ORGANIC AND BIOLOGICAL CHEMISTRY

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

Rates of Solvolysis of Some Deuterated 2-Phenylethyl *p*-Toluenesulfonates[1,2]

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Rates of solvolysis of 2-phenylethyl (Ia), 2-phenylethyl-1,1-d_2 (Ib) and 2-phenylethyl-2,2-d_2 (Ic) *p*-toluenesulfonates were determined in formic and in acetic acid. In formolysis Ia and Ic react at the same rate, but Ia reacts 17 ± 2% faster than Ib. In acetolysis small effects are observed with both deuterated compounds: Ia is 3 ± 1% faster than Ib and 4 ± 3% faster than Ic. The formates and acetates produced in the solvolyses were converted to the corresponding 2-phenylethanols II. Comparison of the infrared spectra of the products with those of synthetic mixture of IIb and IIc revealed that *ca.* 45% phenyl migration had occurred in the formolysis and *ca.* 10% phenyl migration in the acetolysis. These results suggest that phenyl participation predominates in formolysis, but is unimportant in acetolysis. The nature of the transition state in phenyl-participation reactions and the factors contributing to secondary deuterium isotope effects are discussed.

In recent years much interest in secondary deuterium isotope effects[3] has developed. The diminution in rate produced by substitution of deuterium for hydrogen on the β-carbon of a system undergoing SN1-type solvolysis has been the object of numerous studies. The origin of the effect has been variously ascribed to hyperconjugation,[4] elimination-type driving forces[5] or hydrogen participation.[6] The differences between these explanations are more concerned with details such as the role of solvent than with fundamentals. Each assumes that the isotope effect arises from overlap of the C–H σ-orbital on the β-carbon with the developing vacant *p*-orbital on the α-carbon.

Other explanations have been offered. Wiberg[7] has suggested that a simple inductive effect of the developing positive charge on the β-carbon–hydrogen bond may explain the facts. Halevi[8] believes that electron distribution in C–H and C–D bonds may differ sufficiently to account for part or all of the observed effects.

Quite recently three groups have observed appreciable isotope effects in solvolysis when α-hydrogens are replaced by deuterium.[2,9,10] The present investigation was undertaken with the hope of defining more closely the nature of secondary deuterium isotope effects and their possible utility in mechanistic studies.

2-Phenylethanol-1,1-d_2 (IIb) was prepared by the reduction of ethyl phenylacetate with lithium aluminum deuteride. 2-Phenylethanol-2,2-d_2 (IIc) resulted from the action of lithium aluminum hydride on ethyl phenylacetate-α,α-d_2. This deuterated ester in turn was obtained by heating the sodium salt of ethyl phenylmalonate in deuterium oxide. The phenylmalonic ester at first hydrolyzes to the sodium salt of the half ester, which then smoothly undergoes decarboxylation to the desired product. The *p*-toluenesulfonates of the 2-phenylethanols were prepared in conventional fashion. Results of deuterium analyses (Table I) show that the products are somewhat short of isotopic purity. This situation undoubtedly could be remedied (see Experimental), but the materials were satisfactory for the purposes of the present experiments.

TABLE I

RATES OF FORMOLYSIS OF DEUTERATED 2-PHENYLETHYL *p*-TOLUENESULFONATES[a]

Position of D	Atoms D/ molecule	$k^b \times 10^5$ sec.$^{-1}$	k_H/k_D
..	None	3.80[c]	..
α	1.83	3.24	1.17
β	1.62	3.82	1.00

[a] Solvolysis at 75.25° in anhydrous formic acid initially 0.10 *M* in sulfonate and 0.107 *M* in sodium formate. [b] Each constant is the average of three runs with average deviation 0.04 in all cases. [c] S. Winstein and R. Heck, THIS JOURNAL, **78**, 4801 (1956), report 4.10 × 10^{-5} sec.$^{-1}$ at 75.00° with initial concentrations about one-third those used here.

TABLE II

RATES OF ACETOLYSIS OF DEUTERATED 2-PHENYLETHYL *p*-TOLUENESULFONATES[a]

Temp., °C.	$k \times 10^{-6}$ sec.$^{-1}$ for No D	α-D	β-D	$(k_H/k_D)\alpha$	$(k_H/k_D)\beta$
93.90	2.42	2.39	2.26	1.02	1.07
93.95	2.54	2.44	2.51	1.04	1.01
			Average	1.03	1.04

[a] The same materials were used as in the formolyses. See Table I for deuterium analyses. Solutions were initially 0.03 *M* in sulfonate and 0.032 *M* in sodium acetate.

Rates of formolysis at 75.25° of 2-phenylethyl (Ia), 2-phenylethyl-1,1-d_2 (Ib) and 2-phenylethyl-2,2-d_2 (Ic) *p*-toluenesulfonates were determined. The results are recorded in Table I. Rates of acetolysis at 93.9° were determined for the same compounds. Rate constants are give in Table II. The different presentation is employed because temperature control was somewhat poorer at the higher temperature of the acetolysis. Consequently, Ia, Ib and Ic were acetolyzed simultaneously in each of two runs so as to minimize

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(1) This work was supported by the Office of Ordnance Research, U. S. Army.

(2) A portion of this work has been published in preliminary form: W. H. Saunders, Jr., S. Ašperger and D. H. Edison, *Chemistry & Industry*, 1417 (1957).

(3) The term "secondary isotope effect" as used here is defined as an alteration in rate arising from isotopic substitution in a bond which is not broken in the rate-determining step.

(4) E. S. Lewis and C. E. Boozer, THIS JOURNAL, **76**, 791 (1954).

(5) V. J. Shiner, Jr., *ibid.*, **75**, 2925 (1953).

(6) S. Winstein, Abstracts of Papers, Fifteenth National Organic Chemistry Symposium of the American Chemical Society, Rochester, N. Y., June 17-20, 1957.

(7) K. B. Wiberg, *Chem. Revs.*, **55**, 713 (1955).

(8) E. A. Halevi, *Tetrahedron*, **1**, 174 (1957).

(9) A. Streitwieser, Jr., and R. C. Fahey, *Chemistry & Industry*, 1417 (1957); A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey and S. Suzuki, THIS JOURNAL, **80**, 2326 (1958).

(10) K. Mislow, S. Borčić and V. Prelog, *Helv. Chim. Acta*, **40**, 2477 (1957).

the effect of any unavoidable temperature fluctuations during a run.

Interpretation of the rate results requires some knowledge of the extent to which the process of phenyl migration may accompany the solvolyses. Since the phenyl migration would convert α-deuterated starting material to β-deuterated product (and *vice versa*), a method of analyzing mixtures of IIb and IIc was sought. The infrared spectra of the two substances showed numerous differences, of which peaks at 9.92 μ (IIb) and 10.5 μ (IIc) appeared particularly advantageous for analysis. The relevant portions of the spectra of synthetic mixtures are shown in Fig. 1. Calibration curves were prepared and the compositions of the products of the solvolyses obtained by reference to these curves. The formates and acetates were first converted to the alcohols with lithium aluminum hydride and all products were analyzed as the alcohols. Results are given in Table III. Incomplete deuteration of the standards and the solvolysis products renders the figures somewhat less precise than they might be (see Experimental for a more complete consideration of this point), but the over-all precision of the determinations still seems within about 5%. After this work was completed, a report appeared in which rearrangements in solvolyses of 2-phenylethyl-1-^{14}C *p*-toluenesulfonate were studied.[11] The 45% rearrangement in formolysis is in excellent agreement with the mean of our two values, but their value for acetolysis (5.5%) is considerably less than the 10% we obtained. Probably more weight should be attached to their value, since their precision throughout was considerably superior to ours.

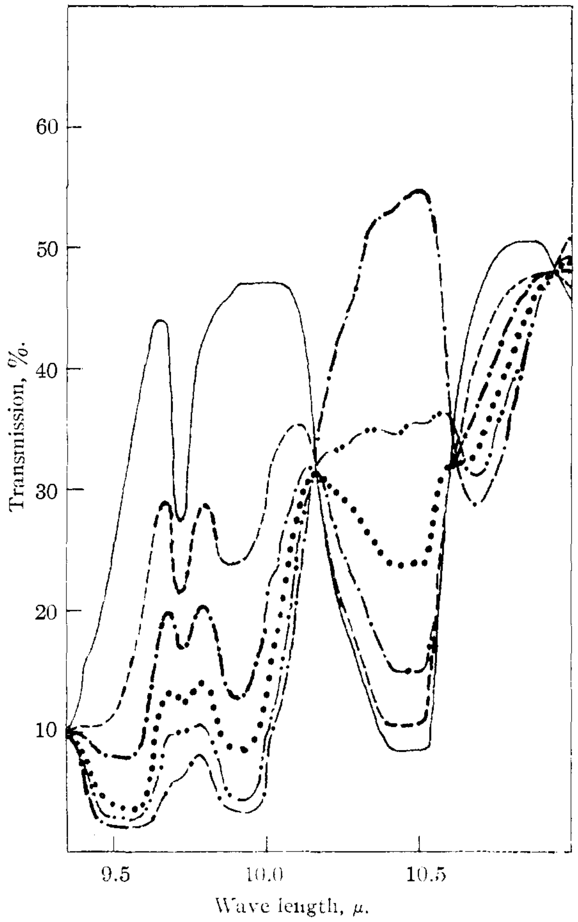


Fig. 1.—Infrared spectra of α- and β-deuterated 2-phenylethanols: ———, α-deuterated; ·——·, β-deuterated. The remaining lines represent mixtures of the two deuterated alcohols.

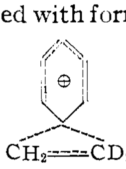
TABLE III

COMPOSITION OF PRODUCTS FROM SOLVOLYSES OF DEUTERATED 2-PHENYLETHYL *p*-TOLUENESULFONATES

Solvent	Starting material	Product	% compn. at 9.92 μ	% compn. at 10.50 μ	Average % comp.
HCOOH	α-D	No D	8.7[a]	8.7[a]	8.7
		α-D	53.2	52.0	52.6
		β-D	37.1	37.0	37.1
					98.4
HCOOH	β-D	No D	18.9[a]	18.9[a]	18.9
		α-D	40.3	45.3	42.8
		β-D	47.5	42.2	44.8
					106.5
HOAc	α-D	No D	8.7[a]	..[b]	8.7
		α-D	81.4	..	81.4
		β-D	10.8	..	10.8
					100.9
HOAc	β-D	No D	..[b]	19.5[a]	19.5
		α-D	..	9.8	9.8
		β-D	..	77.5	77.5
					106.8

[a] The % undeuterated product in each case is calculated from the deuterium analysis and the assumption that only undeuterated and dideuterated species are present (see Experimental for discussion of this assumption). [b] Analyses at these wave lengths were not used because they involve composition ranges where %T changes very slowly with composition.

The results of the formolysis clearly confirm Winstein's[12] contention that the reaction proceeds with predominant phenyl participation. This conclusion follows from the absence of a β-deuterium isotope effect and hence the absence of hyperconjugation or hydrogen participation. The extensive phenyl migration shows that around 90% of the product arises from the symmetrically bridged ion III or its equivalent. A control experiment in which IIb was heated with formic acid demonstrates that the product undergoes no further rearrangement under the conditions of the reaction. Likewise, internal return from a phenonium–tosylate ion pair[13] cannot be appreciable, since in its presence Ib and Ic would be interconverted and their



III

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(11) C. C. Lee, G. P. Slater and J. W. T. Spinks, *Can. J. Chem.*, **35**, 1417 (1957).

(12) S. Winstein and R. Heck, THIS JOURNAL, **78**, 4801 (1956); S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, *ibid.*, **75**, 147 (1953).

(13) For a case where internal return is important in a related system, see S. Winstein and K. Schreiber, *ibid.*, **74**, 2165 (1952).

rate constants would drift toward a common value as the reaction proceeded.

Several additional conclusions may be drawn. The complete absence of a β-deuterium isotope effect in formolysis renders unlikely the inductive[7] explanation of these effects, since an inductive effect should have no stereoelectronic requirements and therefore still be operable in the presence of predominating phenyl participation. Our results thus provide further support for Shiner's[14] claim that β-deuterium isotope effects have definite conformational requirements. If phenyl participation dominates, the β-carbon–hydrogen bonds will be almost orthogonal to the developing p-orbital on the α-carbon in the transition state.

Furthermore, although a symmetrical phenonium ion (III) appears to be involved as an intermediate, the transition state for ionization evidently does not resemble III at all closely. If the transition state did resemble III, the α- and β-carbon–hydrogen bonds would be in closely similar environments and therefore similar α- and β-deuterium isotope effects would be expected, irrespective of the origin of the effect. Cram[15] has noted that rate differences between diastereomers are small in solvolyses in the 3-phenyl-2-butyl and related systems. Since the phenonium ions from diastereomers should show much greater differences in non-bonded repulsions than the diastereomers themselves, he concludes that the transition state for ionization bears more resemblance to reactant than to phenonium ion. One would ordinarily expect a transition state leading directly to a high-energy intermediate to resemble that intermediate rather closely,[16] so the results provide some support for an unsymmetrically bridged intermediate preceding the symmetrical phenonium ion.[17]

The results on acetolysis demonstrate that the major portion of this reaction proceeds without phenyl participation. The α-deuterium effect is much reduced and there now appears to be a small but definite β-deuterium effect. Interpretation of the results is somewhat complicated by the possibility that a part of the reaction may be bimolecular with acetate ion,[12] although the observed extent of rearrangement requires that at least 10–20% of the reaction involve an ionic intermediate.

Streitwieser[9] has observed a 17% isotope effect in the solvolysis of cyclopentyl-1-d p-toluenesulfonate and ascribes the effect to the change in bond hybridization (sp^3 to sp^2) in going from the ground state to a carbonium-ion-like transition state. Examination of reasonable models suggests that the C–H out-of-plane bending frequency in the carbonium ion should be considerably less than the corresponding frequency in the ground state. While this seems to be the most reasonable explanation of the α-deuterium effect, further experimental evidence is desirable. We feel our results offer such evidence on two points.

First, if the α-effect were entirely the result of the development of positive charge, one would expect it to be relayed to a measurable extent to the β-position, contrary to fact. Secondly, a characteristic of the out-of-plane C–H vibration would be a pronounced susceptibility to inhibition by the proximity of departing or displacing groups.[9,18] Our acetolysis appears to be a borderline S_N1–S_N2 reaction and presumably the α-carbon bears an amount of charge in the transition state not markedly less than in the transition state for formolysis. On the other hand, the freedom of the out-of-plane C–H vibration could be greatly reduced if the leaving group (or the displacing group) is close enough to offer hindrance. Such hindrance should be a much more sensitive function of distance than the electron density at the α-carbon atom.

Experimental[19]

2-Phenylethanol-1,1-d_2.—Ethyl phenylacetate was reduced with lithium aluminum deuteride (Metal Hydrides, Inc., 98% deuterium) and the reaction mixture worked up as described by Amundsen and Nelson.[20] 2-Phenylethanol-1,1-d_2, b.p. 110° (20 mm.), 1.83 atoms D/molecule,[21] was obtained in 78% yield.

Ethyl Phenylacetate-α,α-d_2.—A solution of 0.33 mole of ethyl phenylmalonate in 100 ml. of dry AR benzene was treated with 0.33 mole of sodium hydride.[22] The mixture was stirred for an hour, and the white, amorphous product removed by filtration and washed thoroughly with benzene. The solid was then placed in a vacuum desiccator (continuous pumping) for 24 hours. Fifty grams of the resulting sodium salt was added to 50 g. of deuterium oxide (99.5%) and the mixture refluxed for eight hours in a nitrogen atmosphere. The organic layer was separated and the aqueous layer extracted twice with ether. The combined extracts and organic layer were dried over anhydrous magnesium sulfate. Removal of the ether and distillation through a short Vigreux column gave 16.7 g. (63%) of ethyl phenylacetate-α,α-d_2, b.p. 73–74° (0.5 mm.).

2-Phenylethanol-2,2-d_2 was obtained by reduction of ethyl phenylacetate-α,α-d_2 with lithium aluminum hydride in 84% yield, b.p. 102–103° (15 mm.).

2-Phenylethyl p-Toluenesulfonates.—Treatment of the appropriate 2-phenylethanol with p-toluenesulfonyl chloride in pyridine[23] produced the p-toluenesulfonate in yields of around 90%. The undeuterated toluenesulfonate melted 37.5–38.2° (lit.,[12b] 35.5–36.6°). The deuterated toluenesulfonates melted about 0.5° higher. Results of deuterium analyses are recorded in Table I.

Deuterium analyses were performed by the "falling drop" method. The procedure and apparatus were essentially as described by previous workers.[24] Duplicate analyses usually agreed to within 1%.

Products of Solvolyses.—Solutions of 2-phenylethyl-1,1-d_2 and 2-phenylethyl-2,2-d_2 p-toluenesulfonates (0.3 M) in anhydrous formic acid containing a slight excess of sodium formate were heated under reflux for four days. Solutions

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[14] V. J. Shiner, Jr., THIS JOURNAL, **78**, 2653 (1956).

[15] D. J. Cram, H. L. Nyquist and F. A. Abd Elhafez, *ibid.*, **79**, 2876 (1957).

[16] G. S. Hammond, *ibid.*, **77**, 334 (1955).

[17] For another reaction in which both symmetrical and unsymmetrical phenonium ions may be involved, see D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **75**, 3189 (1953); S. Winstein, M. Brown, K. Schreiber and A. H. Schlesinger, *ibid.*, **74**, 1140 (1952). See ref. 15 for a later, and different, view.

[18] V. J. Shiner, Jr., *ibid.*, **74**, 5285 (1952), found no α-deuterium effect in an S_N2 displacement, a fact consistent with this interpretation.

[19] Melting points and boiling points are uncorrected.

[20] L. H. Amundsen and L. S. Nelson, THIS JOURNAL, **73**, 242 (1951).

[21] The lower deuterium content (91%) of product as compared to lithium aluminum deuteride (98%) may be the result of an isotope effect in the reduction. Deuterium should concentrate in the deuteride, which was used in slight excess.

[22] Best results were obtained with a 50% dispersion of sodium hydride in mineral oil (Metal Hydrides, Inc.). Subsequent to the present work, petroleum ether (30–60°) was found to be superior to benzene as reaction medium, giving a purer sodium salt and higher isotopic purity in the final product.

[23] R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

[24] W. von E. Doering and A. K. Hoffman, THIS JOURNAL, **77**, 521 (1955); A. S. Keston, D. Rittenberg and R. Schoenheimer, *J. Biol. Chem.*, **122**, 227 (1937).

of the same concentrations in acetic acid were refluxed for 40 hr. In each case, the cooled reaction mixture was diluted with water and extracted with petroleum ether (b.p. 30–60°). The extract was washed with sodium carbonate solution and water and then dried. The crude ester from evaporation of the extract was treated with lithium aluminum hydride in ether and the resulting 2-phenylethanol purified by distillation under reduced pressure.

Examination of the infrared spectra of α- and β-deuterated 2-phenylethanols revealed a number of regions of distinct difference, of which peaks at 9.92 μ (α-deuterated) and 10.5 μ (β-deuterated) appeared most advantageous for analysis (see Fig. 1). The infrared spectra of synthetic mixtures of α- and β-deuterated alcohols in carbon tetrachloride solution were determined and plots relating composition to % transmission at these wave lengths were prepared. Since the standards were not completely deuterated, it was necessary to make some assumption concerning the distribution of deuterium. For simplicity, it was assumed that only undeuterated and dideuterated species were present. This is undoubtedly incorrect, but the error will largely cancel if the actual distribution is similar in the two standards. We also, of course, do not know whether di- or monodeuterated species (or both) contributed to the observed infrared peaks.

Infrared spectra of the alcohols from the solvolyses were determined in carbon tetrachloride solution and their compositions found by reference to the plots of %T *vs.* composition for the synthetic mixtures. The results are recorded in Table III. The difference in results from α- and β-deuterated starting materials provides a check on the error in our original assumption that deuterium distribution is the same in the two standards. The agreement is not excellent, but adequate for our purposes. The sum of percentages of products from the β-deuterated starting material (Ic) is around 106% in both formolysis and acetolysis (Table III), a result also attributable to error in our assumptions about deuterium distribution.

In a control experiment, a 0.3 M solution of 2-phenylethanol-1,1-d_2 in formic acid (about 0.01 M in sodium formate) was heated at 80° for three days. The resulting 2-phenylethyl formate was converted to 2-phenylethanol, which was found by infrared analysis to be identical with the starting material.

Kinetic Methods.—Anhydrous formic acid was obtained from 98–100% formic acid by drying over finely powdered boric oxide.[25] Anhydrous acetic acid was prepared from 99.8% acetic acid by addition of a small excess of acetic anhydride. Sodium acetate and sodium formate were dried thoroughly over phosphorus pentoxide. All materials were Analytical Reagent grade.

The reactions were carried out in a flask fitted with a side arm for withdrawing samples, and a reflux condenser surmounted by a calcium chloride tube. The flask was immersed in a thermostat held at 75.25 ± 0.05°. Formic acid containing 0.107 M sodium formate was brought to thermal equilibrium and a weighed quantity (calculated to give a 0.100 M solution) of the p-toluenesulfonate introduced. Aliquots of 5 ml. were withdrawn periodically, quenched in cold glacial acetic acid, and titrated potentiometrically[25] with 0.05 N perchloric acid in acetic acid.

The acetolyses were carried out by a procedure closely similar to that for the formolyses. Solutions initially 0.030 M in p-toluenesulfonate and 0.032 M in sodium acetate were used. Higher temperatures (93.9°) were necessary to obtain reasonable rates and it was more difficult to maintain constant temperature over a series of runs. Consequently, rates on undeuterated, α- and β-deuterated toluenesulfonates were run simultaneously so that any temperature change would influence equally all three reactions. For this reason, as well as the lower concentrations, precision was somewhat lower than in the formolyses, but still within 2–3%.

Acknowledgments.—We wish to thank Professor A. Streitwieser, Jr., for several interesting discussions and for information in advance of publication. We also thank Professors K. Mislow and V. Prelog for informing us of their results in advance of publication.

(25) S. Winstein and H. Marshall, THIS JOURNAL, **74**, 1120 (1952).

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, BROOKHAVEN NATIONAL LABORATORY]

Electron Impact Dissociation of Camphene-8-C^{13} [1,2]

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Specific fragmentation mechanisms for the formation of $C_9H_{13}^+$ and $C_8H_{11}^+$ ions are established from a study of the mass spectrum of camphene-8-C^{13}. A cyclic structure for $C_7H_9^+$, the most abundant ion in the camphene spectrum, is proposed.

The $C_7H_9^+$ ion accounts for approximately 30% of the total ion yield in mass spectra of the terpenes α-pinene, cyclofenchene and tricyclene. It is the most abundant ion produced in spectra of the isomeric exocyclic olefins camphene, β-pinene and α-fenchene, but with these compounds competing processes reduce the $C_7H_9^+$ intensity to roughly 15% of the total ion yield. The monocyclic $C_{10}H_{16}$ isomer dipentene cleaves on electron impact to give $C_5H_8^+$ ions with $C_7H_9^+$ as the second most abundant ion in its mass spectrum. Spectra for these compounds are shown graphically in Figs. 1, 2 and 3.

The electron impact dissociation reactions of these compounds present an interesting problem since the processes are essentially those of intramolecular rearrangement and dissociation of excited $C_{10}H_{16}^+$ ions.

The statistical theory of mass spectra[3a,b] gives rate equations for unimolecular ion decomposition reactions which involve energetics of the reaction and frequency factors which are related to steric factors or entropy of activation. Since energetics for dissociation reactions in isomeric systems are expected to be very similar, differences in reaction rates probably arise from differences in the frequency factors. If one assumes that the theory applies, one could assert that the relatively large yield of $C_3H_5^+$, etc., from the exocyclic olefins can be explained by higher excitation of the latter on electron impact. This is a very improbable assumption that would do serious damage to any attempt to apply the statistical theory to systems observable with the mass spectrometer. One is left then with considerations of the effect of structure on mechanisms, and it was for this reason that a C^{13} tracer procedure was investigated.

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(1) Research performed under the auspices of the U. S. Atomic Energy Commission.

(2) A part of this material was presented at the Chicago A.C.S. Meeting, September, 1953.

(3) (a) L. Friedman, F. A. Long and M. Wolfsberg, *J. Chem. Phys.*, **27**, 613 (1957); (b) H. Rosenstock, A. Wallenstein, A. Wahrhaftig and H. Eyring, *Proc. Natl. Acad. Sci. U. S.*, **38**, 667 (1952).