The Mechanism of β-Elimination Reactions in Dimethyl Sulfoxide[1]

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Attempts have been made to elucidate the mechanism of novel base-catalyzed elimination reactions occurring in dimethyl sulfoxide. Kinetic studies in potassium *tert*-butoxide–dimethyl sulfoxide at 30 and 55° have established that the elimination of aliphatic sulfoxides is E2 in nature, *i.e.*, first order in base and first order in sulfoxide. Reproducible kinetic data on aliphatic halides and sulfones could not be obtained because of the rapidity of the elimination reaction. A general conclusion is that the rate depends on both the leaving group and the reactivity of the β-hydrogen. Elimination studies on various compounds in tritiated dimethyl sulfoxide have pinpointed any proton–proton exchange occurring before or after the elimination step. The specific activity of the resulting olefins indicates that exchange occurs only at the α-positions and not at the β-positions.

Introduction

The base-catalyzed elimination reactions of sulfones have received considerable attention by Ingold and his school.[2,3] In sodium ethoxide–ethanol media olefin production from simple aliphatic sulfones required temperatures of 200° or higher depending on the aliphatic sulfone in question. Potassium hydroxide was not a particularly effective catalyst at these temperatures.[4] Studies on the base-catalyzed elimination reactions of sulfoxides have been mainly concerned with the reactions of diphenyl sulfoxide with strong bases such as butyllithium.[5] Elimination reactions with sulfides, *i.e.*, mercaptide elimination, is usually limited to "retro"-Michael reactions and to sulfides containing one or two other sulfide linkages in the molecule.[6]

Previously, we observed that diaralkyl sulfides and sulfoxides undergo base-catalyzed 1,3-rearrangements and subsequent β-eliminations to stilbene derivatives in dipolar solvents.[7] In an extension of our studies in this area, we observed that olefin formation from a large number of aliphatic functional derivatives occurred readily in potassium *tert*-butoxide–dimethyl sulfoxide (DMSO) at 55°.[8,9] For example, aliphatic halides, sulfones, sulfoxides, nitrates, disulfides, thiocyanates, nitrites, sulfides, thiols, and nitriles yielded olefins in 5–95% yields for reaction periods of 17–117 hr. in *t*-BuOK–DMSO. Further, structural variations of the reactant in each series of compounds suggested that a β-elimination was operative in all cases. Owing to the novelty of these findings, a more detailed investigation on the reaction mechanism was undertaken. The present paper is a summary of our kinetic and tritium exchange studies on some of these compounds.

Results

The results of two kinetic experiments on diisopropyl sulfoxide are shown in Table I. In Fig. 1, these data

(1) This work was presented before the Organic Division, 145th National Meeting of the American Chemical Society, New York, N. Y., September 8–13, 1963.

(2) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter 30.

(3) C. K. Ingold, *Proc. Chem. Soc.*, 265 (1962).

(4) See especially G. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 705 (1930), and references therein.

(5) For the most recent review of this area see: H. H. Szmant, "Organic Sulfur Compounds," Vol. I, ed. by N. Kharasch, Pergamon Press, New York 22, N. Y., 1961, Chapter 16, p. 154 *et seq.*

(6) J. F. Arens, ref. 5, Chapter 23, p. 257 *et seq.*

(7) T. J. Wallace, H. Pobiner, J. E. Hofmann, and A. Schriesheim, *Proc. Chem. Soc.*, 137 (1963).

(8) J. E. Hofmann, T. J. Wallace, P. A. Argabright, and A. Schriesheim, *Chem. Ind.* (London), 1243 (1963).

(9) T. J. Wallace, J. E. Hofmann, and A. Schriesheim, *J. Am. Chem. Soc.*, **85**, 2739 (1963); *Nature*, **199**, 1287 (1963).

are plotted according to the classical expression for a second-order reaction. In both cases, the concentration of base and the isopropyl groups of the reactant are approximately equal. Hence, this simplifying assumption has been included. Although these data agree fairly well with second-order behavior, it should be recognized that a rigorous analysis of a number of eliminations is not possible because each reaction leads to *tert*-butyl alcohol as a by-product. As previously demonstrated, *tert*-butyl alcohol inhibited the elimination reactions of sulfones, sulfoxides, and sulfides.[9] Reproducible kinetic data on isopropyl bromide and diisopropyl sulfone could not be obtained because the elimination step is too fast.

TABLE I

KINETIC STUDIES ON DIISOPROPYL SULFOXIDE (DIPSO)

Temp., °C.	55		30
DMSO, ml.	6.9		6.8
t-BuOK, mmoles	1.26	3.92	2.8
DIPSO, mmoles	0.632		1.40

Time, min.	Yield of propylene, mmole	
10	0.057	0.006
20	0.092	.019
30	. . .	.047
40	. . .	.054
60	0.267	.087
90	0.318	.115

For reasons which will subsequently be discussed, the previously unreported elimination of 2-chlorobutane was carried out in 7.0 ml. of 0.56 M *t*-BuOK–DMSO at 30° at a base alkyl halide ratio of 2. The total yield of C-4 olefin after 30 sec. was 67% and the product composition consisted of 32% 1-butene, 45% *trans*-2-butene, and 13% *cis*-2-butene.

The results of the radiotracer experiments with tritiated DMSO are shown in Table II. No specific attempt to measure reaction rates was made, but approximate half-lives for elimination are reported to give an estimate of the relative order of reactivity for each compound studied. The specific activity has been defined in integral units so that a fully equilibrated olefin would have a specific activity equivalent to its total number of hydrogens. As a point of reference, the rate of exchange between diphenylmethane and tritiated DMSO at 30° was found to have a reaction half-life that was less than 3 sec.

Although the rate of base-catalyzed isotope exchange between propylene and dimethyl sulfoxide has been

Table II
Specific Activities[a] of Compounds Studied in Tritiated DMSO

Time, min.	Diisopropyl sulfoxide	Di-tert-butyl sulfoxide	Isopropyl bromide	Di-n-butyl sulfone	Diisopropyl sulfone	Isopropyl nitrate	Diisopropyl sulfide[b]
10	0.92	0.0	0.0	..	1.08	0.0	..
20	0.99	0.011	0.0	..	0.97	0.0	..
30	..	...	...	..	..	...	..
40	..	...	0.0	..	1.11	0.0	..
45	1.16	0.050	...	..	..	...	..
60	..	...	...	..	..	...	..
75	..	...	...	2.16	..	...	..
90	1.35	...	...	..	..	...	..
120	..	...	...	2.25	..	...	0.98
150	1.49	...	...	..	..	...	..
210	..	...	...	..	1.38	...	1.27
22 hr.	..	...	...	2.83	..	...	..
Approx. reaction half-life, min.	100	10	<1	1000	60	5	>100 hr.

[a] As outlined in the Experimental section, the specific activity has been defined in integral units equivalent to one per proton. Thus, a fully equilibrated propene would have a specific activity of 6.0 and a butene 8.0. [b] Owing to the slowness of reaction, the possibility of some exchange with propylene following elimination cannot be excluded.

measured,[10] it is impossible to correct for any exchange that occurs after elimination because the catalytic activity of the system is constantly changing. However, the rate of olefin–dimethyl sulfoxide exchange is fairly slow compared to elimination. Thus, a good approximation of the specific activity of the olefin as it is being eliminated can be made by extrapolating the specific activity data to zero time. The latter point is demonstrated in Fig. 2. Isopropyl bromide, isopropyl nitrate, and di-tert-butyl sulfoxide contain no tritium before elimination. The propylene from diisopropyl
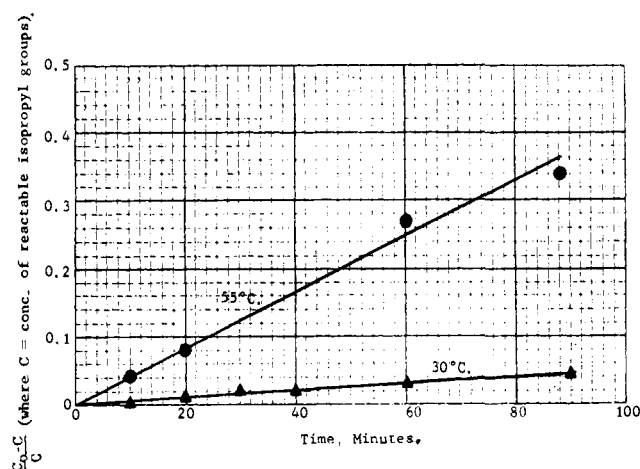
Fig. 1.—Elimination of propylene from diisopropyl sulfoxide.

sulfide, diisopropyl sulfoxide, and diisopropyl sulfone contains tritium equivalent to one fully equilibrated hydrogen before elimination. The butylene from di-n-butyl sulfone contains the equivalent of two fully equilibrated hydrogens before the elimination step. These results indicate that exchange occurs only at the α-positions of these compounds and not at the β-positions.

Discussion

Classical β-elimination reactions have been divided into three major categories: the E1 mechanism, the E2 mechanism, and the carbanion mechanism. These are differentiated by the order of bond breaking and the

(10) The first-order rate constant for tritium exchange with propylene at 55° using 0.56 M t-BuOK in DMSO is 5.4 × 10⁻⁵ sec.⁻¹; see ref. 14 for experimental details.

degree of bond rupture in the transition state.[11] The nature of dimethylsulfoxide affords the opportunity to measure both the kinetic order of the reaction as well as any proton exchange that might occur between the solvent and the reactant. The latter point arises from the fact that dimethyl sulfoxide undergoes rapid base-catalyzed proton exchange with very weakly acidic materials.
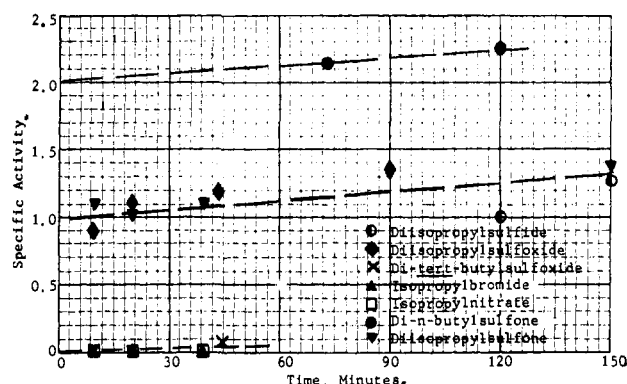
Fig. 2.—Determination of specific activity prior to elimination.

It has been found that the formation of propylene from diisopropyl sulfoxide adheres to over-all second-order kinetics, being first order in both base and reactant. Further, the results indicate that for all compounds studied (sulfides, sulfoxides, sulfones, nitrates, and halides) no exchange occurs at the β-position prior to the elimination reaction. For those compounds containing acidic α-hydrogens, i.e., the sulfoxides and sulfones, complete equilibration of this position is noted prior to any elimination.

The kinetic and isotope exchange work clearly place these elimination reactions in the E2 category. The exact degree of bond rupture in the transition state is impossible to assess, but it is likely that the X group has

$$XCH_2CH_2R + B^{\ominus} \longrightarrow \overset{X\ \delta\ominus}{\underset{\underset{B\delta\ominus}{\overset{|}{H}}}{\overset{|}{C}H_2CHR}} \longrightarrow X^{\ominus} + \\ CH_2=CHR + BH$$
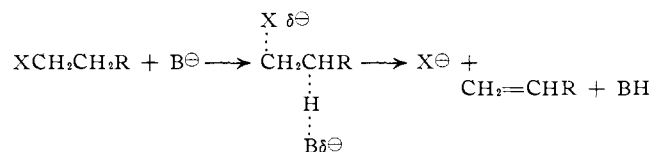
started to leave before the β-C–H bond has been com-

(11) J. F. Bunnett, Angew. Chem. Intern. Ed. Engl., 1, 225 (1962).

pletely broken. An alternative explanation could be presented in which a hydrogen bonded carbanion is formed as an intermediate. This then undergoes further reaction where $k_2 \gg k_3$. The difference between these possibilities is subtle at most and differen-

$$XCH_2CH_2R + B^\ominus \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} XCH_2\underset{\substack{\vdots \\ H \\ B}}{CHR} \overset{k_2}{\longrightarrow} CH_2{=}CHR + \\ HB + X^\ominus$$

$$\Big\downarrow k_3 \, TB$$

$$XCH_2CHTR + B^-$$

tiation based on the current data is impossible. The fact that exchanges occur at the α-position has no bearing on the over-all course of reaction. α-Elimination is ruled out on the basis that dimethyl sulfoxide itself does not undergo any reaction with monoolefins such as cyclohexene.

Additional mechanistic information indicates that the reaction rate is influenced by the nature of both the leaving group and the ease of proton removal. Thus, as shown in Table II, the order of reactivity for the isopropyl derivatives is that which would be generally anticipated, i.e., halide $\simeq$ nitrate > sulfone > sulfoxide > sulfide. A comparison of the reaction half-lives for di-tert-butyl sulfoxide and diisopropyl sulfoxide indicates that the order of hydrogen reactivity is that which would be expected for a β-elimination. The greater reactivity of diisopropyl sulfone in comparison to di-n-butyl sulfone is also in accord with these conclusions. With the alkyl halides, elimination occurs so readily that thermodynamic considerations rather than hydrogen reactivity begin to control product selectivity. Thus, with 2-chlorobutane, under conditions where essentially no isomerization will occur,[12] the product consists of 32% 1-butene, 45% trans-2-butane, and 13% cis-2-butene. The ratio of trans to cis is very close to experimental equilibrium, and there is a slight preference for the initial removal of a secondary rather than a primary hydrogen. Further information on stereoselectivity with less reactive leaving groups is difficult to obtain because of concomitant isomerization of the olefinic product.

In view of the rapid rate of exchange between di-

$$\underset{\substack{\| \\ }}{\overset{O}{}}$$

phenylmethane and $CT_3{-}S{-}CT_3$, the ease of exchange of the acidic α-hydrogen atoms of the sulfones and sulfoxides is not surprising. The sulfur atom in both the sulfones and sulfoxides has a large degree of positive charge. This positive charge is responsible for the acidity of the α-carbon–hydrogen bonds in these compounds and the electron deficiency of the sulfur atom also results in resonance stabilization of the resulting carbanion by p–d overlap. The possibility of exchange at the α-hydrogen of the sulfide would be somewhat more interesting. Unfortunately, because of the slowness of the reaction, it is extremely difficult to differentiate between exchange that occurs before and after elimination.

(12) A. Schriesheim, C. A. Rowe, Jr., and L. Naslund, J. Am. Chem. Soc., **85**, 2111 (1963).

Experimental

Reagents.—Potassium tert-butoxide was obtained from the Mine Safety Appliance Co. (Callery, Pa.) as the sublimed, white powder in wax-sealed containers. All samples were at least 98.5% pure. DMSO was dried and distilled over Linde 13X Molecular Sieves to remove any water that was present.

Most reactants were obtained from either Columbia Organic Chemicals or Matheson Coleman and Bell as reagent grade materials and analyzed for purity by g.c. before use. Materials less than 98% pure were distilled under a nitrogen atmosphere through an 18-in. silvered column equipped with a tantalum-wire spiral. In the case of the sulfoxides and sulfones, distillation was carried out in the presence of Linde 13X Molecular Sieves to ensure complete removal of water. All reagents were stored in a nitrogen drybox equipped with a moisture conductivity cell. Di-tert-butyl sulfoxide was prepared from the oxidation of the sulfide by hydrogen peroxide in acetic acid (m.p. 64°, reported[13] m.p. 63.5–65°).

Tritium Exchange Studies.—For the radiotracer portion of the experimental work, a stock solution of base in tritiated dimethyl sulfoxide was prepared beforehand. Tritiated dimethyl sulfoxide was obtained from Nichem, Inc. The received material had a specific activity of approximately 50 mc./g. Before use, this material was diluted 100-fold with straight DMSO that had been freshly distilled from Linde 13X Molecular Sieves. A 0.56 M solution of potassium tert-butoxide was then prepared in a nitrogen-blanketed drybox, equipped with a moisture conductivity cell. That solutions thus prepared compare favorably in catalytic activity with solutions containing no tritiated dimethyl sulfoxide has been confirmed previously.[14] Individual experiments were performed by placing 7.0 ml. of the stock solution in a 10-ml. glass vial equipped with a self-sealing neoprene cap. After pre-thermostating to reaction temperature, approximately 2 mmoles of the reactant were added.

Aliquot samples were then withdrawn periodically and quenched in water. The hydrocarbon was liberated with the aid of an external extractant, usually 2,3-dimethylbutane. The product was then analyzed for tritium content by measuring its specific activity on a radio-assaying gas chromatograph.[15]

The specific activity as reported is defined by one unit per hydrogen according to the equation

$$\text{spec. act.} = X/(X)_{\text{tol}}$$

where

$$X = \text{counts/molar area}^{16}/\text{total hydrogens}$$
$$(X)_{\text{tol}} = \text{counts/molar area/3 for a fully equilibrated toluene standard}^{14}$$

This definition assumes little or no equilibrium isotope effect of the olefin under question as compared to toluene. This is not unreasonable in lieu of previous data.[14] In any case, the qualitative conclusions would not be affected by an equilibrium isotope effect even if it were as large as 1.5.

Kinetic Measurements.—The general procedure for the kinetic experiments was similar to the tracer work except for minor variations. Straight dimethyl sulfoxide was employed with no radioactive material and an internal standard, usually n-pentane, was added with the reactant so that exact yields could be calculated. Analyses were performed on a Perkin–Elmer, Model 154 chromatograph using a 21-ft. column of Dow Corning (DC-200) silicone oil on Chromosorb at 75°. Molar response corrections were again employed.[16] A detailed description of these experimental techniques have been previously published.[8]

(13) L. Bateman, et al., J. Chem. Soc., 5339 (1961).
(14) J. E. Hofmann, R. J. Muller, and A. Schriesheim, J. Am. Chem. Soc., **85**, 3000 (1963).
(15) J. E. Hofmann and A. Schriesheim, ibid., **84**, 957 (1962). Note: propane is being employed in place of methane.
(16) This is the peak area of the gas chromatograph corrected for molar response. See A. E. Messner, D. M. Rosie, and P. A. Argabright, Anal. Chem., **31**, 230 (1959).