[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE RICE INSTITUTE]

Isotope Effects in Carbonium Ion Reactions. III. The Solvolysis of Methyltolylcarbinyl Chloride[1]

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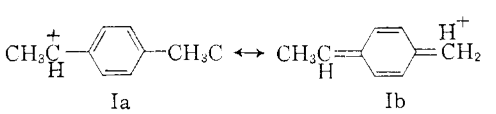
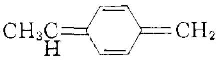
The substitution of deuterium for hydrogen in the *p*-methyl group of methyl-*p*-tolylcarbinyl chloride results in a retardation of solvolysis in acetic acid by about 10% and in aqueous acetone by about 1%. Similar substitution in the *m*-methyl group of the *m*-tolyl isomer gives a 1% acceleration. Substitution in the methyl group next to the chlorine-bearing carbon produces a retardation of 13–20%, depending on solvent and temperature. A 10% retardation results from deuterium substitution in the α-position.

Introduction

The substitution of deuterium for β-hydrogen in alkyl halides and sulfonates has been shown to lead to retardation of solvolysis.[2] A connection has been proposed between this isotope effect in ionization reactions and weakening of the bonds to hydrogen in the transition state by hyperconjugation. When the deuterium substitution is made at the carbon atom adjacent to the incipiently cationic carbon, other explanations involving electrostatic effects, elimination reactions and neighboring group participation are conceivable. A characteristic of conjugation of any sort is that it may be transmitted through unsaturated systems, and we shall here investigate this possibility in the solvolysis of methyltolylcarbinyl chlorides. Since the preliminary publication of a portion of this work,[1] another example of the same type has appeared which show a similar effect of deuterium substitution in *p*-alkylbenzhydryl chlorides.[3] The methyl-*p*-tolylcarbinyl chloride gives on solvolysis the ion I, with the possibility of the pertinent hyperconjugation indicated by the contribution of structure Ib. There is no reason to expect elimination to give the very unstable olefin II, and direct participation of the hydrogen of the *p*-methyl group by the intermediacy of III is absurd. The only reasonable role of hydrogen close to a neighboring group participation would be the possibility of the contribution of structures such as IV. Related structures have been considered in detail under the name "α-hydrogen bonding," and the result of such contributions has been identified with hyperconjugation.[4] We shall not attempt to distinguish between this possible mechanism of hyperconjugation, which presumably affects a hydrogen bending vibration, and that involving "no-bond resonance," which can affect all hydrogen vibrations. Streitwieser[2e] has suggested that isotope effects arise from the weakening of this same bending vibration.



Ia Ib



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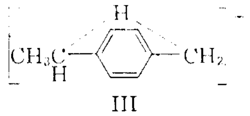

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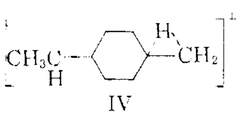
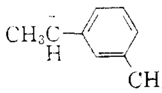


IV

The ion V, without hyperconjugation possibilities as far as the ring methyl is concerned, is the product of solvolysis of the *meta* compound. If the retardation by deuterium substitution is a manifestation of an inductive or electrostatic effect, then the effect of deuterium should be qualitatively the same in the *m*-methyl and in the *p*-methyl groups. Virtually no effect of deuterium in the *m*-methyl group is expected on the basis of a conjugation explanation.



V

Results and Discussion

The various compounds were prepared from deuterated toluene by following the sequences: toluene → *p*-methylacetophenone → methyl-*p*-tolylcarbinol → methyl-*p*-tolylcarbinyl chloride, and *p*-methylacetophenone → *p*-methylacetanilide → 2-bromo-4-methylaniline → m-bromotoluene → methyl-*m*-tolylcarbinol → methyl-*m*-tolylcarbinyl chloride.

Table I shows the rate constants obtained for the various compounds, and the isotope effect expressed as k_H/k_D.

The rate reduction on placing deuterium in the *p*-methyl group is clear in the acetic acid solvent and is still present, but to a much smaller extent, in the aqueous acetone solvent. The usual isotope effect resulting from deuterium substitution at the adjacent carbon is clear in both solvents. In the aqueous acetone solvents the question of the significance of the small rate differences must be raised. The rate constants are the slopes of straight lines fitted to the experimental points in one of the usual logarithmic plots. The accuracy of these slopes may be estimated either by the precision of the fit of the experimental points to the best straight line, or by a comparison of the slopes

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[1] Part of this paper was published in preliminary form: E. S. Lewis and G. M. Coppinger, THIS JOURNAL, **76**, 4495 (1954); another portion was presented at the 130th Meeting of the American Chemical Society in Atlantic City, N. J., September, 1958. All of the work is taken from portions of the Ph.D. theses at the Rice Institute of G. M. Coppinger (1954) and R. R. Johnson (1958).

[2] (a) V. J. Shiner, Jr., THIS JOURNAL, **75**, 5292 (1953); (b) **76**, 1603 (1954); (c) E. S. Lewis and C. E. Boozer, *ibid.*, **74**, 6306 (1952); (d) **76**, 791 (1954); (e) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey and S. Suzuki, *ibid.*, **80**, 2326 (1958).

[3] V. J. Shiner, Jr., and C. J. Verbanic, *ibid.*, **79**, 373 (1957).

[4] M. M. Kreevoy and H. Eyring, *ibid.*, **79**, 5121 (1957).

TABLE I

SOLVOLYSIS RATES OF METHYLTOLYLCARBINYL CHLORIDES

Substance	Solvent	Temp., °C.	$k \times 10^4$ sec.$^{-1}$	k_H/k_D
para				
$CH_3CHClC_8H_4CH_3$	CH_3COOH	50.25	1.14 ± 0.02[a]	
$CH_3CHClC_6H_4CHD_2$	CH_3COOH	50.25	1.04 ± .02	1.10
$CD_3CHClC_6H_4CH_3$	CH_3COOH	50.25	0.89 ± .01	1.28
$CH_3CHClC_6H_4CH_3$	CH_3COOH	65.30	6.02 ± .05	
$CH_3CHClC_6H_4CHD_2$	CH_3COOH	65.30	5.61 ± .04	1.07
$CD_3CHClC_6H_4CH_3$	CH_3COOH	65.30	5.15 ± .07	1.17
$CH_3CHClC_6H_4CH_3$	80% Me_2CO[b]	50.3 ± 0.1	5.76 ± .04	
$CH_3CHClC_6H_4CD_3$	80% Me_2CO	50.3 ± .1	5.68[c]	1.013[c]
$CD_3CHClC_6H_4CH_3$	80% Me_2CO	50.3 ± .1	4.92[c]	1.17[c]
$CH_3CDClC_6H_4CH_3$	80% Me_2CO	50.3 ± .1	5.15[c]	1.12[c]
$CH_3CHClC_6H_4CH_3$	80% Me_2CO	37.6	1.501[d]	
$CH_3CHClC_6H_4CD_3$	80% Me_2CO	37.6	1.489[d]	1.008
$CD_3CHClC_6H_4CH_3$	80% Me_2CO	37.6	1.322 ± 0.004	1.14
$CH_3CDClC_6H_4CH_3$	80% Me_2CO	37.6	1.357 ± .004	1.11
$CH_3CHClC_6H_4CH_3$	80% Me_2CO	34.0	1.066 ± .003	
$CH_3CHClC_6H_4CD_3$	80% Me_2CO	34.0	1.052 ± .006	1.01
meta				
$CH_3CHClC_6H_4CH_3$	70% Me_2CO[e]	49.65	1.409 ± 0.013	
$CH_3CHClC_6H_4CD_3$	70% Me_2CO	49.65	1.419 ± .006	0.993
$CH_3CHClC_6H_4CH_3$	70% Me_2CO	37.6	0.3640 ± .0011	
$CH_3CHClC_6H_4CD_3$	70% Me_2CO	37.6	.3662 ± .0007	0.994
$CH_3CHClC_6H_4CH_3$	80% Me_2CO[f]	62.4[f]	.823 ± .003	
$CH_3CHClC_6H_4CD_3$	80% Me_2CO	62.4	.843 ± .010	.976

[a] ± indicates maximum deviation from the mean of 2 to 4 runs. [b] 8 volumes of acetone + 2 volumes of water, 0.1 *M* NaCl. [c] The temperature fluctuations made these runs rather uncertain, and since only one run was made on each compound the k_H/k_D values are unprecise. [d] Two runs with identical results. [e] 7 volumes of acetone + 3 volumes of water. [f] Same as *b*, except no NaCl.

from successive experiments. Of these the latter is more reliable since there are some sources of error which affect the slope of the line without a large effect on the linearity. The standard error of the fit to a straight line for the aqueous acetone data varied from 0.2 to 1%; in most cases it was less than 0.5%. The errors in the table for the reproducibility of the runs are not standard errors; the numbers preceded by ± represent the maximum deviation from the mean of all the data, which is less than the standard deviation when there were only two runs, and usually more when there were three or four runs. It is clear that both ways of estimating the error are in this case comparable. For any one temperature k_H/k_D for the *p*-methyl compound is greater than unity by an amount only slightly greater than the standard deviation of a run. However, if one ignores the possibility of a temperature effect and combines all the runs on this compound, the repetition of this barely significant effect becomes more significant and the value $k_H/k_D = 1.011 \pm 0.003$ includes all the results for the *para* compound in aqueous acetone. It is believed that systematic errors attributable to gradual change in solvent composition, or to contaminants capable of solvolysis, are absent.

In the runs in "80% acetone," the necessity for added sodium chloride to get a first-order reaction is disturbing. It is conceivable that a common ion retardation[5] is being made constant by the added chloride ion, although this effect has not been observed previously in these compounds. The initial rates in the absence of chloride ion were the same as in its presence, suggesting that, if a common ion retardation is the source of the effect of sodium chloride, the isotope effect in the ionization step alone is similar to that found in the presence of chloride ion. It also suggests that the normal salt effect cancels the retarding effect. A second possibility is that in this solvent the reaction is perceptibly reversible, as it is in acetic acid,[6] but it is not clear why the addition of sodium chloride would lead to clean first-order kinetics. Finally it is possible that the electrolyte merely has an effect on the glass electrode and makes the end-point more reliable. No such effect was noted on the *meta* compound in either "70%" or "80%" acetone, but non-reproducibility of electrodes in these systems reduces the significance of this observation.

The change in isotope effect with solvent is interesting but complex. There are several possible contributions to this effect which have been discussed. Two factors which have a profound influence on rate can be dismissed from consideration. These are the dielectric constant of the medium and the solvation of that part of the transition state which will become the anion. We shall ignore, with less justification, the relatively minor solvation of the initial state and consider only solvation of the incipiently cationic portion of the transition state. It has been suggested that the nucleophilic participation of the solvent is the major source of the variation of isotope effect with solvent.[2d] With the not unreasonable assumption that aqueous acetone is more nucleophilic than acetic acid, the smaller isotope effect in the former

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(5) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 360.

(6) J. Steigman and L. P. Hammett, THIS JOURNAL, **59**, 2536 (1957).

solvent then results from the smaller electron deficiency and hence the smaller demand for hyperconjugation. It is seen, however, that the effect of the isotopic substitution in the *p*-methyl is more sensitive to the solvent change than that from isotopic substitution at the neighboring carbon. It seems unlikely that a change in electron deficiency at the α-carbon would have a very different influence on the weakening of bonds in the two methyl groups. The differential effect may therefore result from a difference in the extent of solvation on hydrogen, as suggested by Shiner,[2ab] or on the benzene ring, as suggested in a different connection by Schubert.[7]

The effect of deuterium in the *m*-methyl group is novel. The difference between the two compounds is nearly as significant as that in the *para* compound, and the use of all the data as described before gives $k_H/k_D = 0.988$ with a standard deviation of 0.005. Since deuterium substitution in the *m*-methyl group gives an effect opposite from that of deuterium substitution in the *p*-methyl group, one is forced to conclude that a resonance effect operates from the *p*-position; hence the connection between isotope effect and hyperconjugation is well established. Similarly, the effect from the change in the *m*-substituent cannot be a resonance effect and, unless it is an effect on the pre-exponential factor, is therefore an inductive effect, with deuterium more electron releasing than hydrogen. While there is no evidence that this is a potential energy effect, there is precedent for an inductive effect. Halevi first observed this in measuring acid and base strengths and concluded that deuterium was more electron releasing than hydrogen.[8] Tiers has drawn the same conclusion from the n.m.r. spectra of *n*-C_3F_7H and *n*-C_3F_7D.[9] Since the CH stretching is anharmonic, the equilibrium distance even in the lowest vibrational state is less for C–D than for C–H, and both these authors suggest that the chemical differences result only from the difference in this distance. Streitwieser[2e] has suggested that there is an inductive effect on the C–H bond, so that the vibrations are different in acetic acid and in the acetate ion, and therefore giving an isotope effect on the ionization equilibrium. Evidence from infrared spectra shows that the CH bonds in acetic acid and acetate ion are indeed different, but other evidence (summarized by Halevi[8c]) shows that dipole moments and bond distances are altered by isotopic substitution. We shall therefore only conclude that an inductive interaction between the methyl group and the electron deficient center exists and leads to an isotope effect. The presence of an inductive effect does not substantially alter the arguments about solvation, although the inductive effect must also operate from the *p*-position. If there is an unexpected substantial solvent dependence of this possible inductive effect, then the solvation arguments presented may be unnecessarily complicated.

The large variation of isotope effect with solvent may account for the very small isotope effect in the bromination of methyl-d_3-benzene in aqueous acetic acid solution.[10] It is now not necessary to abandon a connection between isotope effect and hyperconjugation. The new problem introduced is that our understanding of solvent effects is quite imperfect, so that the detection of hyperconjugation by isotope effects is of less value than was at first supposed.[2e]

The effect of α-deuterium substitution (k_H/k_D = 1.1) can be added to a growing list of these effects[2e,11]; it was the first that we had seen. The explanation of this isotope effect by Streitwieser and co-workers[2e] appears quite adequate.

We therefore conclude that a resonance or hyperconjugation effect and possibly an inductive effect contribute to the isotopic rate difference, and that these contributions are modified by an as yet unpredictable solvent influence. We conclude that incipient elimination or neighboring group participation are not the sources of isotope effects in all cases, although the latter has been shown to contribute in favorable situations.[12]

Experimental

Toluene-α-d_3.—Dimethyl phenylmalonate (118 g., 0.57 mole) was mixed with sodium hydride (14 g., 0.58 mole) in 500 ml. of anhydrous ether. One ml. of methanol was added and the mixture was stirred and heated under reflux for 16 hours, then filtered. The resulting sodium salt was dried in air and weighed 124.5 g. (95%). Of this 111 g. (0.5 mole) was mixed with deuterium oxide (24.5 g., 1.2 moles) in a 1-liter autoclave and heated to about 400° for 7 hours, during which time the pressure rose to 1050 p.s.i. The autoclave after cooling was further cooled in ice and the carbon dioxide was released. The residue was extracted with 20–40° petroleum ether, dried over magnesium sulfate, and fractionally distilled. Toluene was recovered in yield of 38–41%, and further distillation of some of the runs yielded dibenzyl ketone, identified as its 2,4-dinitrophenylhydrazone, in a yield of about 30%. Analysis by mass spectrometry showed 2.92 atoms deuterium per molecule, and nuclear magnetic resonance spectra indicated roughly 0.5 atom protium in the methyl group per molecule. Analyses by mass spectra on the various derivatives showed about 2.9 atoms of deuterium per molecule in all samples, with the following exception. The toluene used to prepare the samples used in the solvolysis in acetic acid was prepared by a similar process, but the starting materials were dimethyl phenylmalonate, anhydrous sodium carbonate and deuterium oxide. This gave toluene containing 2.01 atoms of deuterium per molecule by combustion analysis.

p-Methyl-d_3-acetophenone.—To a solution of 6.6 g. of toluene-α-d_3 and 23 g. of anhydrous aluminum chloride in 50 ml. of carbon disulfide cooled to 0° was added 7.0 g. of acetic anhydride. The carbon disulfide was removed by distillation and the product complex was decomposed by the addition of cold 10% sulfuric acid. The ketone was extracted with ether and purified by distillation, b.p. 92–9° at 2 mm., yield 7.5 g. (82%). After one distillation, analysis by vapor phase chromatography showed the presence of 2% of the *o*-isomer, which was reduced by further distillation. The same reaction carried out at the boiling point of carbon disulfide yielded 7% of the *o*-isomer. The same synthesis was used to prepare ketone with normal isotopic distribution.

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[7] W. M. Schubert, J. Robins and J. L. Hawn, THIS JOURNAL, **79**, 910 (1957).

[8] (a) E. A. Halevi and M. Nussim, *Bull. Res. Council. Israel*, **5A**, 263 (1956); Abstrs. 16th Intl. Cong. Pure Appl. Chem., II, 27 (1957); (b) E. A. Halevi, *Tetrahedron*, **1**, 174 (1957); (c) E. A. Halevi, *Trans. Faraday Soc.*, **54**, 1441 (1958).

[9] G. V. D. Tiers, THIS JOURNAL, **79**, 5585 (1957).

[10] C. G. Swain, T. E. C. Knee and A. J. Kresge, *ibid.*, **79**, 505 (1957).

[11] A. Streitwieser, Jr., and R. C. Fahey, *Chemistry & Industry*, 1417 (1957); W. H. Saunders, Jr., S. Asperger and D. H. Edison, *ibid.*, 1417 (1957); K. Mislow, S. Borcic and V. Prelog, *Helv. Chim. Acta*, **40**, 2477 (1957); R. R. Johnson and E. S. Lewis, *Proc. Chem. Soc.*, 52 (1958).

[12] S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958).

Methyl-d_3 p-Tolyl Ketone.—Ordinary methyl p-tolyl ketone (10 g.) was exchanged by heating under reflux with 99$^+$% deuterium oxide (2 g.) in the presence of 0.1 g. of anhydrous sodium carbonate and 20 ml. of dioxane. After exchange, water and dioxane were removed by vacuum distillation and the ketone decanted from the sodium carbonate. The exchange was repeated six times. One sample (eventually used in the runs in acetic acid) had 2.4 atoms of deuterium per molecule by combustion and water density. The other sample had about 2.8 atoms of deuterium per molecule by mass spectrometric analysis. Oxidation of this ketone with hypochlorite gave p-toluic acid free from deuterium in the p-methyl group, as shown by its infrared spectrum.

Methyl-p-tolylcarbinol.—The variously deuterated ketones were reduced with lithium aluminum hydride to the corresponding carbinols, b.p. 90° at 2 mm. Similarly, the α-deutero compound was prepared by the reduction of ordinary ketone with lithium aluminum deuteride.

Methyl-p-tolylcarbinyl Chloride.—The carbinol was treated with excess thionyl chloride and the product distilled, b.p. 92° at 12 mm., yields from 90–95%.

p-Methyl-d_3-acetanilide.—p-Methyl-d_3-acetophenone (30 g., 0.136 mole) was dissolved in a mixture of 25 ml. of concd. sulfuric acid and 180 ml. of glacial acetic acid. Sodium azide (21.4 g., 0.33 mole) was added slowly to the stirred mixture kept at 60–70° over a period of 4 hours. The resulting mixture was poured into one liter of ice and water, and the resulting crystals were removed by filtration and air-dried. The yield of crude product was 18.5 g. (55%).

2-Bromo-4-methyl-d_3-aniline Hydrochloride.—The bromination of the crude p-methyl-d_3-acetanilide to 2-bromo-4-methyl-d_3-acetanilide (m.p. 115–117°), in 78% yield followed the directions of Gilman[13] as did the subsequent hydrolysis to 2-bromo-4-methyl-d_3-aniline hydrochloride in a yield of 90%.

m-Methyl-d_3-bromobenzene.—2-Bromo-4-methyl-d_3-aniline hydrochloride (35 g., 0.156 mole) was dissolved in a solution of 175 ml. of water and 35 ml. of concentrated sulfuric acid, and cooled to 0°. Sodium nitrite (28 g., 0.4 mole) in cold water was added slowly with cooling, then 453 g. (2.16 moles) of 30–32% hypophosphorous acid cooled to 0° was added, and the resulting solution was kept in the refrigerator for 60 hours, then extracted with ether. The ether solution was washed, dried and distilled, yielding 21.7 g. (80%) of m-methyl-d_3-bromobenzene, b.p. 180°.

Methyl-m-methyl-d_3-phenylcarbinyl Chloride.—The Grignard reagent from m-methyl-d_3-bromobenzene (21 g., 0.12 mole) was made in the usual manner in ether solution, and freshly distilled acetaldehyde (5 g., 0.144 mole) was added to the stirred solution. When the addition was complete, dilute sulfuric acid was added, and the ether phase was washed with sodium bicarbonate solution, water and saturated sodium chloride solution and then dried over magnesium sulfate. Distillation yielded 11.7 g. (74%) of the carbinol, b.p. 61° at 0.5 mm. Treatment with a 10% excess of thionyl chloride yielded on distillation the corresponding methyl-m-methyl-d_3-phenylcarbinyl chloride, b.p. 65° at 1.7 mm., in 85% yield. The synthesis of the same compound without deuterium followed the same course from commercial m-bromotoluene, which, like the deuterium-substituted product, was not contaminated with a detectable amount of isomer on vapor phase chromatography.

Solvents.—The acetic acid was ordinary reagent grade glacial acetic acid made up to 0.1005 mole/liter lithium acetate. Aqueous acetone was made up from distilled water and reagent grade acetone; "70%" was the mixture obtained from 300 ml. of water and 700 ml. of acetone, "80%" was the mixture of 200 ml. of water with 800 ml. of acetone. No series of runs on the same compound were made from different batches of a solvent, and there were no chronological drifts fast enough to influence the isotope effect, indicating a changing solvent composition, although a slow shift in rate constants of about 4% over a period of four weeks was observed in the acetic acid only.

Kinetic Measurements.—In acetic acid the runs were done in the presence of lithium acetate to suppress the reverse reaction.[6] A solution of the chloride of about 0.08 molar concentration was placed in the thermostat and 2-ml. samples were diluted and titrated with 0.05 M perchloric acid in acetic acid, using a pH meter modified to put the readings on scale.[14] As completion was approached, the end-points became uncertain, and it was necessary to use the method of Guggenheim to get the rates, rather than a method using a titer after a long period of time. This end-point also apparently was sensitive to the condition of the glass electrode and was therefore not suitable for runs of any higher precision.

In aqueous acetone solvents the samples were titrated with aqueous sodium hydroxide solution after diluting a 2-ml. sample with 20 ml. of acetone, again using the pH meter to detect the end-point. In the 80% aqueous acetone, a first-order law was not followed strictly, the reaction apparently slowed down with time slightly. In the presence of 0.100 molar sodium chloride this difficulty disappeared, although the apparent initial rates were not affected. Near the end-point in this solvent, the response of the pH meter was quite slow, although the end-point was apparently sharply defined.

The amount of alkyl chloride was not measured in every run, but in some of the later runs the yield of acid could be determined as follows: p-$\mathrm{CH_3C_6H_4CHClCH_3}$, 90.7%; p-$\mathrm{CD_3C_6H_4CHClCH_3}$, 96.7%; p-$\mathrm{CH_3C_6H_4CHClCD_3}$, 96.6%; p-$\mathrm{CH_3C_6H_4CDClCH_3}$, 93.6%. A contamination by the corresponding styrene was detected in some cases, and the low values probably represent loss of acid by this decomposition, possibly accompanied by hydrolysis with atmospheric moisture. The presence of substances which would interfere with the kinetics is unlikely both because of the excellent fit to a first-order reaction course, and because of the method of synthesis which would not give other substances capable of solvolysis at a comparable rate.

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HOUSTON, TEX.

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(13) H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 111.

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