopropane. They provided an alternate mechanism involving alkoxide attack on the nitroso moiety of the urea (Scheme II). A third mechanism which involved proton abstraction as the first step (Scheme III) was also excluded on the basis of several observations. Jones, *et al.*,[9] were careful to limit their discussion to the decomposition of *N*-nitroso-*N*-(2,2-diphenylcyclo-

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[8] D. E. Applequist and D. E. McGreer, *J. Amer. Chem. Soc.*, **82**, 1965 (1960).

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