

refrigerator in the solid state and liquefied on the steam-bath under nitrogen. The tubes were sealed under nitrogen and placed in an oil-bath at the appropriate temperature. At the proper time each tube was removed, opened, and the contents were poured into 5 ml. of water which was promptly extracted with 2 ml. of pentane. The pentane extracts were washed with 5-ml. portions of 10% sodium hydroxide solution and then analyzed by gas chromatography. Table III records the results.

Equilibration of the Three Olefins.—The equilibration experiments were conducted with the same techniques employed in the kinetic experiments, and the results are recorded in Table II.

Elimination Reactions of 2-Phenyl-2-butyl Chloride (Runs 1 and 2).—Dry glacial acetic acid, or a dry solution of 0.011 *M* *p*-toluenesulfonic acid in acetic acid (4 ml.), was preheated to 49.85 ± 0.05°. Sufficient chloride was added to make each solution 0.1 *M* in substrate. After the appropriate times (see below), reaction aliquots were extracted with pentane, with water, dried and analyzed by V.P.C. In run 1 where *p*-toluenesulfonic acid was present, aliquots were taken after 9, 10, 11, 14 and 20 min., and in run 2 (absence of the same acid), aliquots were taken after 10, 15 and 20 minutes. The logarithm of each concentration found for each olefin was plotted against time and was extrapolated back to 0 time to correct for isomerization of olefin after it was formed. The amounts of unreacted chloride were determined after isolation by titrating with standard alcoholic silver nitrate solution; in no case was less than 90% of the chloride unreacted. The chloride was found to pyrolyze under the V.P.C. analytical condition to give 63.8% *cis*-II, 32.8% III, and 3.5% *trans*-II. The amount of each olefin contributed to the observed products by pyrolysis of unreacted starting material and by the small amount of *cis* contaminant in the starting chloride was calculated and deducted from the observed values. These corrections never exceeded 1.5%. The final results are recorded in Table I.

Elimination Reactions of 2-Phenyl-2-butyl Acetate (Runs 3 and 4).—In run 3, a stock solution of 0.009 *M* *p*-toluenesulfonic acid in dry glacial acetic acid was prepared, and to 4.00-ml. portions was added sufficient acetate (*ca.* 0.090 g.) to give solutions 0.10 *M* in substrate. Reaction mixtures were placed in a constant temperature bath at 49.85 ± 0.05°, and were quenched after 5, 7.5 and 10 min. by shaking them with water and pentane.

The pentane solutions were washed with dilute base, dried and submitted to V.P.C. analysis. The results of each of the 3 samples agreed within the probable errors of Table I. Run 4

was made in the same way except that no *p*-toluenesulfonic acid was present and a reaction time of 120 hr. was employed.

Elimination Reactions of 2-Phenyl-2-butanol (Runs 5 and 6).—In each of three test-tubes, 4 ml. of a stock solution 0.010 *M* in *p*-toluenesulfonic acid was preheated to 49.85 ± 0.05°. Sufficient substrate was then added (*ca.* 0.080 g.) to make the solutions 0.1 *M* in substrate. The reactions were quenched and worked up as with the acetate. Prior to analysis by gas chromatography, each sample was chromatographed on neutral alumina to remove any unreacted alcohol. The reactions run for 5 and 7.5 minutes yielded analyses agreeing within experimental error (see run 5, Table I).

In a sealed rate tube, 4 ml. of a solution 0.1 *M* in the carbinol in acetic acid was heated at 49.85 ± 0.05° for 150 hours, then quenched, extracted, chromatographed and analyzed as with the samples containing acid catalyst. Table I, run 6, records the results.

Deamination of 2-Phenyl-2-butylamine (Run 7).—A solution (4 ml.) 0.1 *M* in the amine hydrochloride in acetic acid was preheated to 49.85 ± 0.05° in the oil-bath and a stoichiometric amount (*ca.* 25 mg.) of sodium nitrite was added. After the nitrogen evolution subsided (*ca.* 2 min.), the white, cloudy mixture was poured into 5 ml. of water and 2 ml. of pentane to yield two clear phases. The pentane extract was worked up and analyzed as with the extracts from the other reactions. See run 7, Table I, for results.

Elimination Reaction of 2-Phenyl-2-butyl Hydrazine (Run 8).—To 16 ml. of a solution 0.009 *M* in *p*-toluenesulfonic acid in acetic acid which had been preheated to 49.85 ± 0.05° in the oil-bath was added enough of the pure hydrazine (32 mg.) to make the solution 0.012 *M* in substrate. After 15 minutes at the oil-bath temperature, the reaction was quenched with 15 ml. of water and extracted with 5 ml. of pentane. The pentane extract was washed with an equal volume of 10% sodium hydroxide and analyzed by the usual procedure.

A control experiment was run in which 2-phenyl-1-butene was substituted for the produced olefins, and pure hydrazine (Eastman Kodak Co. white label) for produced hydrazine or unreacted starting material. Identical conditions to those of the elimination reaction were employed, and the maximum extent of isomerization of produced olefin during the course of the elimination reaction was found to be 5%. This value was taken into consideration in evaluating the uncertainty in the product distribution from the elimination experiment.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, LOS ANGELES 24, CALIF.]

Studies in Stereochemistry. XXXV. Mechanism of E_i Reaction of Amine Oxides¹

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The first-order kinetics of the E_i (elimination) reaction of *threo*- and *erythro*-*N,N*-dimethyl-3-phenyl-2-butylamine oxide have been measured in tetrahydrofuran-water and dimethyl sulfoxide-water mixtures as well as in the pure solvents. Variations in rates as great as 10⁶ were observed as solvent was varied, the rates being lowest in water and highest in dry tetrahydrofuran. The rate was higher in wet dimethyl sulfoxide than in wet tetrahydrofuran because dimethyl sulfoxide acts as an internal drying agent and competes with aniline oxide for the water present. From pure tetrahydrofuran to 50 mole % tetrahydrofuran-50 mole % water as solvent, a linear relationship between ΔF^\ddagger and $\log(1/N_{H_2O})$ was observed. From pure dimethyl sulfoxide to 20 mole % dimethyl sulfoxide-80 mole % water as solvent, a linear relationship between ΔF^\ddagger and N_{H_2O} was found. The reaction was completely stereospecific in the *cis* sense over temperature ranges from 0° to 138°. Ratios of $k_{threo}/k_{erythro}$ ranged from 4.5 to 1.2, and $k_{conj.}/k_{unconj.}$ from 50 to 6 as solvent was changed.

Pyrolysis of esters, xanthates, carbonates, halides and amine oxides results in elimination reactions uncatalyzed by acids or bases, predominantly *cis* in steric direction and intramolecular in character.³ The term E_i is suggested for this class of reaction. Although the reaction in some cases occurs in the gas phase and appears to be one stage,⁴ the term E_i is meant to name the reaction class, whether or not all examples possess a common detailed mechanism. A recently discovered example of a dichotomy of mechanism was observed in

the pyrolysis of sulfoxides,⁵ which was *cis* and stereospecific in mechanism at about 80°, and was non-stereospecific at higher temperatures.

The present paper deals with a kinetic investigation of the Cope reaction, in which an amine oxide is pyrolyzed to produce an olefin and a hydroxylamine.⁶ Previous work has established that in amine oxides whose functional group is attached to branched carbon, the proportions of different products produced correlates with the number of hydrogens attached to the β-carbons.⁷ The reaction is highly stereospecific and

(1) This work was supported in part by the U. S. Army Research Office (Durham). Results were announced in a Communication to the Editor; D. J. Cram, M. R. V. Sahyun and G. R. Knox, *J. Am. Chem. Soc.*, **84**, 1734 (1962).

(2) National Science Foundation predoctoral fellow, 1961-1962.

(3) See D. J. Cram in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 305, for a review.

(4) (a) D. H. R. Barton, *J. Chem. Soc.*, 2174 (1949); (b) A. Maccoll and R. H. Stone, *ibid.*, 2756 (1961), and many previous papers.

(5) C. A. Kingsbury and D. J. Cram, *J. Am. Chem. Soc.*, **82**, 1810 (1960).

(6) Although the first example was first reported in 1898 by W. Werwick and R. Wolfenstein [*Ber.*, **31**, 1553 (1898)]; the scope, utility and general course of the reaction has been established by A. C. Cope and co-workers.

(7) A. C. Cope, N. A. LeBel, H. H. Lee and W. R. Moore, *J. Am. Chem. Soc.*, **79**, 4720 (1957).

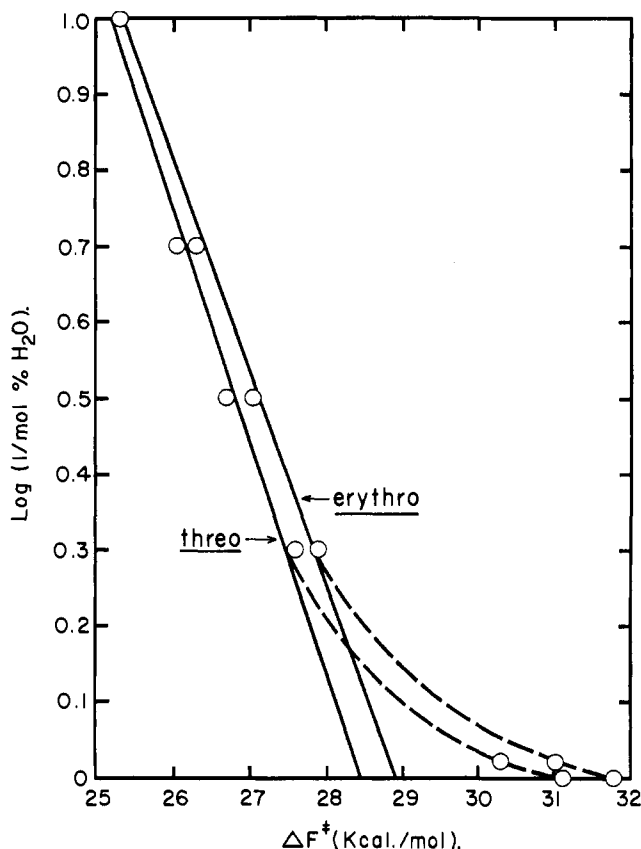
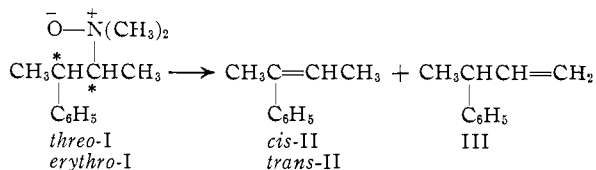


Fig. 1.—Plot of free energy of activation for pyrolysis of *threo*- and *erythro*-N,N-dimethyl-3-phenyl-2-butylamine oxides against log (1/mole % H₂O) in water-tetrahydrofuran mixtures.

cis in direction,⁸ and normally occurs at 85–150°.⁹ The oxides of *threo*- and *erythro*-N,N-dimethyl-3-phenyl-2-butylamine (I) were chosen for kinetic study for several reasons: (1) Other studies⁸ established that the reaction occurred in high yield at suitable temperatures. (2) The starting materials I and products II have been thoroughly characterized,¹⁰ and the latter can be readily analyzed by vapor phase chromatography. (3) The steric course of the reaction can be readily followed. (4) The tendency of the reaction to produce conjugated II *vs.* unconjugated olefin III can be determined. (5) The magnitude of eclipsing effects can be assessed.



Results

Pure samples of *threo*- and *erythro*-I were prepared⁸ and water was removed by evaporation to constant weight. The resulting materials were shown to contain one mole of water by Karl Fischer titration. This material was used in the kinetic measurements. Pure samples of *cis*- and *trans*-II and III were prepared, as well as 2-phenyl-1-butene, which served as an added "internal standard" in the V.P.C. analyses of the reaction products. Use of known mixtures of olefins demonstrated that results could be duplicated within 0.5% with an accuracy of $\pm 2\%$.

When *threo*-I-hydrate was dissolved in a dioxane solution and the water removed with molecular sieves

(8) D. J. Cram and J. E. McCarty, *J. Am. Chem. Soc.*, **76**, 5740 (1954).

(9) A. C. Cope, T. T. Foster and P. H. Towle, *ibid.*, **71**, 3929 (1949).

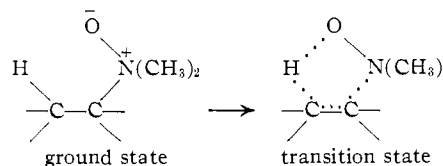
(10) D. J. Cram, *ibid.*, **74**, 2137 (1952).

at 25°, the reaction had gone to completion in the course of drying. The presence of the water of hydration stabilizes the amine oxide during storage. Exploratory kinetic runs in dimethyl sulfoxide, tetrahydrofuran, water, dioxane and methanol demonstrated that the reaction was first order in the amine oxide over at least 85–90% of the reaction. Systematic studies were carried out with both racemates in tetrahydrofuran–water and dimethyl sulfoxide–water mixtures. The immiscibility of tetrahydrofuran–water mixtures from about 55 to 90 mole % in water at 75–125° prevented this range from being studied. In each run a minimum of 5 points was taken, and solutions 0.05 M in amine oxide hydrate were employed. In runs made in pure tetrahydrofuran, the amine oxide hydrate was dissolved in tetrahydrofuran at –78°, and the water was removed with molecular sieves at that temperature. The rate constant for *threo*-I hydrate in dimethyl sulfoxide did not change when the solution was made 0.1 N in water. Apparently dimethyl sulfoxide acts as a drying agent for the amine oxide hydrate. No reaction occurred with either isomer at 132° in water, 0.1 N in formic acid.

The yields of product varied with temperature, ranging between 63 and 100% at temperatures of 0° to 75°, and decreasing to values as low as 27% at 75–132°. At the higher temperatures, yields of olefin produced decreased with longer reaction times. The infrared spectrum of products from the *threo*-oxide decomposed at 132° in water (10 hr., run 36) exhibited bands only characteristic of saturated hydrocarbons, which presumably arose by olefin polymerization. This destruction of reaction products prevented carrying the reactions to completion in those runs made at higher temperatures. The results are set forth in Table I, which includes the thermodynamic parameters associated with the rate constants obtained in tetrahydrofuran and dimethyl sulfoxide, and their mixtures with water.

Discussion

Importance of Hydrogen Bonding to Rate.—Extrapolation of the rate data of Table I to 52.4° provides a convenient means of comparing the effect of various solvents on reaction rate of the Cope reaction. The following comparisons are made at that temperature. Although tetrahydrofuran and dimethyl sulfoxide differ greatly in dielectric constant ($\epsilon^{\text{THF}} = 7.4$ and $\epsilon^{\text{DMSO}} = 45$ at 20°, respectively), $k_{\text{threo}}^{\text{THF}}/k_{\text{threo}}^{\text{DMSO}} \cong 3$ and $k_{\text{erythro}}^{\text{THF}}/k_{\text{erythro}}^{\text{DMSO}} \cong 9$. As expected on the basis of a one-stage cyclic mechanism,⁹ charge is dispersed and solvation energy decreased in passing from the ground to the transition state. Thus in the more



polar dimethyl sulfoxide, more solvation energy has to be overcome in the transition state than in tetrahydrofuran, and the rate in the latter solvent is slightly faster. However, the effects are remarkably small.

Much more striking is the dramatic rate-decreasing role played by hydrogen-bonding media. Although methanol has a lower dielectric constant than dimethyl sulfoxide ($\epsilon^{\text{MeOH}} = 33$ *vs.* $\epsilon^{\text{DMSO}} = 45$, respectively), $k_{\text{threo}}^{\text{DMSO}}/k_{\text{threo}}^{\text{MeOH}} \cong 3 \times 10^3$. In Table II are listed ratios of rate constants (based where necessary on data extrapolated to 52°) in which the rate constants obtained in water are used as standard and are

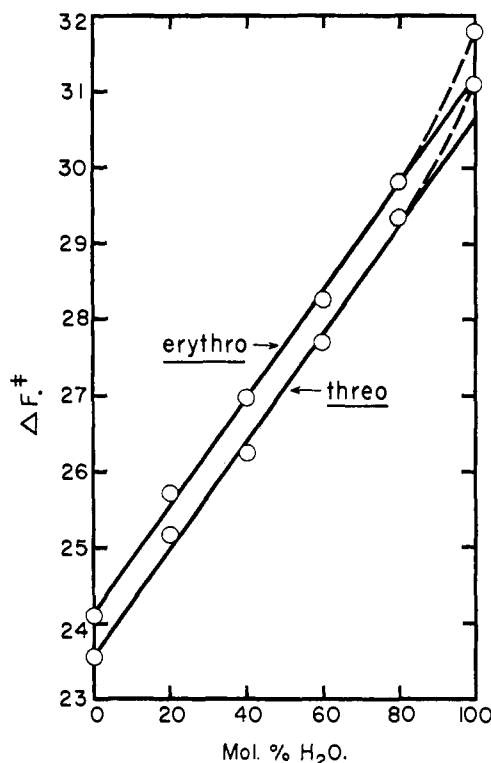


Fig. 2.—Plot of free energy of activation for pyrolysis of *threo*- and *erythro*-*N,N*-dimethyl-3-phenyl-2-butylamine oxides against mole % water in water-dimethyl sulfoxide mixtures.

$K[\text{H}_2\text{O}] \gg 1$, k_{obs} is linear with $1/[\text{H}_2\text{O}]$, and ΔF^\ddagger is linear with $\ln(1/[\text{H}_2\text{O}])$, or $\log(1/N_{\text{H}_2\text{O}})$. Implicit in this derivation are the assumptions that k_0 and K are little changed by medium over the solvent range covered by the linear relationship.

TABLE II

RELATIVE VALUES OF RATE CONSTANTS, EXTRAPOLATED WHEN NECESSARY TO 52.4°, IN VARIOUS SOLVENT SYSTEMS

Solvent ^a	$k_{\text{erythro}}^{\text{solvent}}/k_{\text{erythro}}^{\text{H}_2\text{O}}$	$k_{\text{threo}}^{\text{solvent}}/k_{\text{threo}}^{\text{H}_2\text{O}}$	$k_{\text{threo}}/k_{\text{erythro}}$
THF	ca. 2×10^{6c}	ca. 9×10^{6c}	4.5
90% THF-10% H ₂ O	1×10^4	1×10^4	1.6
80% THF-20% H ₂ O	3×10^3	3×10^3	1.2
70% THF-30% H ₂ O	1×10^3	1×10^3	1.5
50% THF-50% H ₂ O	1×10^{1c}	3×10^{2c}	1.7
5% THF-95% H ₂ O	2.1
DMSO	7×10^4	1×10^5	2.0
80% DMSO-20% H ₂ O	7×10^3	1×10^4	2.3
60% DMSO-40% H ₂ O	9×10^2	1.5×10^3	2.2
40% DMSO-60% H ₂ O	2×10^{2c}	2×10^2	2.4
20% DMSO-80% H ₂ O	2×10^{1c}	2×10^{1c}	2.0
MeOH	...	3×10^{1c}	...

^a THF = tetrahydrofuran, DMSO = dimethyl sulfoxide.

^b Rate for pure water at 52.4° estimated by assuming rate increased by factor of $3.5/10^0$; $k_{\text{erythro}}^{\text{H}_2\text{O}} = 7 \times 10^{-9}$ sec.⁻¹; $k_{\text{threo}}^{\text{H}_2\text{O}} = 9 \times 10^{-9}$ sec.⁻¹. ^c Rate extrapolated to 52.4°.

The linear relationship between the free energy of activation and the mole % water in dimethyl sulfoxide as solvent (Fig. 2) can be expressed in eq. 3. In this equation, $\Delta F_{\text{obs}}^\ddagger$ is the observed free energy of activation

$$\Delta F_{\text{obs}}^\ddagger = \Delta F_0^\ddagger + X_{\text{R}_2\text{NO}\cdot\text{H}_2\text{O}} \Delta F^{\text{H}} \quad (3)$$

in the various dimethyl sulfoxide-water mixtures, ΔF_0^\ddagger the free energy of activation for non-hydrogen-bonded amine oxide molecules, $X_{\text{R}_2\text{NO}\cdot\text{H}_2\text{O}}$ is the mole fraction of amine oxide molecules hydrogen bonded at equilibrium and ΔF^{H} the free energy involved in breaking the amine oxide-hydrogen bond. Implicit

in this equation are the assumptions that ΔF_0^\ddagger and ΔF^{H} do not change with added water over the range of the linear relationship.¹¹ From the slopes of the lines of Fig. 2, ΔF^{H} is estimated to be approximately 7 kcal./mole, which is greater than the energy of hydrogen bonds in ice (4.5 kcal. per mole).¹²

In the SN2 reaction of hydroxide ion with methyl iodide in dimethyl sulfoxide-water mixtures, the second-order rate constant is logarithmically linear with the mole fraction of water.¹³ This relationship is mathematically identical with the linearity of ΔF^\ddagger with mole % water observed here.

In a second study,¹⁴ the rate constants (k) for the racemization of 2-methyl-3-phenylpropionitrile by potassium methoxide in methanol-dimethyl sulfoxide mixtures were measured. From about 20-60 mole % methanol, a plot of $\log k$ against mole % dimethyl sulfoxide was linear (Fig. 4, ref. 14). The value of k increased by an estimated 9 powers of 10 in passing from pure methanol to pure dimethyl sulfoxide. Clearly some of the same mechanistic features are common to the solvent effects on rate in the three studies.

In another investigation,⁵ the rate of the E_i reaction of certain sulfoxides decreased by 3 powers of 10 in passing from dioxane to methanol. The same effects in a less extreme form are visible in these results.

The lower drop in rate when water is added to dimethyl sulfoxide as compared to tetrahydrofuran is undoubtedly associated with the much stronger hydrogen bonding abilities of dimethyl sulfoxide. In this connection, some evidence has been offered¹⁵ that water-water hydrogen bonds are stronger than water-dimethyl sulfoxide hydrogen bonds. The authors point out that heat is liberated when water is mixed with dimethyl sulfoxide and conclude that strong interactions of a non-hydrogen bonding variety must also be present between water and dimethyl sulfoxide. The fit between Fig. 2 and eq. 14 probably reflects many compensating effects implicit in the derivation of the latter.

Activation Parameters.—Although the kinetic data were not refined enough to provide accurate activation parameters, the changes of ΔH^\ddagger and ΔS^\ddagger with changes in solvent are large enough to have mechanistic implications. In tetrahydrofuran-water mixtures, ΔH^\ddagger increases by approximately 10 kcal. in passing from 100% tetrahydrofuran to 90 mole % tetrahydrofuran-10 mole % water. A somewhat compensating entropy effect is seen in the increase in ΔS^\ddagger of about 20 e.u. with the same solvent change. Within experimental error, further additions of water have no effect on ΔH^\ddagger , but gradually reduce the entropy by over 10 e.u.

These effects are consistent with the mechanism suggested in the last section. In eq. 2, when $[\text{H}_2\text{O}]$ is negligibly small, only the non-hydrogen-bonded reactive form of the amine oxide is present. As water is added to the medium, the hydrogen-bonded unreactive form predominates, being largely in that form when the solution is 10 mole % in water. This change in composition of the medium adds to ΔH^\ddagger , the enthalpy associated with breaking an amine oxide-hydrogen bond. However, once most of the amine oxide is hydrogen bonded, further increases in water

(11) Some justification for the presumption that ΔF_0^\ddagger does not change is found in the fact that rates in pure dimethyl sulfoxide and tetrahydrofuran differ by factors of only 3-9. Furthermore, in the E_i reaction (ref. 5) with sulfoxide as leaving group, insensitivity of rate to medium was observed when hydrogen bonds were not involved.

(12) K. Pitzer, "Quantum Chemistry," Prentice-Hall, Inc., New York, N. Y., 1953, p. 198.

(13) J. Murto, *Suomen Kemi*, **B39**, 92 (1961).

(14) D. J. Cram, B. Rickborn, C. A. Kingsbury and P. Haberfeld, *J. Am. Chem. Soc.*, **83**, 3678 (1961).

(15) W. Drinkard and D. Kivelson, *J. Phys. Chem.*, **62**, 1494 (1958).

content effect the concentration of hydrogen bonded species very little, and hence ΔH^\ddagger is little effected. The ΔS^\ddagger associated with reactions whose transition states involve making five- or six-membered rings and whose starting states are neutral range from -2 to -17 e.u.¹⁶ The large negative entropy observed in pure tetrahydrofuran supplements this generalization. When 10 mole % water is added, a large positive entropy becomes associated with the almost completely hydrogen-bonded amine oxide in equilibrium with a relatively non-hydrogen-bonded solvent. In the over-all reaction, hydrogen bonded substrate is converted to non-hydrogen bonded transition state, and a mole of water is liberated to a relatively non-hydrogen bonding medium. Thus the large positive entropy associated with the equilibrium state must be added to the smaller negative entropy associated with passage of non-hydrogen-bonded amine oxide to the transition state, and an over-all positive entropy of activation results. Further increases in the amount of water decrease the entropy of the hydrogen-bonded amine oxide relative to that of the solvent since the solvent itself has become highly hydrogen bonding. At 50 mole % water, the entropy of liberation of amine oxide-bound water to the medium appears to have decreased in value to the point where the over-all entropy for reaction has again become negative.

In dimethyl sulfoxide-water mixtures, ΔH^\ddagger increases gradually by about 5 kcal. in passing from pure dimethyl sulfoxide to 40 mole % dimethyl sulfoxide-60 mole % water, and does not change further (within experimental error) in passage to 20 mole % dimethyl sulfoxide-80 mole % water. The values for ΔS^\ddagger are almost within experimental error of one another over the whole solvent composition range, and average out to about $+2$ e.u.

Because dimethyl sulfoxide competes with amine oxide for the water in the medium, most of the amine oxide is hydrogen bonded only when the water in the medium passes the 60 mole % mark, at which point ΔH^\ddagger becomes constant. It is significant that ΔH^\ddagger becomes constant at about the point where equal numbers of water and dimethyl sulfoxide compose the medium. The entropy associated with water hydrogen bonded to amine oxide is approximately the same as water hydrogen bonded to dimethyl sulfoxide, and therefore little change in entropy is associated with transferring a mole of water from amine oxide to sulfoxide. These conclusions are compatible with the interpretations of the previous section.

Eclipsing Effects.—The values of $k_{threo}/k_{erythro}$ listed in Table II provide a measure of the magnitude of eclipsing effects in the Cope reaction, and of their variation with medium. At equilibrium, *threo*-I/*erythro*-I is probably only slightly less than unity,¹⁷ whereas at equilibrium, *cis*-II/*trans*-II = 5. To some extent, the values of $k_{threo}/k_{erythro}$ provide a measure of how far along is the transition state in geometry between starting material and olefin.¹⁸ The values of this kinetic ratio vary between extremes of 4.5 and 1.2, a fact which demonstrates for the E_i reaction that the structure of the transition state is capable of considerable variation. The transition state most resembles olefin ($k_{threo}/k_{erythro} = 4.5$) when the reaction is conducted in dry tetrahydrofuran, in which the highest reaction rates are observed. The lowest

value for the ratio (1.2) is observed in 80 mole % tetrahydrofuran-20 mole % water. As the mixture is increased in water, the value of the ratio increases somewhat, arriving at 2.1 in 95 mole % water. In the dimethyl sulfoxide-water solvent system, the values range only between extremes of 2.0 and 2.4. These data suggest that the less polar the medium, the greater is the requirement of the transition states to distribute charge internally, and the greater is the carbon-carbon double bond character. The small changes in the kinetic ratios, once substantial amounts of water enter the medium, probably reflect as much the small changes in ground state energy (between hydrogen-bonded and non-hydrogen-bonded species) as they do changes in transition state energies. In this connection, it is interesting that the discontinuities in the kinetic ratio occur at about the same solvent compositions as those for ΔH^\ddagger .

Product Distribution.—Within limits of experimental detection, these reactions appear to be completely stereospecific and *cis* in stereochemical direction. The very small amount of non-stereospecific reaction observed in an earlier study⁸ was due to slightly impure olefinic standards (this study was made before vapor phase chromatographic techniques were available). Thus the Cope reaction is unique among the E_i reactions in this stereochemical feature. The low temperature required for reaction coupled with the probable instability of radical pairs which would be required by competing homolytic elimination⁵ probably both contribute to the stereospecificity.

Small trends are visible in the ratios of conjugated to terminal olefin ($k_{conj.}/k_{term.}$). Values of this ratio vary from extremes of about 50 to 6. As expected, the values are higher for the *threo* isomer which produces the more stable *cis*-olefin than for the *erythro* isomer in dimethyl sulfoxide, and its mixtures with water. Surprisingly, the values are about the same in the other solvent systems. The highest values for the ratios are observed in those solvents (dimethyl sulfoxide and tetrahydrofuran) which permit the reaction to be run at the lowest temperature.

When correction is made for the 3/1 statistical advantage enjoyed by the reactions leading to terminal olefin, $k_{conj.}/k_{term.}$ amounts to about one power of ten. Thus the phenyl group lends considerable stability to the transition state, a fact which also indicates that in the transition, the double bond is partially formed.

Experimental

Starting Materials and Products.—The diastereomeric amines were prepared and purified through crystalline derivatives as before,⁸ the melting point of *threo*-3-phenyl-2-butylammonium benzoate being 119.0–119.5°, and that of *erythro*-3-phenyl-2-butylammonium chloride, 218.2–218.8°. These materials were converted to their respective N,N-dimethyl-3-phenyl-2-butylamine oxides as previously,⁸ which were dried to constant weight on a rotary evaporator at room temperature. Karl Fischer titration of the material indicated the presence of one mole of water in each sample.

Samples of *cis*- and *trans*-2-phenyl-2-butene pure to vapor phase chromatographic analysis (see later section) were available from a previous investigation.¹⁹ A sample of 3-phenyl-1-butene, prepared as before,¹⁰ exhibited physical properties identical with previously obtained material, and was pure to vapor phase chromatography (see later section).

Solvents.—Solvents used for kinetics were purified as follows. Tetrahydrofuran was treated with solid sodium hydroxide, distilled from lithium aluminum hydride, and stored over molecular sieves. J. T. Baker analyzed dimethyl sulfoxide was shown by Karl Fischer titration to contain less than 0.02% water (limit of sensitivity), and was used as such. Methanol was dried by distillation from lithium aluminum hydride, and dioxane was purified by refluxing over solid potassium hydroxide and distillation from

(16) Literature is summarized in ref. 5, footnote 25.

(17) In a similar case [D. J. Cram and F. A. Abd Elhazef, *J. Am. Chem. Soc.*, **75**, 339 (1953)], equilibrated open-chain diastereomers without large intramolecular dipole-dipole interactions gave a ratio of 0.82.

(18) The principles involved here have been applied in more detail to the E₂ reaction [D. J. Cram, F. D. Greene and C. H. DePuy, *ibid.*, **78**, 790 (1956)].

(19) D. J. Cram and M. R. V. Sahyun, *ibid.*, **85**, 1257, (1963).

lithium aluminum hydride, and was dried over molecular sieves.

Kinetics.—For the kinetic runs, the amine oxide monohydrate was accurately weighed into a clean, dry flask, and the desired solvent added from a volumetric pipet to give a solution 0.05 *M* in amine oxide. For runs made at 0°, 25° and 36°, the reactions were conducted in the same flasks placed in an appropriate water-bath, 2-ml. aliquots being removed and quenched with 10 ml. of water at proper times. For runs made at higher temperatures, 2-ml. aliquots were sealed in ampoules which were placed in appropriate oil-baths and withdrawn at the proper times, opened, and the reaction was quenched with 10 ml. of water. For those runs conducted in dry tetrahydrofuran, the solutions were prepared at -80°, and the water of hydration was removed with molecular sieves at that temperature. The solutions were then warmed to 0° or 25°. A minimum of 5 points was used for each kinetic run.

As an internal standard for quantitative analysis by gas chromatography, 5 μ l. of 2-phenyl-1-butene¹⁹ was added to the aqueous quench mixture, and the olefin was extracted with 2 ml. of pure pentane. The pentane extract was submitted to gas chromatography, and the amount of each component relative to the internal standard estimated from the areas under the peaks. Synthetic mixtures were prepared which approximated the unknowns in each component, and the unknowns were corrected to the

known mixtures. Use of known mixtures demonstrated that results could be duplicated within 0.5% to an accuracy of $\pm 2\%$. The rate constants were calculated with the assumption that the maximum yield of olefin obtained in any of the runs with a given lot of amine oxide represented the maximum obtainable yield for that particular lot. Only one lot was employed for *erythro* material, while two lots were used for the *threo*-oxide. Duplicate runs were made on each lot in pure dimethyl sulfoxide at 52.4° to confirm the reproducibility of yields and rate constants. Only minor differences were observed in rate constants calculated this way and those based on the weight of the amine oxide hydrate employed.

The V.P.C. analysis was conducted as follows: After each aliquot of the reaction mixture was quenched with cold water, 4.7 mg. (5.0 μ l.) of 2-phenyl-1-butene was added as internal standard with a microliter syringe. The solution was then mixed thoroughly and extracted with 2 ml. of pure pentane. A 50- μ l. sample of this extract was then subjected to vapor phase chromatography with a Perkin-Elmer model 154C vapor fractometer using a 23% γ -methyl- γ -nitropimelonitrile on firebrick column at 110° with helium at 15 p.s.i. as carrier gas. Control experiments with known mixtures of the three olefins were used to determine the proper factors for relating the relative peak area to composition of the mixtures.

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Studies in Stereochemistry. XXXVI. Radical Anions as Neighboring and Electron Transfer Groups in Substitution-Reduction Reactions¹

BY DONALD J. CRAM AND CECILE K. DALTON²

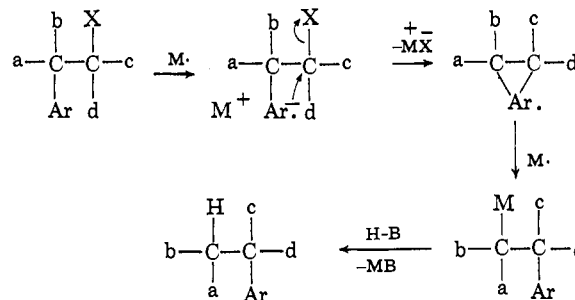
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Examples have been found of reactions in which alkali metals transfer electrons to β -phenylalkyl methanesulfonates, and the aromatic radical anions generated act as neighboring groups in nucleophilic substitution-reduction reactions. Reaction of *threo*-2-phenyl-3-pentyl methanesulfonate with potassium in 1,2-dimethoxyethane gave hydrocarbon, 94% of which was 2-phenylpentane and 6% was 3-phenylpentane (product of phenyl migration). Treatment of *threo*-3-phenyl-2-pentyl methanesulfonate with sodium in liquid ammonia gave hydrocarbon, 75% of which was 3-phenylpentane and 3% was 2-phenylpentane (product of phenyl migration). Another type of reaction has been discovered in which alkali metals transfer electrons to 1-methoxy-2-(1-naphthyl)ethane, the naphthyl group serving as an electron-transfer agent in reductive substitution of the methoxyl group. Treatment of 1,1-dideuterio-1-methoxy-2-(1-naphthyl)ethane or 1,1-dideuterio-2-(1-naphthyl)ethyl methanesulfonate with potassium in 1,2-dimethoxyethane gave 1-ethylnaphthalene deuterated only in the methyl group. In contrast, 1,1-dideuterio-2-(1-naphthyl)ethyl *p*-toluenesulfonate when acetolyzed gave acetate in which deuterium was distributed equally in the two positions of the ethyl group. An ethylene naphthionium ion must have intervened in the solvolysis, but electron transfer occurred in the reductive substitution reaction without carbon participation.

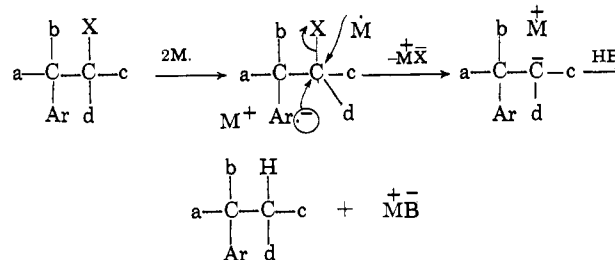
The ability of aryl groups to form ethylene phenonium ions as intermediates in solvolytic reactions has been well established,³ as has the formation of a spiro-dienone from the anion of 2-(4-hydroxyphenyl)-ethyl bromide in a 1,3-elimination reaction.⁴ These observations coupled with the fact that alkali metals transfer electrons to aromatic nuclei in the course of reduction⁵ suggested that aryl radical anions might serve as neighboring groups in nucleophilic substitution-reduction reactions. Two general types of criteria might be used for detection of aryl involvement in reduction at saturated carbon: (1) If an aryl group migrates in the course of reduction (see formulas), it probably acts as a nucleophile in the process; one of a number of possible reaction schemes is formulated. (2) If the presence of an aryl group in the molecule is a condition for reductive substitution at saturated carbon, but no rearrangement occurs, aryl may serve as an electron transfer group without itself directly participating in displacement of the leaving group (see formulas for one of several possible mechanisms). In connection with the latter possibility, electron

transfers from one aromatic ring to a second in paracyclophanes,⁶ diphenylmethane⁷ and 1,2-diphenylethane⁷ have been found to occur at very high rates.

Aryl radical anion participation in reductive substitution



Aryl electron transfer without direct participation



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