

Mechanisms of Elimination Reactions. IX. The Effect of Added Dimethyl Sulfoxide on Rates and Sulfur Isotope Effects in the Reaction of 2-Phenylethyldimethylsulfonium Bromide with Hydroxide Ion in Water¹

Anthony F. Cockerill and William H. Saunders, Jr.

Contribution from the Department of Chemistry, University of Rochester, Rochester, New York. Received May 24, 1967

Abstract: The rate of reaction of hydroxide ion with 2-phenylethyldimethylsulfonium bromide is relatively little affected by small amounts of dimethyl sulfoxide, but strongly increased by larger amounts (40-fold increase at 7.0 *M*, and nearly 1000-fold increase at 9.8 *M* dimethyl sulfoxide). Concomitant with the acceleration is a decrease in the sulfur isotope effect (0.7% in water to 0.1% in 7.0 *M* dimethyl sulfoxide). The rate increase undoubtedly results from a combination of the increased basicity of the hydroxide ion and the solvent effect on the reaction of two ions of opposite charge. The decrease in the sulfur isotope effect appears, in conjunction with other evidence, to indicate a more reactant-like transition state.

We have used sulfur isotope effects on several occasions to test the theory of the variable transition state² in E2 reactions. Although the isotope effects in E2 reactions are appreciably less than in SN1-E1 reactions, there was relatively little change in isotope effect between E2 reactions of *t*-butyldimethylsulfonium ion³ and 2-phenylethyldimethylsulfonium ion.⁴ The present study was undertaken to see whether changes in the reaction medium would change the isotope effect.

The results in Table I show that the rate of reaction of 2-phenylethyldimethylsulfonium ion with hydroxide

ion in water is increased by the addition of dimethyl sulfoxide. While the increase is moderate at first, it becomes nearly 10³-fold at 9.80 *M* (35 mole %) dimethyl sulfoxide.

There are two obvious sources of this increase in rate. Dimethyl sulfoxide is a less polar solvent than water, as measured by dielectric constant, E_T , and Z values.⁵ Consequently, addition of dimethyl sulfoxide to water is expected to increase the rate of reaction between two ions of unlike charge.⁶ The other factor is the increased basicity which results when a dipolar aprotic solvent is added to aqueous hydroxide.^{7,8} This factor will be discussed in more detail below.

The determination of the sulfur isotope effect presents a number of possible pitfalls. There must be no dimethyl sulfoxide in the methyl sulfide collected for isotope-ratio determination, since dimethyl sulfoxide has peaks in the same region as the parent peaks of dimethyl sulfide (62–64). None of our samples showed an appreciable peak at 78 (parent peak for dimethyl sulfoxide). We also demonstrated that no dimethyl sulfide comes from dimethyl sulfoxide, for no dimethyl sulfide is obtained in the absence of sulfonium salt or when the reaction of the sulfonium salt is quenched immediately after it is started.

The isotope effects reported in Table I change little up to 2.80 *M* (5 mole %) dimethyl sulfoxide, but thereafter show a distinct decrease concomitant with the more rapid increase in rate. The decrease is undoubtedly real, and the precision of the results is comparable to or better than that which we have obtained before.^{3,4} There is somewhat more scatter to the results at 7.0 *M* (20 mole %) dimethyl sulfoxide, perhaps because the relatively high speed made it more difficult to stop at the same extent of reaction in every run.

These results clearly show that the extent of C–S bond stretching in the transition state is decreased by added dimethyl sulfoxide. A simple and obvious explanation would be that a decrease in activation energy results in

Table I. Rates and Sulfur Isotope Effects in the Reaction of 2-Phenylethyldimethylsulfonium Bromide with Hydroxide Ion in Mixtures of Water and Dimethyl Sulfoxide at 40°

Dimethyl Sulfoxide, moles/l.	$k_2 \times 10^5$, l. mole ⁻¹ sec ⁻¹	Isotope effect, % ^a
0.00	1.12 ^b	0.74 ^c
1.40	1.38	0.68, 0.67, 0.60 Av 0.65 ± 0.025 ^d (0.107) ^e
2.80	2.62	0.67, 0.66, 0.57, 0.64 Av 0.64 ± 0.023 ^d (0.073) ^e
4.20	6.22	0.44, 0.37, 0.35, 0.36 Av 0.38 ± 0.021 ^d (0.067) ^e
7.00	47.4	0.00, 0.21, 0.28, 0.05, 0.02 Av 0.11 ± 0.056 ^d (0.156) ^e
8.40	210.9	<i>f</i>
9.80	1001	<i>f</i>

^a $[(k_{32}/k_{34}) - 1]100$. ^b Extrapolated from the data of Saunders and Ašperger.^{4a} ^c Single measurement. This effect should be, and is, slightly higher than the precisely known value of 0.64 ± 0.012 at 59°. ^d Standard deviation of mean. ^e 95% confidence limit. ^f Isotope effects not determined under these conditions.

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a more reactant-like transition state.⁹ This explanation has the deficiency of not considering explicitly the possible effect of change in base strength on the C-H bond in the transition state. No conclusions about the C-H bond are possible from the present results alone.

Recent studies by Cockerill¹⁰ have shed light on this problem by means of deuterium isotope effects with 2-phenylethyl-2,2-*d*₂-dimethylsulfonium ion and Hammett ρ values with substituted (*p*-Cl, H, *p*-Me, and *p*-OMe) 2-phenylethyldimethylsulfonium ions. The k_H/k_D value increases modestly in the range of solvent composition covered by our results, from 5.42 in water¹¹ to 5.76¹⁰ at 19.1 mole % (ca. 7 M) dimethyl sulfoxide at 40°. The ρ value increases from +2.11¹² in water to +2.54¹⁰ in 19.4 mole % dimethyl sulfoxide at 50°. Cockerill's work¹⁰ extends to higher dimethyl sulfoxide concentrations than ours. The ρ value undergoes little further change above 19.1 mole %, remaining near +2.6 up to 60 mole %, while k_H/k_D goes through a maximum (6.21 at 47.3 mole % and 40°) between 40 and 50 mole %. The subsequent decrease in k_H/k_D continues up to 84.1 mole % dimethyl sulfoxide, the highest concentration studied.

We propose that these additional results indicate a decrease in the extent of hydrogen transfer in the transition state as dimethyl sulfoxide is added. If the results in water indicate a transition state where the proton is more than half transferred,² the isotope effect is expected to go through a maximum as the extent of proton transfer decreases.¹³ To our knowledge, this is the first example of a k_H/k_D maximum with a single substrate under changing conditions. It is entirely reasonable that an increase in base strength should result in less complete proton transfer in the transition state.¹⁴

The increase in ρ is more difficult to interpret. It could result from a slower decrease in C-H than of C-S stretching in the transition state, so it need not be in conflict with conclusions from the sulfur and deuterium isotope effects. In addition, ρ is also expected to increase with decreasing dielectric constant of the medium.¹⁵ The constancy of ρ at higher dimethyl sulfoxide concentrations may reflect a balance between a decrease from decreasing carbanion character and an increase from the solvent effect.

Our final conclusion, then, is that addition of dimethyl sulfoxide to the reaction medium produces concomitant decreases in the extent of C-S and C-H bond stretching in the transition state. A comparison should be made of this conclusion with our previous one that addition of dimethyl sulfoxide to *t*-butyl alcohol-*t*-butoxide did not affect the transition-state structure in the E2 reaction of 2-arylethyl bromides with *t*-butoxide.¹⁶ The solvent effect on a reaction between oppositely charged ions is expected to be much greater than on a reaction between an ion and a neutral mole-

cule.⁶ More important, we believe, is the differing character of the changes in base strength in the two media.

In *t*-butyl alcohol, *t*-butoxide ion is presumably hydrogen bonded to only a single alcohol molecule for steric reasons. The *t*-butoxide ion must be desolvated to form the E2 transition state, and the ease of desolvation is increased by added dimethyl sulfoxide, leading to an increase in rate. The transition state with its diffuse charge is little affected by changes in medium. Hydroxide ion in water is believed to be hydrogen bonded to three water molecules.¹⁷ Formation of the E2 transition state requires displacement of only one of these. As dimethyl sulfoxide is added, this displacement becomes easier. In addition, the type of solvation of the partially neutralized hydroxide ion in the transition state should change. As water of hydration is replaced by dimethyl sulfoxide, the ion becomes a distinctly stronger base—in effect, a different base. With these differences in mind, it is not surprising that a change in the extent of proton transfer was noted as composition changed in mixtures of water and dimethyl sulfoxide, but not in mixtures of *t*-butyl alcohol and dimethyl sulfoxide.

Experimental Section

Materials. 2-Phenylethyldimethylsulfonium bromide was prepared by the procedure of Saunders and Ašperger.⁴ Solutions were prepared by diluting weighed amounts of dimethyl sulfoxide to 1000 ml with distilled water. The dimethyl sulfoxide was purified as described before.¹⁶

Kinetic Studies. Solutions in the desired solvent of sodium hydroxide and of 2-phenylethyldimethylsulfonium bromide were equilibrated in the thermostat, mixed, and diluted with solvent so as to give initial concentrations of 0.19–0.20 M in base and 0.1 M in sulfonium salt. Aliquots of 5 ml were withdrawn periodically, quenched in 50 ml of distilled water, and titrated with standard 0.1 M hydrochloric acid, using a phenolphthalein indicator. Rate constants were reproducible to within 1–2%. Styrene yields, determined in a Beckman DU spectrophotometer after dilution of an aliquot from a complete reaction with ethanol, were always $100 \pm 1.0\%$.

Preparation of Samples for Mass Spectra. Reactions were carried out in a three-necked round-bottom flask immersed to the necks in a constant-temperature bath and equipped with a gas-inlet tube, a sealed stirrer, and, in the third neck, a tube surmounted by a serum cap and having a side-arm outlet. The outlet led successively to an acetone–Dry Ice trap, a phosphorus pentoxide drying tube, a liquid nitrogen trap, and a tube containing Drierite. The base solution was added to the flask and the apparatus flushed with nitrogen (previously passed over Ascarite and Drierite) for 30 min. Nitrogen flow was stopped, and the sulfonium salt solution added by a syringe through the serum cap. Concentrations were the same as in the kinetic runs, and the volume of solution was 100 ml. The reaction was allowed to run to 4–5% completion (from 290 min for 1.4 M to 40 min for 4.20 M dimethyl sulfoxide). During the last 20–30 min, the Dry Ice–acetone bath was removed and the nitrogen flow recommenced so as to flush all of the dimethyl sulfide into the liquid nitrogen trap. In 7.00 M dimethyl sulfoxide the time for 4% reaction was only 9 min, so the reaction mixture was diluted with 400 ml of water and nitrogen bubbled through for 20–30 min. The liquid nitrogen trap was then transferred to a high-vacuum line. The dimethyl sulfide was distilled twice through phosphorus pentoxide and then twice more, the final distillation being into a sample tube for the mass spectrometer.

The 100% samples of dimethyl sulfide were obtained in a similar fashion from dilution of 2 ml of the sulfonium salt solution (the same sample in the same water–dimethyl sulfoxide solution as for the 5% sample) in 20 ml of aqueous sodium hydroxide, followed by heating at 90–95° for 3 hr. In neither the 5 nor 100% samples was any dimethyl sulfide obtained when a blank without added sulfo-

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nium salt was run, or when the reaction was quenched with hydrochloric acid immediately after starting.

Mass Spectrometry. An Atlas CH-4 instrument was used. Inlet temperatures ranged from ambient to 140°, and about 500–600 units of sample pressure were used. The same precautions as before^{3,4} were taken to keep initial scale deflection and attenuator settings the same for all samples compared. The entire mass spectrum (up to *m/e* 100) was scanned for each sample as a precaution against impurities. Minor peaks (0.3–1.0% of the *m/e* 62 peak) were noted at 74 and 76 in some samples, but the *m/e* 78 peak (dimethyl sulfoxide) was always less than 0.1%. Masses 62 and

64 were then scanned successively 20 times.¹⁸ At least 10, and almost always 15–20 scans were used in each calculation. The *m/e* 62/64 ratios use each peak twice: a given peak is compared both with the peak preceding and the peak following. This procedure minimizes the effect of the slow decrease in peak height resulting from sample depletion. Standard deviation of the mean for the ratios usually ran around 0.05–0.1%, and never above 0.15%.

(18) Though the instrument is capable of simultaneous collection, the dual collector available for this work would have collected *m/e* 62 and 63 together, and *m/e* 63 contains both S³² and S³⁴ species.

7,12-Dihydropleiadenes. VII. Application of Nuclear Overhauser Effects to Stereochemical Problems

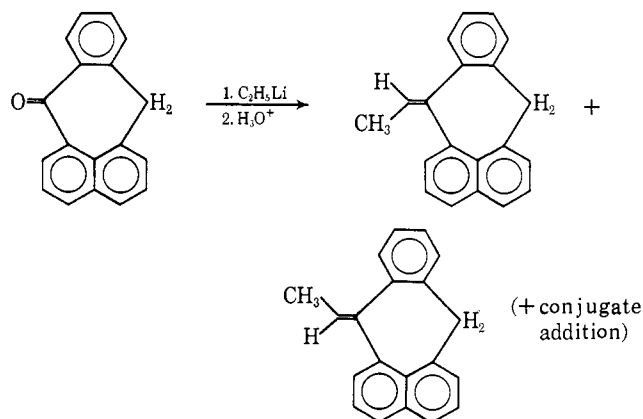
James G. Colson,¹ Peter T. Lansbury,^{2a} and Franklin D. Saeva^{2b}

Contribution from the Central Research Center, Hooker Chemical Corporation, Niagara Falls, New York 14302, and Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214.

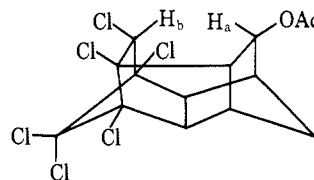
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Abstract: Nuclear Overhauser Effects (NOE) between axial C₇ and C₁₂ protons and between equatorial C₇ protons and adjacent aromatic methyl groups in 7,12-dihydropleiadenes have been observed, in accord with the proximity of such groups to each other. Several structural assignments which were otherwise tenuous could be conclusively made by using NOE's.

In some previous studies of 7,12-dihydropleiadene (DHP) chemistry,^{3–5} we have determined the preferred conformations of various groups on the C₇ and C₁₂ positions of the DHP molecule.^{4,5} In addition, it was clearly established that axial protons on these positions always appeared at lower field in the nuclear magnetic resonance (nmr) spectrum in chloroform than their equatorial counterparts from nmr chemical shift studies of model compounds,^{4,5} spin decoupling of axial benzylic protons from aromatic protons,⁴ and relative kinetic acidities in conformationally fixed com-



pounds.³ These findings were insufficient, however, to allow unambiguous stereochemical assignments to be made for certain isomeric dihydropleiadenes. For example, the geometric isomers resulting from carbonyl addition of ethyllithium to 7-(12H)-pleiadenone and subsequent dehydration could not be readily distinguished by existing chemical and physical techniques.⁶ We hoped that this problem, as well as several others (*vide infra*), could be efficiently solved by investigating intramolecular nuclear Overhauser effects (NOE). Anet^{7a} and others^{7b} have shown that this technique has great promise for identifying adjacent protons in molecules, such as in the example below.



These Overhauser effects are best observed in conformationally rigid molecules^{7a} in which magnetic nuclei are proximal and show no scalar spin-spin coupling, but are coupled by a direct dipole-dipole interaction. As a result of this coupling, the populations of the nuclear energy levels are not independent of each other. In the case of two protons A and B coupled only by the above-mentioned dipole-dipole interaction, in a conformation such that $1/T_1^A = 1/T_1^{AB}$, any changes in the populations of the nuclear energy levels of proton

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