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Kinetic Studies of Solvolysis. XII.* The Question of a Single Mechanism for the "Borderline" S_N Reactions — The Solvolysis of Optically Active α-Phenylethyl Chloride in Aqueous Ethanol

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Competitive solvolysis has been conducted in binary solvents of water and ethanol on optically active α-phenylethyl chloride at 40.0°C. The extents of inversion ($\alpha\%$) for solvolysis products, i. e., α-phenylethyl alcohol and α-phenylethyl ethyl ether, have been calculated from the optical rotations of these products isolated after ten half-lives, and the values of $\alpha\%$ have been plotted vs. the volume percentage of water. In the region of 90% aqueous ethanol, the two $\alpha\%$ lines for the alcohol and the ether intersect with each other. This intersection of the two lines conflicts with any single mechanism for the borderline S_N reactions, whereas the dual mechanism can explain this phenomenon without any difficulty. In the region of a 100% water-solvent (a typical medium for the S_N1 solvolysis), the two lines do not converge to the same $\alpha\%$ value. On the basis of these findings, a general mechanism of racemization for the S_N1 solvolysis has also been discussed.

The single and the dual mechanisms for the "borderline" S_N reactions have been a longstanding question, and there have been several arguments in support of both sides.[1-6]

On the basis of reaction kinetics, which describes the homogeneous reaction in a solution or in the gas phase as a combination of elementary reactions (Urreaktionen[7]) with "integral" molecularity, the view[4,6] that a borderline reaction must be expressible as a sum of concurrent elementary reactions, i. e., the unimolecular (S_N1) and the bimolecular (S_N2) process, seems to be only the self-evident representation of the borderline cases; there have been in the literature several examples of borderline cases which cauld be explained on the basis of the dual mechanism.[8]

On the other hand, if one ignored the significance of the reaction-kinetical mechanism mentioned above, the view[1-3] that a single mechanism of an intermediate character operates in borderline S_N reactions might be superficially tempting inasmuch as there have been presented no definitive experimental results which are inexplicable by this single mechanism.

Thus, the question as to which picture is more reasonable has been currently described as "difficult"[9] or "to some extent a question of definition."[10]

However, Weiner and Sneen[5] recently presented data which they interpreted to mean that two distinct paths, i. e., the S_N1 and the S_N2 processes, were followed in a borderline case. Namely, when the hydrolysis of optically active 2-octyl brosylate was conducted in the presence of large amounts of sodium azide, the resulting inverted 2-octanol, formed in competition with 2-octyl azide, proved to be 100% optically pure. If one recognized that sodium azide (a strong nucleophile) would react preferentially with the S_N1 intermediate to form alkyl azide, thus preventing its conversion to alcohol, and that a nucleophilic S_N2 displacement by water would furnish inverted alcohol, the data mentioned above would consequently mean the presence of two distinct paths for the hydrolysis of 2-octyl brosylate.

In this paper we will report on a new phenomenon observed in the competitive hydrolysis and ethanolysis of optically active α-phenylethyl chloride, a phenomenon which also seems to favor the dual mechanism.

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* Part XI of this series: K. Okamoto, H. Yamada, I. Nitta and H. Shingu, This Bulletin, **39**, 299 (1966).

[1] S. Winstein, E. Grunwald and H. W. Jones, *J. Am. Chem. Soc.*, **73**, 2700 (1951).

[2] M. L. Bird, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, **1954**, 634.

[3] C. G. Swain, *J. Am. Chem. Soc.*, **70**, 1119 (1948).

[4] V. Gold, *J. Chem. Soc.*, **1956**, 4633.

[5] H. Weiner and R. A. Sneen, *J. Am. Chem. Soc.*, **84**, 3599 (1962).

[6] H. Shingu and K. Okamoto, "Theoretical Significance of Differentiation of the S_N1 and S_N2 Mechanism," presented at Organic Reaction Mechanism Symposium of the Chemical Society of Japan, Osaka, October, 1952.

[7] A. Skrabal, "Homogenkinetik," T. Steinkopf, Dresden (1941), p. 39.

[8] E. g. a) H. Shingu and K. Okamoto, *J. Chem. Soc. Japan, Pure Chem. Sect.* (*Nippon Kagaku Zassi*), **78**, 547 (1957); b) Y. Pocker, *J. Chem. Soc.*, **1959**, 3944, 3939; c) P. Casapieri and E. R. Swart, ibid., **1963**, 1254.

[9] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York (1959), p. 258.

[10] J. Hine, "Physical Organic Chemistry," 2nd ed., McGraw-Hill Book Co., New York (1962), p. 138.

The Extent of Inversion for the Products of the Competitive Solvolyses of Optically Active α-Phenylethyl Chloride in Aqueous Ethanol.—Solvolysis was conducted in mixtures of water with ethanol at 40.0°C on optically active α-phenylethyl chloride. After ten half-lives, as calculated from the rate constants interpolated from the data[11] at other temperatures, α-phenylethyl alcohol and α-phenylethyl ethyl ether with an inverted configuration, accompanied by racemization, were isolated by elution chromatography over basic alumina. The styrene were found to amount at most to 3% of the chloride in the solvent range from 50 to a 95% aqueous ethanol (see Table II). The extent of inversion for the alcohol and that for the ether were calculated from the optical rotations of these reaction products. The results are shown in Fig. 1 in the form of a plot of α% (the degree of inversion) vs. the volume percentage of water in aqueous ethanol solvents.

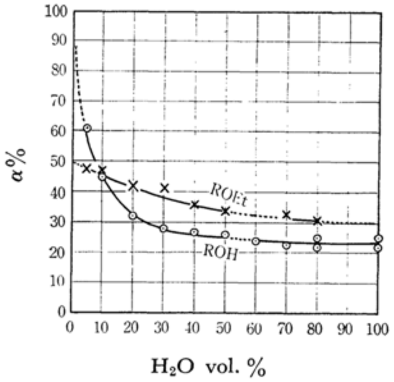


Fig. 1. Extent of inversion (α%) of solvolysis products of α-phenylethyl chloride in aqueous ethanol at 40.0°C.

For the solvent ranges of 60 to 100% water, the solvolyses were conducted under heterogeneous conditions; the reaction was continued until at least 98% of the chloride has been converted to hydrogen chloride. Despite the difference in stirring conditions, the extents of inversion for duplicate runs carried out in 100% water and in 80% water were similar to each other (see Fig. 1). Therefore, these results in heterogeneous regions seem actually to be caused by homogeneous reactions with rather low concentrations of the chloride.

As is illustrated by the α% line in Fig. 1, the degree of inversion for the α-phenylethyl alcohol so formed decreases from 61 to 25% as the water content of these binary solvents is increased from 5 to 50%; then at higher water contents it remains relatively constant at a level of from 22 to 25%.

The extent of inversion for α-phenylethyl ethyl ether also diminishes from 47 to 34% upon an increase in water content from 5 to 50%, while at higher water contents it remains at a level of about 30%.

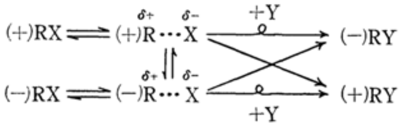
The possible racemization of α-phenylethyl alcohol in the presence of hydrogen chloride under the reaction conditions has been ruled out, since it was found that in 90 and 70% aqueous ethanol and in water optically active α-phenylethyl alcohol was not appreciably racemized (less than 3%) in the presence of 0.1 to 0.5 N hydrogen chloride at 40.0°C for the reaction time for which each solvolysis was conducted (Table III).

An Interpretation of the Results in Solvent Ranges Close to 100% Water.—In 100% water or in the solvent ranges close to it, the solvolysis of α-phenylethyl chloride proceeds by a typical S_N1 mechanism; this may be understood as follows.

The solvolysis rate of this compound is known to be 10[5,12] as high in water as in 100% ethanol; this rate ratio is enormously high compared with the ratio (10-10[2,13]) to be expected in "S_N2" solvolyses in water and in 100% ethanol. Therefore, the possibility of inversion due to the S_N2 hydrolysis may be ruled out in these solvent ranges and the observed extent of inversion may be derived exactly from the stereochemical characteristics of the "S_N1" solvolysis.

If one assumes for the S_N1 solvolyses that an optically active S_N1 intermediate reacts with all molecules of the nucleophile on its back-side as a result of the presence of the anionic-leaving group on the front-side, and that the racemization of the product is caused only by the intramolecular inversion of the intermediate to its antipode,[14] the extents of the inversions of the products of two kinds, formed by the competitive back-side attack of nucleophiles of two kinds, should be the same as one another. Actually, however, this is not the case. The α% line for α-phenylethyl ethyl ether runs at a higher level than that for α-phenylethyl alcohol, as is illustrated in Fig. 1.

This gap in the α% lines can be explained by the following general mechanism for the racemization, a mechanism which contains a third path to the product, i. e., the front-side attack of a nucleophile on the intermediate, in addition to the above mentinoed two paths to the products (an intramolecular inversion of the intermediate and a back-side attack of a nucleophile on the intermediate). This may be schematically illustrated as follows.



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[11] A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **79**, 1597 (1957).

[12] At 50°C, Ref. 11.

[13] e. g., for the S_N2 solvolyses of methyl bromide k_{H_2O} : k_{EtOH} ratio is estimated to be 26.8 at 50°C.[1]

[14] See a) K. Okamoto, K. Takeuchi and H. Shingu, This Bulletin, **35**, 525 (1962); b) H. Weiner and R. A. Sneen, *J. Am. Chem. Soc.*, **87**, 292 (1965).

According to this general mechanism for racemization, the extent of the inversion of the product is controlled not only by the intramolecular inversion of the optically active intermediates, but also by the competition of the front- and backside attack of a nucleophile. As a result of this competition, the extents of inversion (or retention) should vary significantly with the nature of the nucleophile. In our experiments, as may be expected from this mechanism, the extents of inversion for α-phenylethyl alcohol and α-phenylethyl ethyl ether are not the same; this is reflected by the different natures of the two attacking nucleophiles, water and ethanol.

An Interpretation of the Results in Solvent Ranges Close to 100% Ethanol.—In 95% aqueous ethanol, both α-phenylethyl alcohol and α-phenylethyl ethyl ether show rather high optical purities, 61 and 47% respectively. In addition, as is illustrated in Fig. 1, the α% line of α-phenylethyl alcohol for the solvent ranges close to 100% ethanol can be extrapolated to 100% from the values for 95 and 90% aqueous ethanol solvents, whereas the α% line for α-phenylethyl ethyl ether points to a value of about 50% for a 100% ethanol solvent.

According to the dual mechanism, this would indicate that in the solvent ranges from 95 to 100% ethanol most of the water molecules react with α-phenylethyl chloride by means of S_N2 mechanism, whereas in the same solvent ranges ethanol molecules react by means of both S_N1 and S_N2 mechanisms and a significant part (at least 50%) of the ethanol molecules still react by means of the S_N1 mechanism.

The facts observed in these solvent ranges might also be explicable by the single mechanism. According to the single mechanisms,[1-3] which postulate only one transition state for a single borderline case, one could assume transition states of two kinds corresponding to the competitive hydrolysis and ethanolysis in 95% aqueous ethanol. Thus, if one uses the representation for the transition state of the single mechanism proposed by Winstein et al.,[1] the greater extent of inversion for α-phenylethyl alcohol as compared with that for α-phenylethyl ethyl ether would be explained by the greater contribution of the sturcture II[1] (see below) for the transition state containing more nucleophilic water molecules as compared with that for the transition state composed of less-nucleophilic ethanol molecules.

$$\underset{\text{I}}{\text{Z: R–X}} \longleftrightarrow \underset{\text{II}}{\text{Z–R: X}} \longleftrightarrow \underset{\text{III}}{\text{Z: R: X}}$$

(RX, α-phenylethyl chloride; Z, water or ethanol)

Furthermore, if one uses the terms[15] derived from the conception of a "concerted" displacement reaction, i. e., a single mechanism proposed by Swain,[3,15] this fact would be explicable as due to the greater "bond-making" extent at the transition state of hydrolysis as compared to that of the ethanolysis, since the extents of "bond-breaking" in ethanolysis and hydrolysis would be identical in this binary solvent.

However, as will be illustrated in the following section, the intersection of two α% lines for α-phenylethyl alcohol and for α-phenylethyl ethyl ether seems difficult to explain by any single mechanism.

The Inadequacies of the Single Mechanism in Interpreting the Intersection of Two α% Lines.—According to the single mechanism, the greater extent of inversion for α-phenylethyl alcohol than that for α-phenylethyl ethyl ether may be anticipated not only for a 95% aqueous ethanol solvent but also for the solvent ranges with a much greater water content in this binary solvent, because the contribution of the structure II or the extent of "bond-making" for the transition state composed of the water molecule with the greater nucleophilic reactivity should become greater as the content of water is increased in aqueous ethanol solvents, whereas the extent of "bond-breaking" or the contribution of the structure III in the transition state would be of the same magnitude for both hydrolysis and ethanolysis in this binary solvolytic medium.

As is illustrated in Fig. 1, however, the two α% lines intersect with each other in the region of 90% aqueous ethanol, and in the solvent ranges with a higher water content the α% line for α-phenylethyl alcohol runs at a lower level than that for α-phenylethyl ethyl ether. This is in conflict with the above-mentioned anticipation of the single mechanism, which expected the α% line for the alcohol to run at a higher level than that for the ether over the entire range of this binary solvent.

On the other hand, the intersection of two α% lines does not conflict with the dual mechanism; it may be interpreted as an incidental result of the superposition of two α% lines corresponding to the concurrency of two independent reaction, i. e., hydrolysis and ethanolysis, each of which is composed of S_N1- and S_N2-type reactions.

Experimental[16]

Materials.—The preparation of optically active and racemic α-phenylethyl chloride followed previous practice.[17] The solvolysis infinity values indicated a purity of from 98 to 99% for the chloride. Ethanol

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[15] C. G. Swain and W. P. Langsforf, *J. Am. Chem. Soc.*, **73**, 2813 (1951).

[16] Optical rotations were measured with a Zeiss-Winkel "Kreis-Polarimeter 0.01°." The infrared spectra were obtained on a Shimadzu model IR-27. The ultraviolet spectra were obtained with an Shimadzu model UV-50M. The gas-liquid chromatograms were obtained with an Ohkura model 2100 equipped with a flame ionization detector.

[17] K. Okamoto, K. Takeuchi and H. Shingu, This Bulletin, **34**, 1142 (1961).

TABLE I. THE EXTENTS OF INVERSION ($\alpha\%$) OF PRODUCTS IN SOLVOLYSES OF OPTICALLY ACTIVE α-PHENYLETHYL CHLORIDE IN AQUEOUS ETHANOL AT 40.0±0.05°C

Run No.	Solvent vol. %[a] EtOH	RCl[b] M	Reaction time hr.	α_D (neat, 0.5 dm.)[c] RCl	ROH	ROEt	$\alpha\%$[d] ROH	ROEt
	100							(27.8)[e]
10	95	0.149	524	+9.975°	−2.15°	−3.585°	61.0	47.4
1	90	0.149	118	−21.44°	+3.44°	+7.59°	45.4	46.7
11	80	0.151	30.2	−13.240°	+1.475°	+4.20°	31.5	41.9
3	70	0.148	15.4	+12.225°	−1.190°	−3.815°	27.5	41.1
7	60	0.044	4.0	+5.755°	−0.540°	−1.580°	26.5	36.2
15	50	0.0226	1.8	−7.635°	+0.690°	+1.985°	25.6	34.4
21	40	0.0770[f]	0.8	+15.645°	−1.335°	—	24.2	—
3′	30	0.363[f]	3.9	+14.120°	−1.160°	−3.565°	23.3	33.3
20	20	0.0746[f]	0.9	+15.815°	−1.405°	—	25.1	—
4′	20	0.333[f]	1.5	−13.650°	+1.070°	+3.210°	22.2	31.0
6	H_2O	0.0750[f]	1.1	+6.060°	−0.540°	—	25.2	—
4	H_2O	0.127[f]	1.1	+6.155°	−0.488°	—	22.4	—

a) See Experimental.
b) Initial concentration of optically active α-phenylethyl chloride.
c) Taken at 24—30°C.
d) Rotations for optically pure substances were taken to be 125° for α-phenylethyl chloride (H. M. R. Hoffmann and E. D. Hughes, *J. Chem. Soc.*, **1964**, 1244.), 44.2° for α-phenylethyl alcohol (D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, *J. Am. Chem. Soc.*, **81**, 5754 (1959)), and 94.8° for α-phenylethyl ethyl ether (K. Mislow, *J. Am. Chem. Soc.*, **73**, 4043 (1951)).
e) At 70.0°C, calculated from the data by Hughes et al. (E. D. Hughes, C. K. Ingold and A. D. Scott, *J. Chem. Soc.*, **1937**, 1201).
f) Heterogeneous conditions, mol. of RCl/1 l. of the solvent.

TABLE II. COMPOSITION OF SOLVOLYSIS PRODUCTS OF α-PHENYLETHYL CHLORIDE IN AQUEOUS ETHANOL AT 40.0±0.05°C

Run No.	Solvent vol. %[a] EtOH	RCl[b] M	Reaction time hr.	Product compositon ROH[d] %	ROEt[d] %	Styrene[e] %	$10^5 k_1$ (sec^{-1})[c]
101	95	0.100	524	30	67	3	—
102	90	0.100	118	38	60	2	1.26
103	80	0.100	30	49	50	1	5.75
105	70	0.140	17	58	41	1	19.5
104	60	0.100	4.0	68	31.5	0.5	63.1
106	50	0.0226	2.0	78.5	21	0.5	174

a) and b) See foot notes a) and b) Table I.
c) Interpolated from the data at other temperatures.[11]
d) Analyses by gas-liquid chromatography, ROH%=ROH% (estimated by g. l. c.) - Styrene%, See Experimental.
e) Analyses by ultraviolet spectroscopy.

TABLE III. RACEMIZATION OF α-PHENYLETHYL ALCOHOL IN THE PRESENCE OF HYDROGEN CHLORIDE IN AQUEOUS ETHANOL AT 40.0°C

Run No.	Solvent vol. %[a] EtOH	ROH M	HCl N	Reaction time hr.	α_D (neat, 0.5 dm.)[a] of ROH Initial	After the reaction	Racemization %
1	90	0.150	0.150	120	+5.965°	+5.965°	0.0
2	70	0.140	0.120	16	+5.985°	+6.010°	(0.0)
3	H_2O	0.120	0.100	1.3	+5.980°	+5.785°	3.3

a) Taken at 25—28°C.

was purified by the process of Lund and Bjerrum.[18] Aqueous ethanol solvents (x vol.%) were prepared by mixing x volumes of ethanol and $100-x$ volumes of water, each with temperatures of from 20 to 25°C before mixing. Racemic α-phenylethyl ethyl ether for an authentic sample was prepared by refluxing α-phenylethyl chloride (6.7 g.) in 99% ethanol (175 cc.) for 10 hr. After the usual treatment, 5.19 g. (71.2% yield) of racemic α-phenylethyl ethyl ether, b. p. 54.0°C/5 mmHg; $n_D^{30.0}$ 1.4821, was obtained. Racemic α-phenylethyl alcohol, the commercial material, was distilled in vacuo b. p. 85—86°C/7 mmHg.

Results.—The details of the results for solvolyses in aqueous ethanols are tabulated in Table I. The results of composition analyses of the solvolysis products are illustrated in Table II. α-Phenylethyl alcohol and α-phenylethyl ethyl ether were estimated by the gas-liquid chromatography of the reaction mixtures. The column was made from 4.0 mm. i. d. × 4 m. annealed copper tubing. The packing was prepared from Diasolid (60—80 mesh) using PEG 6000 as a liquid; the packing was 5% liquid phase by weight. The retention times for α-phenylethyl alcohol and α-phenylethyl ethyl ether were, respectively, 7.5—8.5 and 17.5—18.0 min.; these times were determined at 160°C using nitrogen as the carrier gas (flow rate 50—60 cc./min.). Because of the failure to separate the styrene peak and the α-phenylethyl alcohol peak under the operation conditions of this chromatography, the concentration of styrene in the reaction mixtures was estimated by ultraviolet spectroscopy, using 244 mμ as a characteristic band for styrene. The cell length was 1 cm.; one volume of the reaction mixture was diluted with 99 volumes of distilled water. Absorbances caused by the benzenoid absorption of α-phenylethyl alcohol and α-phenylethyl ether were subtracted from the observed styrene absorbance of the sample. The precentage of α-phenylethyl alcohol as estimated by gas-liquid chromatography was corrected by the subtraction of the styrene percentage.

The results of racemization experiments for α-phenylethyl alcohol in the presence of hydrogen chloride are illustrated in Table III. The details of procedures for the isolation of the solvolysis products and for the racemization experiments of α-phenylethyl alcohol are illustrated in the descriptions of some representative runs which follow.

The Solvolysis of Optically Active α-Phenylethyl Chloride in 80 vol.% Aqueous Ethanol at 40.0°C.—To 100 cc. of 80 vol.% aqueous ethanol in a 200-cc. round-bottomed flask maintained at 40.0°C, 2.16 g. (0.0154 mol.) of α-phenylethyl chloride, $\alpha_D^{24.9}$ $-13.240°$ (0.5 dm., neat); b. p. 56.0°C/3 mmHg. was added. After it has been maintained for 30.2 hr. at 40.0±0.05°C, the reaction mixture was neutralized with 0.65 g. of sodium hydroxide pellets and then fractionally distilled to give 80 cc. of ethanol, b. p. 77—80°C. To the residue 7.0 g. of sodium chloride was added, and the organic layer was extracted with three 15-cc. portions of ether. The concentration of the combined ether solutions, dried with magnesium sulfate, afforded an oily material which was distilled in vacuo to give 1.01 g. of the mixture of α-phenylethyl alcohol and α-phenylethyl ethyl ether, b. p. 55—60°C/5—4 mmHg. The mixture was then chromatographed over 25 g. of basic alumina. The fractions (No. 1—5, for each 25 cc.) eluted with n-hexane consisted of α-phenylethyl ethyl ether, (0.29 g., b. p. 37°C/2 mmHg; $\alpha_D^{24.2}$ $+4.20°$ (0.5 dm., neat) n_D^{30} 1.4840). α-Phenylethyl alcohol (0.309 g.; b. p. 64°C/3 mmHg; $\alpha_D^{25.2}$ $+1.475°$ (0.5 dm., neat) n_D^{30} 1.5231) was eluted with 99% ethanol fractions (Nos. 8 and 9, for each 15 cc.). The alcohol and the ether showed infrared spectra identical with those of the authentic samples.

The Heterogeneous Solvolysis of Optically Active α-Phenylethyl Chloride in Water.—To 110 cc. of water, maintained at 40.0°C, in a 100-cc. four-necked flask equipped with a reflux condenser, a stirrer and a thermometer, there was added 2.00 g. (0.0142 mol.) of α-phenylethyl chloride, $\alpha_D^{24.1}$ $+6.155°$ (0.5 dm., neat); b. p. 54.0°C/5 mmHg, in one portion. After a 0.7 hr. stirring, the reaction mixture was extracted with five 20-cc. portions of ether. The concentration of the combined ether solutions, dried with magnesium sulfate, afforded 1.76 g. of an oily material which was then distilled in vacuo to give 1.47 g. of α-phenylethyl alcohol, $\alpha_D^{24.4}$ $-0.488°$ (0.5 dm., neat); n_D^{30} 1.5239; b. p. 66°C/5 mmHg; identical infrared spectrum with an authentic sample.

An Examination of the Racemization of Optically Active α-Phenylethyl Alcohol in 90% Aqueous Ethanol in the Presence of 0.15 N Hydrogen Chloride.—To 54 cc. of 0.15 N hydrogen chloride in 90% aqueous ethanol, prepared by mixing 7.00 cc. of concentrated hydrogen chloride and 63 cc. of 100% ethanol in a 100-cc. round-bottomed flask, 1.00 g. (0.00821 mol.) of α-phenylethyl alcohol ($\alpha_D^{22.9}$ $+5.965°$ (0.5 dm., neat)) was added. After it had stood for 120 hr. at 40.0°C, the mixture was neutralized with 0.30 g. of sodium hydroxide pellets (silightly basic to litmus) and then fractionally distilled to give 36 cc. of ethanol. To the residue 10 g. of sodium chloride was added; it was then extracted with five 15-cc. portions of ether. The combined ether extracts were concentrated and distilled in vacuo to give 0.80 g. of α-phenylethyl alcohol, b. p. 84°C/6 mmHg, $\alpha_D^{24.9}$ $+5.965°$ (0.5 dm., neat.)

The authors wish to thank Mr. Yoshihisa Matsui for his assistance in the analyses of styrene.

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[18] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston (1955), p. 286.