seen that the selectivity is not appreciably different from that of toluene and the xylenes. This affords added support to the conclusion that resonance effects are not of appreciable importance in determining selectivity.

The three xylenes have the same reactivity toward propylene as judged by the yield of monoadduct based on methyl groups available (see Table I). This reactivity is essentially the same as that exhibited by toluene. About 80–90% of the reacted xylenes are accounted for as monoalkylation products. Diadducts and diarylalkanes account for the remainder of the alkylbenzene reacted. In reactions with the xylenes, 30–40% of the propylene charged were converted to monoalkylation products. Polymerization of propylene was less important than in the 1-butene experiments.[4] Some diadducts were also formed, but these were not analyzed. The remainder of the propylene charged was recovered unchanged.

Reactivity of *p*-methylanisole toward alkylation by propylene cannot be accurately assessed by the results obtained in the present study. Approximately 5% of the *p*-methylanisole was converted to phenols. The nature of these was not determined. The analysis of monoalkylated *p*-methylanisole given in the table was arrived at on the assumption that the alkylcyclohexanes obtained by the procedure described in the Experimental section were derived from the corresponding *p*-methoxy- or *p*-hydroxyalkylbenzenes. That some dimethylcyclohexane was also detected shows that probably some rearrangement of *p*-methylanisole to xylenols took place or, alternately, ring methylation of *p*-methylanisole by methyl radicals took place. Such pyrolytic reactions of alkyl phenyl ethers to form alkylphenols have been reported.[8]

(8) W. J. Hickinbottom, *Nature*, **142**, 830 (1938); **143**, 520 (1939); N. M. Cullinane and S. J. Chard, *J. Chem. Soc.*, 821 (1945); R. D. Obolentzev, *J. Gen. Chem.* (*U.S.S.R.*), **16**, 1459 (1946).

[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE UNIVERSITY, EAST LANSING, MICH.]

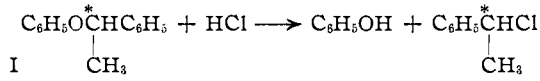
Cleavage of Optically Active α-Phenethyl Phenyl Ether with Hydrogen Chloride

BY HAROLD HART AND RAYMOND J. ELIA[1,2]

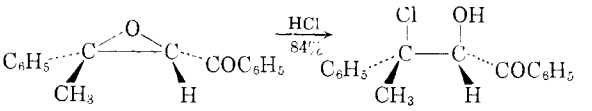
RECEIVED OCTOBER 7, 1960

Hydrogen chloride cleaves optically active α-phenethyl phenyl ether at 40° to give α-phenethyl chloride and phenol with a minimum of 85–90% retention of configuration, in toluene, 3-pentanone or isobutyl alcohol as solvent (0.25 *M* solutions). The reaction is kinetically first order in each reactant; the second-order rate constants show a rather small increase with increasing dielectric constant and/or hydroxylic nature of the solvent.

Some years ago we reported[3] that α-phenethyl phenyl ether is cleaved by hydrogen chloride at 50° in benzene with a minimum of 38% retention of configuration (62% racemization). A similar configurational result, with varying retentions of optical purity, was obtained with the corresponding *p*-tolyl and mesityl ethers, neat, in benzene or in acetone. Retention of configuration required a mechanism for ether cleavage different from those which had previously been considered,[4] and it was suggested that, consonant with the behavior of α-phenethyl systems in other reactions,[5] an SNi ion-pair mechanism was operative.



Subsequently it was shown that *cis*- and *trans*-dypnone oxides react stereospecifically with hydrogen chloride, in acetic acid or ethanol, to give chlorohydrin with retention of configuration.[6] Brewster pointed out[7] that the acidic hydrolysis (dilute hydrochloric acid) of *trans*-α-methylstilbene oxide[8] also proceeds with retention; attention has also been called[6,7] to earlier acidic hydrolyses of cyclic epoxides which give *cis*-diols. In all cases, a phenyl group is attached to the epoxide carbon at which cleavage occurs.



In view of the high stereospecificity of the epoxide cleavages,[6,7] it seemed desirable to establish with greater precision than in our exploratory study[3] the extent of retention of optical purity in the cleavage of I. It is the purpose of this paper to describe both the stereochemical results and the reaction kinetics in several solvents.

Results

Stereochemistry.—A solution approximately 0.25 *M* in hydrogen chloride and α-phenethyl phenyl ether was maintained at 40° for a given time, then extracted with 20% alkali to remove the phenol and hydrogen chloride, washed with water, dried and distilled. The rotation of recovered α-phenethyl chloride was compared with the rotation of the chloride originally used to synthesize the ether (*via* the Claisen procedure). The observed loss in rotation should, in the absence of other factors, represent the total racemization in the two reactions (ether

(1) Taken from the Ph.D. Thesis submitted by R. J. E. to Michigan State University, 1957.

(2) Financial support in the form of a fellowship from the Research Corporation, New York, is gratefully acknowledged.

(3) H. Hart and H. S. Eleuterio, *J. Am. Chem. Soc.*, **76**, 1379 (1954).

(4) For a review, see R. L. Burwell, Jr., *Chem. Revs.*, **54**, 625 (1954).

(5) Numerous examples are cited by E. L. Eliel in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 79 ff.

(6) H. H. Wasserman and N. E. Aubrey, *J. Am. Chem. Soc.*, **78**, 1726 (1956).

(7) J. H. Brewster, *ibid.*, **78**, 4061 (1956).

preparation and cleavage). Some slight racemization is known[9] to occur during the ether preparation, so that a maximum limit can be set on the racemization accompanying cleavage.

Three interfering reactions caused adventitious racemization of the α-phenethyl chloride produced from the cleavage; they were examined separately and corrected for. Both phenol[10] and hydrogen chloride can racemize α-phenethyl chloride. Furthermore, they had to be removed by alkali extraction, before the chloride could be isolated, and this alkaline extraction also caused some racemization of the chloride. The results of control experiments are summarized in Tables I and II, which show that about 30% of the racemization may occur independently of the cleavage. In Table III the observed and corrected retention percentages are summarized. It is clear that cleavage is *at least 85-90% stereospecific, with retention of configuration,* in toluene, 3-pentanone or isobutyl alcohol as solvent.

TABLE I

RACEMIZATION OF α-PHENETHYL CHLORIDE DURING WORK-UP[a]

Solvent	Time, hr.	[α]²⁵D Init.	[α]²⁵D Final	Rac., %[b]
Toluene	0	26.50°	20.08°	24.2
	1		19.98	24.5
	4		19.90	24.9
	6		19.60	26.1
	26		19.46	26.6
3-Pentanone	0	−44.45	−33.92	23.5
	1		−33.00	25.3
	26		−32.75	26.1
i-BuOH	0	19.30	13.95	27.8
	1		13.60	29.5
	26		13.39	30.6

[a] α-Phenethyl chloride, 0.25 *M* in the solvent indicated, was maintained at 40° for the time shown, then extracted with 20% KOH, washed, dried and distilled. [b] The gradual increase with time may be due to traces of moisture; the observed values are nearly time-independent, and due largely to the alkali extraction.

TABLE II

RACEMIZATION OF α-PHENETHYL CHLORIDE BY PHENOL AND/OR HYDROGEN CHLORIDE[a]

Solvent	Time, hr.	[α]²⁵D Init.	[α]²⁵D Final	Rac., % Total[b]	Rac., % Corr.[c]
Toluene	1	−33.22°	−24.90°	25.1	0.6
	4		−23.25	28.8	6.6
	26		−21.42	35.4	12.1
3-Pentanone	1	−23.64	−16.70	29.5	5.1
	26		−14.71	37.9	15.7
i-BuOH	1	30.20	20.45	32.0	4.0
	26		18.67	39.9	10.9

[a] Solutions 0.1 *M* each n α-phenethyl chloride, phenol and hydrogen chloride were maintained at 40° for the time shown, then worked up by alkali extraction, etc.; see footnote *a* of Table I. [b] Intermediate values, at intermediate time intervals, are omitted to conserve space; see ref. 1. [c] Represents racemization in excess of the work-up procedure. A sample calculation, for toluene after 26 hours, is: 100(33.22-21.42/0.734)/33.22 = 12.1 = % racemization due to phenol and/or hydrogen chloride.

Kinetics.—Rates of cleavage were measured in the several solvents used for the stereochemical studies. Solutions containing varying concentrations (0.1–0.3 *M*) of hydrogen chloride and α-phenethyl phenyl ether (I) were thermostated at 40°; aliquots diluted with a relatively large volume of benzene were extracted with alkali, and the quantity of phenol produced was determined by a suitably tested colorimetric method described in the Experimental part. The colorimetric method was superior to either hydrogen chloride titration (rapid solvolysis of α-phenethyl chloride interferred) or quantitative bromination of the phenol. Reactions were followed to 50 ± 10% completion, and the HCl/ether concentration ratio was varied from about 0.4 to 3.0. Data for a typical run are given in Table IV, and Table V summarizes the rate measurements.

TABLE III

RETENTION IN CLEAVAGE OF α-PHENETHYL PHENYL ETHER, 40°

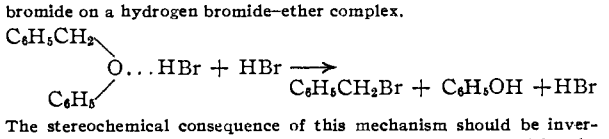
Solvent	Time, hr.	[α]²⁵D of chloride Init.[a]	[α]²⁵D of chloride Final[b]	Retention, % Obsd.	Retention, % Corr.[c]
Toluene	1	−45.30°	29.43°	65.0	86.8
	6		27.08	61.4	90.0
	26		26.45	58.5	90.3
3-Pentanone	1	38.25	−23.65	61.8	87.8
	6		−21.42	56.1	86.3
	26		−21.18	55.3	89.2
i-BuOH	1	30.45	−18.50	60.5	89.3
	6		−16.70	54.8	85.3
	26		−15.97	52.4	87.3

[a] The α-phenethyl phenyl ether prepared from these chloride samples had rotations of −14.88°, + 12.75° and + 11.50°, respectively. [b] Comparable values obtained after 2 and 4 hours are omitted to conserve space. Values are opposite in sign to those for the chloride used to prepare the ether, indicating one net inversion for the two reactions. Since the ether preparation occurs with inversion,[9] the cleavage must occur with retention of configuration.[3] [c] Corrections were made using the values in Table II, or similar values. A sample calculation, for toluene at 26 hours, is: 100[(26.45/0.646)/45.30] = 90.3 = % retention.

Discussion

In view of the report that hydrogen bromide cleaves benzyl phenyl ether at a rate first order in ether but second order in hydrogen bromide,[11] the present data were also calculated to determine the fit with over-all third-order kinetics.[12] The fit was poorer than for the second-order kinetics, but more important, values of k_3 varied with the ratio of initial reactant concentrations. The third-order process, if it occurs at all in the present case, must be a relatively minor reaction path.

It is likely that in their reactions with hydrogen halides, protonated ethers may run the usual gamut



The stereochemical consequence of this mechanism should be inversion at the benzyl carbon, quite the opposite of that observed for the α-phenethyl ether. Although different mechanisms for the benzyl and α-phenethyl systems are not unlikely, it would appear worthwhile to put the matter to experimental test, using deuterium-labeled active benzyl phenyl ether.

(9) H. Hart and H. S. Eleuterio, *J. Am. Chem. Soc.*, **76**, 516 (1954).
(10) H. Hart and W. L. Spliethoff, *ibid.*, **77**, 833 (1955).
(11) A. Y. Drummond and A. M. Eastham, *J. Am. Chem. Soc.*, **79**, 3689 (1957). Only initial rates (to 5–10% cleavage) were measured. The rate-determining step was considered to be attack by hydrogen bromide on a hydrogen bromide–ether complex.
(12) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 21.

TABLE IV

CLEAVAGE OF α-PHENETHYL PHENYL ETHER BY HYDROGEN CHLORIDE IN TOLUENE, 40°

a_0 = (HCl) = 0.2931 M; b_0 = (ether) = 0.0975 M

t, sec. × 10^{-3}	$a - x^a$	$b - x^a$	k_2, l. mol.$^{-1}$ sec.$^{-1}$ × 10^5
5.0	0.2911	0.0955	1.41
11.0	.2889	.0933	1.37
28.0	.2827	.0871	1.40
33.0	.2814	.0858	1.35
45.0	.2788	.0832	1.28
52.0	.2771	.0815	1.21
63.0	.2731	.0775	1.29
76.8	.2690	.0734	1.32
85.6	.2658	.0702	1.38
206.3	.2433	.0477	1.31
		Av.	1.30 ± 0.06

[a] x = concentration of phenol (moles/liter) produced in time t, as determined colorimetrically (see Experimental).

TABLE V

SUMMARY OF RATE CONSTANTS, 40°

Solvent	Init. concn., mole/l. HCl	Ether	k_2, l. mol.$^{-1}$ sec.$^{-1}$ × 10^5	Mean k_2
Toluene	0.1315	0.2010	1.25 ± 0.03	
	.1208	.3045	1.43 ± .06	
	.1217	.0979	1.35 ± .08	
	.2230	.1006	1.30 ± .05	
	.2931	.0975	1.30 ± .06	1.33 ± 0.05
3-Pentanone	.1580	.1000	2.48 ± .07	
	.1250	.2003	2.42 ± .12	
	.1350	.2984	2.34 ± .06	
	.2071	.0997	2.40 ± .06	
	.2610	.0992	2.42 ± .05	2.41 ± 0.03
i-BuOH	.1275	.1054	3.17 ± .10	
	.1005	.2000	3.07 ± .08	
	.1250	.2884	3.24 ± .24	
	.2256	.1000	3.15 ± .10	
	.2800	.0984	3.54 ± .33	3.23 ± 0.12

of solvolytic displacement mechanisms, depending upon the nature of the groups attached to oxygen.[13] Although few examples have been worked out in detail, and structural variations have not been delineated as precisely as with other solvolytic displacements,[14] it is clear that primary and most secondary alkyl ethers are cleaved by an SN2 mechanism,[15] whereas tertiary alkyl, benzhydryl and trityl ethers probably cleave by an SN1 mechanism.[13] It should be anticipated that variant solvolytic mechanisms (SN2^1, SNi, etc.) will be found.

The nearly complete retention of configuration and second-order kinetics for the cleavage of I are consistent with an SNi mechanism.[5] It is significant that the rates and stereochemistry are only slightly affected by increasing the dielectric constant of the solvent from 2.4 (toluene) to 17.3 (3-pentanone) or changing to the hydroxylic solvent isobutyl alcohol (dielectric constant 18.7). These results suggest a rather tight ion-pair intermediate. Studies with more polar solvents are precluded by the experimental difficulty that the initial cleavage product, α-phenethyl chloride, solvolyzes further.

(13) R. L. Burwell, Jr., *Chem. Revs.*, **54**, 615 (1954).

(14) A. Streitwieser, Jr., *ibid.*, **56**, 571 (1956).

(15) For example, optically active methyl *sec*-butyl ether reacts with hydrogen bromide in glacial acetic acid to form methyl bromide and *sec*-butyl acetate of the same configuration as the ether. In excess hydrogen bromide, inverted *sec*-butyl bromide is formed with little or no racemization; see R. L. Burwell, Jr., L. M. Elkin and L. G. Maury, *J. Am. Chem. Soc.*, **73**, 2428 (1951).

Experimental

Materials.—Optically active I was synthesized as described previously.[16] C.P. toluene was distilled and a middle cut used. Reagent grade 3-pentanone was refluxed with calcium chloride for 2 hours. Fresh drying agent was added and the mixture allowed to stand overnight, filtered and distilled. C. P. isobutyl alcohol was dried with calcium oxide and distilled. Hydrogen chloride was dried with concentrated sulfuric acid.

Stereochemical Studies. General Procedure.—One liter of solvent containing 0.25 mole each of hydrogen chloride and α-phenethyl phenyl ether, $[\alpha]^{25}D$ −14.88° (prepared from α-phenethyl chloride, $[\alpha]^{25}D$ −45.30°) was maintained at 40° for the desired time, then extracted with 200 ml. of 20% potassium hydroxide. The organic layer was washed twice with 200 ml. of water, then dried over anhydrous sodium sulfate. Extraction and wash times were standardized. The α-phenethyl chloride was distilled *in vacuo*, after removal of the solvent; its refractive index was used as a criterion of purity and its optical rotation was determined. Recovered I was used in subsequent experiments. Results are summarized in Table III.

Effect of Work-up Procedure on the Rotation of α-Phenethyl Chloride.—A 0.25 M solution of α-phenethyl chloride (known rotation) in the particular solvent was maintained at 40° for the desired time, then worked up as just described. The rotations are summarized in Table I.

Effect of Phenol and Hydrogen Chloride on the Rotation of α-Phenethyl Chloride.—Solutions 0.1 M each in α-phenethyl chloride (known rotation), phenol and hydrogen chloride were maintained at 40° for the desired time, then worked up as described above.[17] The rotations are summarized in Table II.

Kinetic Procedure.—Anhydrous hydrogen chloride was passed into purified solvent at 40.0 ± 0.10° until the desired concentration was approximated. The exact normality was determined by shaking aliquots with 25 ml. of distilled water, followed by titration with standard sodium hydroxide (phenolphthalein). All volumes were corrected to 20°.[18]

For each run, the thermostated standardized acidic solution was transferred to a thermostated volumetric flask which contained a weighed quantity of the ether I. When the mark was reached, the flask was quickly stoppered and shaken. A sample removed immediately and titrated for hydrogen chloride showed no loss during transfer. At various intervals, aliquots were removed, extracted and analyzed colorimetrically for phenol as described below. Approximately 10 aliquots were withdrawn in each run.

Analytical Method.[19]—The general procedure involved adding sodium nitrite and sulfuric acid to an acetic acid solution of the phenol, to form a nitrosophenol whose color intensity in ammonia was measured with a photoelectric colorimeter. The concentration of phenol was determined from a calibration curve prepared with standard phenol solutions. Reagents required were *buffer solution* (800 ml. of glacial acetic acid, 150 ml. of 10% potassium hydroxide and 50 ml. of water), *alcoholic ammonium hydroxide* (450 ml. of ethanol, 300 ml. of 14 N ammonia and 250 ml. of water) and *saturated sodium nitrate* (prepared by filtering the excess solid from a mixture of 73 g. of sodium nitrite and 100 ml. of water maintained at room temperature).

Extraction.—Aliquots (1 ml.) of the reaction mixture from a kinetic experiment were added to 50 ml. of benzene and shaken for 5 minutes with 10 ml. of 10% potassium hydroxide. The extraction was repeated, followed by washing for 2 minutes with 5 ml. of water. Control experiments demonstrated that this extraction procedure was quantitative.

Analysis.—Glacial acetic acid was slowly added to the combined extracts in an ice-cooled 100-ml. volumetric flask. Before the mark was reached, the flask was allowed to come

(16) H. Hart and H. S. Eleuterio, *ibid.*, **76**, 519 (1954).

(17) Equimolar amounts of chloride and phenol were used, since they are produced simultaneously in the cleavage experiments.

(18) "International Critical Tables," McGraw-Hill Book Co., Inc., New York, N. Y., 1928, Vol. 3, p. 27.

(19) L. Lykken, R. S. Treseder and V. Zahn, *Anal. Chem.*, **18**, 103 (1946).

to room temperature, and the final addition was then made. A 1-ml. aliquot of this solution (it is desirable that the phenol content be about 0.05–0.5 mg. for the colorimetric method) was transferred to a 50-ml. volumetric flask, 4 ml. of buffer solution was added, then 5 drops of 36 *N* sulfuric acid and 2 drops of saturated sodium nitrite solution. After 30 to 45 minutes, alcoholic ammonium hydroxide was added while cooling the flask in ice-water. The volume was made up to the mark at room temperature and the solutions were allowed to stand overnight, or at least 5 hours. Colorimetric readings were made with a Klett–Summerson photoelectric colorimeter using a No. 42 violet filter. A small blank correction was necessary. Phenol concentrations were determined from a nearly linear calibration curve, with an accuracy of about 3%.

The rate constants were calculated by standard procedures.[12]

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, THE FLORIDA STATE UNIVERSITY, TALLAHASSEE, FLA.]

Acetolysis of Bicyclo[2.2.2]octyl-2 *p*-Bromobenzenesulfonate and the Absolute Configurations of Bicyclo[2.2.2]octanol-2 and *cis*- and *trans*-Bicyclo[3.2.1]octanol-2

BY H. M. WALBORSKY, M. E. BAUM AND A. A. YOUSSEF

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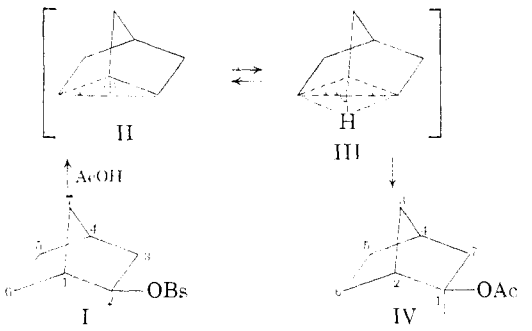
The titrimetric and polarimetric acetolysis rates of bicyclo[2.2.2]octyl-2 *p*-bromobenzenesulfonate have been measured at 25° and found to be 9.07×10^{-6} and 9.4×10^{-6} sec.$^{-1}$, respectively. The acetolysis product was shown to contain, besides bicyclo[2.2.2]octyl-2 acetate, 35 ± 3% of the rearranged bicyclo[3.2.1]octyl-2 acetate. The residual activity found in the acetolysis product of the optically active bicyclo[2.2.2]octyl-2 *p*-bromobenzenesulfonate was shown to reside in both the rearranged and unrearranged alcohols. Retention of activity and configuration in the unrearranged alcohol is discussed in terms of non-classical ion formation. On the basis of the negative Cotton effect exhibited by (−)-bicyclo[3.2.1]octanone-2 and by the application of the Octant rule, absolute configurations have been assigned to (2S)-(+)-bicyclo[2.2.2]octanol-2,(1R:2S:5R)-(−)-*cis*-bicyclo[3.2.1]octanol-2 and (1R:2R:5R)-(−)-*trans*-bicyclo[3.2.1]octanol-2.

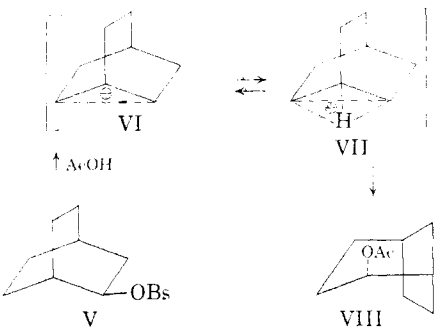
Introduction

The bridged-ion intermediate was originally postulated by Wilson[1] for the transformation of camphene hydrochloride to isobornyl chloride. Subsequent work on the norbornane derivatives gave support to this hypothesis. It was shown that in the acetolysis of optically active *exo*-[2] and *endo*-norbornyl *p*-bromobenzenesulfonate (I)[3] both compounds produced racemic *exo*-norbornyl acetate (IV). This result coupled with the observation that the *exo* isomer solvolyzed 350 times faster than the *endo* was interpreted as evidence for the briged-ion intermediate II.



The skeletal rearrangement (I→IV) implied in the above solvolysis was investigated[4] by tagging the carbon atoms at positions 2 and 3. The results of this experiment demonstrated that rearrangement did occur but that it was more extensive than expected from a bridged-ion such as II. These results could be rationalized by assuming that 55% of the reaction proceeded by II, and 45% by III. The bridged ion III can lead to a 1,3-hydride shift.

The above work prompted the investigation of the analogous bicyclo(2.2.2)octane derivative (V). This system has a number of unique features. In



the first place, if a bridged-ion comparable to II is formed, this ion (VI), in contrast to II, does not possess a plane of symmetry. The bridged ion VII which is analogous to the one proposed by Roberts does, however, possess a plane of symmetry. Secondly, any skeletal rearrangement leads to the formation of an entirely different ring system: a bicyclo(3.2.1)octane derivative (VIII). Finally, this system is essentially free of angle strain, whereas the norbornane system is not.[5] A study of the solvolysis of racemic and optically active V was undertaken to determine the effect of this bridged bicyclic system on the rates as well as on the products of this reaction.

Results

Titrimetric Rates.—Bicyclo(2.2.2)octanol-2 and the *p*-bromobenzenesulfonate ester were prepared as previously described.[6] The solvolysis was conducted in acetic acid, freed of water by reaction with acetic anhydride, and containing sufficient sodium acetate to neutralize the *p*-bromobenzene-

(1) T. P. Nevell, E. de Salas and C. L. Wilson, *J. Chem. Soc.*, 1188 (1939).

(2) S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, **71**, 2953 (1949).

(3) S. Winstein and D. Trifan, *ibid.*, **74**, 1147, 1154 (1952).

(4) J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., *ibid.*, **76**, 4501 (1954).

(5) R. B. Turner, W. R. Meador and R. G. Winkler, *ibid.*, **79**, 4116 (1957).

(6) H. M. Walborsky and D. F. Loncrini, *ibid.*, **76**, 5396 (1954).