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# Kinetic Studies of Solvolysis. XIII.[*1] The Solvolyses of Optically-active α-Phenylethyl Chloride in Binary Mixtures of Phenol and Water—The $S_N1$ Hydrolysis with the Retention of the Configuration

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The competitive $S_N1$ hydrolysis and $S_N1$ phenolysis of optically-active α-phenylethyl chloride in aqueous phenols (75 to 90 wt% phenol) give partially-retained α-phenylethyl alcohol and α-phenylethyl phenyl ether in the presence of added triethylamine at 14 and 30°C. The extent of the retention of the configuration is almost independent of the reaction temperature, whereas it shows a tendency to increase from 13 to 23% for the alcohol and from 5 to 20% for the ether with an increase in the phenol concentration. A predominant four-center ($S_Ni$-like) attack of a water molecule, with the assistance of a specific solvation of phenol molecules, has been suggested as a possible interpretation for the unusual hydrolysis with a retained steric course for this simple secondary alkyl system. In connection with the nature of the specific solvation of phenol molecules, the applicability of the concept of the back-side shielding of the $S_N1$ ion-pair intermediate by a phenol molecule has been discussed.

Solvolysis reactions on aliphatic secondary and tertiary alkyl derivatives without a configuration-retaining group are typically known to proceed with a net inversion of configuration. Thus, solvolyses of optically-active *s*-octyl bromide,1a) *s*-octyl arenesulfonates,1b−d) α-phenylethyl chloride,1e−g) isobutylethylmethylcarbinyl hydrogen phthalate,1h) and phenylethylmethylcarbinyl hydrogen phthalate,1i) in such hydroxylic solvents as aqueous ethanol,1a,c) aqueous dioxane,1b) aqueous acetone,1a) methanol,1e,h,i) cyclohexanol,1f) acetic acid,1c,d,g) formic acid,1f) pimelic acid,1f) and trifluoroacetic acid,1f) give a net inversion of the configuration, accompanied by various degrees of racemization. However, in contrast to these findings, we have earlier established2) that the phenolysis of optically-active α-phenylethyl chloride in various mixtures of phenol and non-hydroxylic co-solvents gives partially-retained α-phenylethyl phenyl ether in the presence of added bases. More recently, Goering and his collaborators3) have reported that the $S_N1$ hydrolysis (alkyl-oxygen cleavage) of optically-active *p*-chlorobenzhydryl *p*-nitrobenzoate proceeds with an excessive retention of the configuration in 80 to 90% aqueous acetone.

These unusual findings led us to extend our search for a solvolysis with a retained steric course to a mixed solvent system of phenol and water. Thus, in a preliminary communication4) we presented a further example in the case of the hydrolysis of optically-active α-phenylethyl chloride in 75 to 90 wt% aqueous phenol at 30°C. In this paper we will describe the details of the previous data, partly reexamined, together with similar results observed at a lower temperature, 14°C. We will also consider in detail the retention mechanism in the solvolysis for this simple secondary alkyl system.

## Results

Solvolyses of optically-active α-phenylethyl chloride (0.106 M) were conducted in 75, 80, 85 and 90 wt% aqueous phenols in the presence of added triethylamine (0.114—0.118 M) for at least ten half-lives at 14 and 30°C. The products of the competitive hydrolysis and phenolysis

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[*1] Presented at the 19th Annual Meeting of the Chemical Society of Japan, Yokohama, April, 1966. Part XII: K. Okamoto, N. Uchida, S. Saitô and H. Shingu, This Bulletin, **39**, 307 (1966).

1) a) E. D. Hughes, C. K. Ingold and S. Masterman, *J. Chem. Soc.*, **1937**, 1196; *cf.* C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London (1953), p. 382; b) H. Weiner and R. A. Sneen, *J. Am. Chem. Soc.*, **87**, 287, 292 (1965); c) A. Streitwieser, Jr., T. D. Walsh and J. R. Wolfe, Jr., *ibid.*, **87**, 3682 (1965); d) A. Streitwieser, Jr., and T. D. Walsh, *ibid.*, **87**, 3686 (1965); e) E. D. Hughes, C. K. Ingold and A. D. Scott, *J. Chem. Soc.*, **1937**, 1201; f) K. Okamoto and Y. Matsui, unpublished results; g) J. Steigman and L. P. Hammett, *J. Am. Chem. Soc.*, **59**, 2536 (1937); h) W. von E. Doering and H. H. Zeiss, *ibid.*, **75**, 4733 (1953); i) H. H. Zeiss, *ibid.*, **75**, 3154 (1953).

2) a) K. Okamoto, K. Takeuchi and H. Shingu, This Bulletin, **35**, 525 (1962); b) K. Okamoto, H. Yamada, I. Nitta and H. Shingu, *ibid.*, **39**, 299 (1966).

3) a) H. L. Goering, R. G. Briody and J. F. Levy, *J. Am. Chem. Soc.*, **85**, 3059 (1963); b) H. L. Goering and J. F. Levy, *ibid.*, **86**, 120 (1964).

4) K. Okamoto, M. Hayashi and H. Shingu, This Bulletin, **39**, 408 (1966).

(*i. e.*, $\alpha$-phenylethyl alcohol, $\alpha$-phenylethyl phenyl ether, and *o*- and *p*-$\alpha$-phenylethylphenol) were chromatographed over silica gel. From the rotations[5] of the products, the configurations and the extent of the retention of the optical purities were determined. The $S_N1$-character of these solvolyses was examined kinetically, and satisfactory first-order behavior was observed for each run; the results are illustrated in Tables 1 and 2 and in Figs. 1 and 2.

TABLE 1. THE EXTENTS OF RETENTION OF THE OPTICAL PURITY FOR THE PRODUCTS OF THE COMPETITIVE SOLVOLYSES OF $\alpha$-PHENYLETHYL CHLORIDE IN AQUEOUS PHENOL SOLVENTS

| Run No. | Solvent | | $\alpha_D$, 0.5 dm, neat[a] | | | | | $\alpha$%[b] Retention | | $\alpha$%[b] Inversion | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | PhOH wt% | $H_2O$ wt% | RCl[c] | ROH | ROPh | RPhOH[c] (*o*-) | RPhOH[d] (*p*-) | ROH | ROPH | RPhOH (*o*-) | RPhOH (*p*-) |
| | Reaction temperatures: 14.3—14.7°C | | | | | | | | | | |
| 4[e] | 75 | 25 | −24.18°<br>(±0.04°) | −1.07°<br>(±0.06°) | +0.47°<br>(±0.04°) | +1.40°<br>(±0.13°) | — | 12.5 | 5.2 | 26.0 | — |
| 1 | 80 | 20 | −23.06°<br>(±0.04°) | −1.61°<br>(±0.25°) | +0.71°<br>(±0.03°) | +0.80°<br>(±0.10°) | −2.09°<br>(±2.09°) | 19.7 | 8.3 | 15.6 | 55 |
| 3 | 85 | 15 | −23.86°<br>(±0.05°) | −1.92°<br>(±0.04°) | +1.19°<br>(±0.04°) | +0.78°<br>(±0.04°) | −1.60°<br>(±0.96°) | 22.8 | 13.4 | 14.7 | 41 |
| 2 | 90 | 10 | −23.86°<br>(±0.05°) | −1.88°<br>(±0.06°) | +1.72°<br>(±0.06°) | +0.62°<br>(±0.02°) | −1.42°<br>(±1.14°) | 22.2 | 19.3 | 11.6 | 36 |
| | Reaction temperatures: 29.6—30.0°C | | | | | | | | | | |
| 11[e] | 75 | 25 | −16.00°<br>(±0.07°) | −0.91°<br>(±0.02°) | +0.34°<br>(±0.01°) | — | — | 16.0<br>(16.3)[f] | 5.7<br>(6.08)[f] | — | — |
| 14 | 80 | 20 | +18.91°<br>(±0.01°) | +1.22°<br>(±0.04°) | −0.67°<br>(±0.01°) | −0.97°<br>(±0.06°) | +1.07°<br>(±0.43°) | 18.3<br>(17.6)[f] | 9.5<br>(7.76)[f] | 23.1 | 35 |
| 12 | 85 | 15 | +18.91°<br>(±0.01°) | +1.27°<br>(±0.08°) | −0.99°<br>(±0.01°) | −0.89°<br>(±0.07°) | +1.66°<br>(±0.67°) | 18.9 | 14.0 | 21.0 | 54 |
| 16 | 90 | 10 | −24.08°<br>(±0.08°) | −1.64°<br>(±0.08°) | +1.82°<br>(±0.04°) | +0.62°<br>(±0.02°) | −1.26°<br>(±0.90°) | 19.3<br>(12.1)[f] | 20.3<br>(19.5)[f] | 11.5 | 32 |

a) Taken at 20—22°C. b) See Ref. 5. c) R=$\alpha$-Phenylethyl; RPhOH=$\alpha$-Phenylethylphenol. d) $[\alpha]_D$ in benzene. e) The reaction mixture was initially heterogeneous. Basic alumina was used for the chromatography. f) The value cited in the preliminary communication.[4] See Ref. 6.

TABLE 2. THE YIELDS OF THE PRODUCTS AND THE RATE CONSTANTS FOR THE COMPETITIVE SOLVOLYSES OF OPTICALLY-ACTIVE $\alpha$-PHENYLETHYL CHLORIDE IN AQUEOUS PHENOLS

| Run No. | Solvent | | Reaction temp. °C | Initial concn. | | Yield, %[a] | | | | $10^3 \times k_1$ sec$^{-1}$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | PhOH wt% | $H_2O$ wt% | | RCl M | $Et_3N$ M | ROH | ROPh | RPhOH (*o*-) | RPhOH (*p*-) | | |
| 4[b] | 75 | 25 | 14.4 | 0.106 | 0.119 | 12.5 | 36.9 | 2.8 | 0.4 | 1.69[b] | (14.4°C) |
| 1 | 80 | 20 | 14.3 | 0.106 | 0.116 | 2.4 | 49.0 | 7.3 | 2.7 | 1.65 | (14.4°C) |
| 3 | 85 | 15 | 14.7 | 0.106 | 0.116 | 8.0 | 54.8 | 7.7 | 2.3 | 1.65 | (14.4°C) |
| 2 | 90 | 10 | 14.3 | 0.106 | 0.117 | 6.9 | 58.2 | 7.1 | 2.0 | 1.81 | (14.3°C) |
| 11[b] | 75 | 25 | 29.8 | 0.106 | 0.118 | 10.5 | 40.6 | 9.5[c] | — | 8.14[b] | (29.5°C) |
| 14 | 80 | 20 | 30.0 | 0.106 | 0.117 | 11.4 | 52.9 | 7.8 | 4.2 | 7.66 | (29.5°C) |
| 12 | 85 | 15 | 30.0 | 0.106 | 0.117 | 10.7 | 54.8 | 7.3 | 2.6 | 7.01 | (29.5°C) |
| 16 | 90 | 10 | 29.6 | 0.106 | 0.114 | 7.1 | 59.9 | 6.8 | 1.9 | 7.60 | (29.7°C) |

a) Based on the starting chloride; R=$\alpha$-Phenylethyl.

b) The reaction mixture was initially heterogeneous. The first aliquot for the kinetic measurement was removed 10 min after the addition of the chloride when the mixture became homogeneous. Basic alumina was used for the chromatography.

c) The percentage yield for the mixture of *o*- and *p*-isomers.

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[5] The maximum rotations of R-(+)-$\alpha$-phenylethyl alcohol, R-(−)-$\alpha$-phenylethyl phenyl ether, *o*-R-(+)-$\alpha$-phenylethylphenol, and *p*-R-(−)-$\alpha$-phenylethylphenol were taken to be +44.2° (1 dm, neat; D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, *J. Am. Chem. Soc.*, **81**, 5754 (1959)), −46.6° (1 dm, neat; Ref. 2b), +27.9° (1 dm, neat; Ref. 2b), and −10.3° ($[\alpha]_D$ in benzene; Ref. 2b) respectively. The maximum rotation of R-(+)-$\alpha$-phenylethyl chloride was taken to be +125° (1 dm, neat; H. M. R. Hoffmann and E. D. Hughes, *J. Chem. Soc.*, **1964**, 1244).

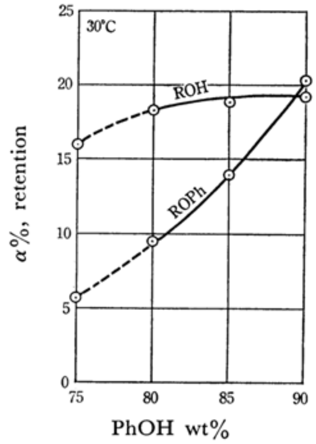

Fig. 1a.

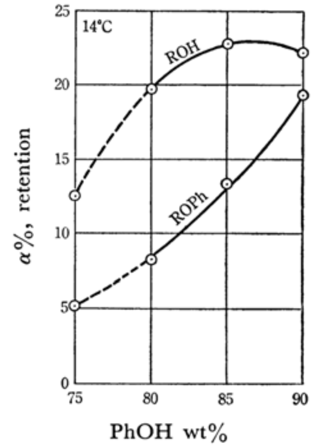

Fig. 1b.

Fig. 1a and 1b. The extents of retention of the configuration for the products of the competitive solvolysis of optically-active $\alpha$-phenylethyl chloride in aqueous phenol solvents.

As expected, the configurations of the starting chlorides were retained, accompanied by predominant racemization, for both the hydrolysis and the phenolysis product, *i. e.*, $\alpha$-phenylethyl alcohol and $\alpha$-phenylethyl phenyl ether, over the entire solvent range examined at 14 and 30°C. The relationships between the extent of the retention of the configuration ($\alpha$%) and the concentration of phenol in aqueous phenol solvents are illustrated in Figs. 1a and 1b.⁶⁾ The runs in 75 wt% aqueous phenol at 14 and 30°C were initially carried out under heterogeneous conditions because of the low solubility of the starting chloride in the reaction mixture.

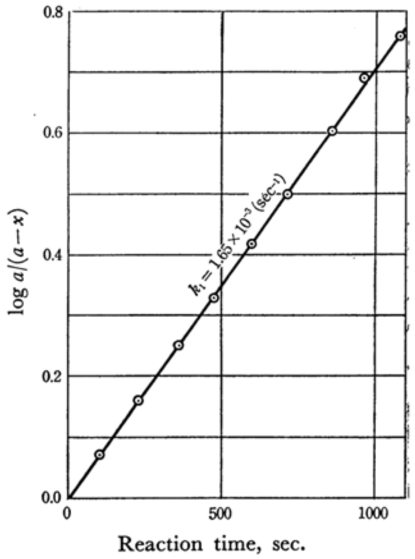

Fig. 2. The first-order plot of the solvolysis of $\alpha$-phenylethyl chloride in 80 wt% aqueous phenol at 14.35±0.05°C (Run 1′). $[\mathrm{RCl}]_0=0.106$ M, $[\mathrm{Et_3N}]_0=0.116$ M.

The extent of retention ($\alpha$%) for $\alpha$-phenylethyl alcohol slightly decreases at the higher temperature, whereas the $\alpha$% for $\alpha$-phenylethyl phenyl ether is practically invariable over the temperature range examined (Figs. 1a and 1b).

The *C*-alkylation products, *i. e.*, *o*- and *p*-$\alpha$-phenylethylphenol, were found to possess net inverted configurations over the entire solvent range examined (Table 1).

## Discussion

In previous papers,²⁾ regarding the retentive phenyl ether formation in binary mixtures of phenol and several non-hydroxylic co-solvents, we suggested a mechanism involving a $\mathrm{S_N}i$-like four-center reaction between a molecule of phenol and a $\mathrm{S_N}1$ ion-pair intermediate. Analogously, for the retentive hydrolysis in aqueous phenol a $\mathrm{S_N}i$-like four-center attack of a water molecule to the $\mathrm{S_N}1$ ion-pair intermediate would be responsible. Furthermore, it was suggested in a previous communication⁴⁾ that this water molecule virtually acts as a chain-end member of a phenol-water polymeric complex.

As for the role of the phenol solvent in this retentive hydrolysis, we may add another suggestion that there is a specific solvation of the ion-pair intermediate by phenol molecules and that, as a result, such solvation enables the water molecule predominantly to attack from the retentive side. The nature of this specific solvation is still elusive

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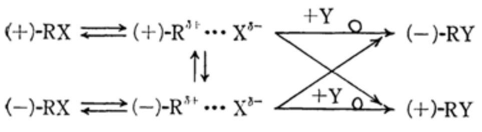
6) The $\alpha$% values for $\alpha$-phenylethyl alcohol at 30°C, reported in a preliminary communication,⁴⁾ were proved to be too low, partly as a result of contamination by phenol. The absorbate in succeeding experiments was changed from alumina to silica gel to give a satisfactory separation of all the components in the reaction products.

at our present state of knowledge. In this connection, a concept of back-side (inversive side) shielding7) or a concept of double inversion, including a $\pi$ complex formation between an ion-pair intermediate and a specified solvent molecule with a conjugate system,8) seems attractive. However, as yet we have neither physical evidence nor kinetic consequences to establish the existence of such a state of intermediate complexes.

To account for the tendency of the $\alpha\%$ values of $\alpha$-phenylethyl alcohol to decrease with a lowering of the water content (Figs. 1a and 1b), two possible causes can be considered: (a) the occurrence of an inversive $S_N2$ hydrolysis, relatively magnified in a solvent with a low dielectric constant,9) or (b) the decrease in the concentration of the water-phenol complex, which might play an important role in the four-center attack of a water molecule, as has been suggested in the preliminary communication.4) The discrimination or verification of these two mechanisms remains as a problem for the future.

If the following reaction scheme, previously10) postulated as being a general racemization mechanism in the course of $S_N1$ solvolysis, is applied to these retentive hydrolyses, the slight decrease in the extent of the retention of $\alpha$-phenylethyl alcohol at the higher reaction temperature (Fig. 1) may be ascribed to the increasing interconversion rate between two antipodal intermediates, since the rate of a retentive or of an inversive attack by a water molecule would have a relatively slight temperature dependence due to their rapidity:



It is of interest to note that the racemization rates, *i. e.*, the interconversion rates, of the antipodal $\alpha$-phenylethyl chlorides through carbonium-ion intermediates in various organic solvents are knwon to increase as much as two to four times11) for a temperature rise of 10°C.

According to the mechanistic scheme shown above, the temperature invariability of the extents of retention for $\alpha$-phenylethyl phenyl ether, observed in the temperature range from 14 to 30°C (Fig. 1), may be explained as a result of how the temperature increment for the rate of the retentive course fortuitously compensates the temperature increment both for the inversive rate and the interconversion rate of the antipodal intermediates.12)

The net inversion of the steric course for the *C*-alkylation, *i. e.*, *o*- and *p*-$\alpha$-phenylethylphenol formation, found over the entire solvent range (Table 1), may be explained as due to the inversive attack of the phenoxides (or a phenol molecule) on the $S_N1$ intermediate, as has been considered to hold for the phenolysis in the other co-solvent system.2b)

## Experimental13)

**Optically-active $\alpha$-Phenylethyl Chloride.** This was prepared by a modified method of an old procedure.1c) In a typical run, 12.0 cc (0.185 mol) of thionyl chloride, purified with quinoline and linseed oil,14) was placed in a small Claisen flask (25-cc capacity), which was equipped with a thermometer inserted into the bottom of the flask through a capillary-neck, and with a dropping funnel into the thermometer-neck. A Liebig condenser, equipped with an adapter, was then connected to the side-arm of the flask and the system was evacuated by a water pump. Under a reduced pressure (20—50 mmHg), 6.0 cc (0.050 mol) of optically-active $\alpha$-phenylethyl alcohol ($[\alpha]_D^{21}$ −17.55°, neat, 0.5 dm; bp 68—71°C/2—3mmHg), resolved by a previously-reported method,15) was added drop by drop, over a period of 10 min at 0—2°C. After 40 min *in vacuo* at 0°C, the thermometer and the dropping funnel were removed; after ordinary equipping with a thermometer and a capillary, the reaction mixture was distilled *in vacuo* to give some unchanged thionyl chloride, trapped in a dry-ice trap, and 5.48 g of $\alpha$-phenylethyl chloride (78% yield; bp 53—55°C/5 mmHg; $[\alpha]_D^{11}$ −23.86°, neat, 0.5 dm; the extent of the retention of the configuration,5) 48.1%).

**Results.** The details of the experimental results are shown in Tables 1 and 2; the details of the procedure will be illustrated in the following description of a representative run.

**The Solvolysis of Optically-active $\alpha$-Phenylethyl Chloride in 85 wt% Aqueous Phenol in the Presence of Added Triethylamine at 14.7°C.** A solution of triethylamine (0.116 M; titrated with 0.05 N perchloric acid in acetic acid, using crystal violet as the indicator) was prepared by mixing 1.06 g of triethylamine (bp 87.0—89.5°C) and 90 cc of 85 wt% aqueous phenol (80 parts of phenol, bp 181.0—181.5°C.

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7) a) W. von E. Doering and A. Streitwieser, Jr.; *cf.* A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956); b) A. Streitwieser, Jr. *et al.*, Refs. 1c and 1d; c) H. Weiner and R. A. Sneen, Ref. 1b.

8) Suggested for the tentative "heterogeneous" substitution of $\alpha$-phenylethyl chloride with silber nitrate and nitrite; a) N. Kornblum, W. J. Jones and D. E. Hardies, *J. Am. Chem. Soc.*, **88**, 1704 (1966); b) N. Kornblum and D. E. Hardies, *ibid.*, **88**, 1707 (1966).

9) For an example, see K. Okamoto, N. Uchida, S. Saitô and H. Shingu, This Bulletin, **39**, 307 (1966).

10) K. Okamoto *et al.*, Ref. 9.

11) K. Bodendorf and H. Böhme, *Ann.*, **516**, 1 (1935).

12) A strict interpretation of this phenomenon will be presented in a forthcoming paper.

13) The infrared sepctra were obtained from a Shimadzu model IR-27 spectrometer. For the measurement of the optical rotations a Zeiss-Winckel Kreispolarimeter, 0.01°, was used.

14) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston (1957), p. 345.

15) E. Downer and J. Kenyon, *J. Chem. Soc.*, **1939**, 1156.

and 20 parts of distilled water). In a 100 cc glass-stoppered Erlenmeyer flask there was placed 70 cc of the triethylamine solution; the mixture was then kept for 0.5 hr in a thermostat maintained at 14.7±0.1°C. Optically-active $\alpha$-phenylethyl chloride (1.045 g, 1.00 cc; $[\alpha]^{20}_{\mathrm{D}}$ $-23.86°$, 0.5 dm, neat; bp 50.0—52.7°C/2.5 mmHg) was added in one portion, after which the mixture was kept at 14.7°C for 1.25 hr. The reaction mixture was cooled at 0°C; 80 cc of water and 95 g of 30% aqueous sodium hydroxide was added in several portions; the mixture was extracted with four 50-cc portions of ether; the combined extracts were washed with two 50-cc portions of 10% aqueous sodium hydroxide, then with two 50-cc portions of 20% aqueous sodium chloride, dried with magnesium sulfate, and concentrated to 10-cc. The evaporation of the solution gave 1.147 g of a water-white oil, which was then chromatographed over 30 g of silica gel (Nakarai, No. II-A, 100—200 mesh). The column was successively eluted with benzene - *n*-hexane (1 : 1 by volume), benzene, benzene-ether (97.5 : 2.5 by volume), and ether, 40-cc portions being taken. Fractions 1—7, using benzene - *n*-hexane, gave 0.807 g of $\alpha$-phenylethyl phenyl ether (54.8% yield; bp 87°C/0.38 mmHg; $n^{31}_{\mathrm{D}}$ 1.5610; the same infrared spectrum as the authentic sample; $[\alpha]^{20}_{\mathrm{D}}$ $+1.19° \pm 0.04°$, 0.5 dm, neat; 13.4% of retention of the configuration). Fractions 7—12, using benzene, gave 0.123 g of *o*-$\alpha$-phenylethylphenol (7.7% yield; bp 135°C (bath temp.)/0.35 mmHg; $n^{35}_{\mathrm{D}}$ 1.5849; the same infrared spectrum as the authentic sample; $[\alpha]^{20}_{\mathrm{D}}$ $0.78 \pm 0.04°$, 0.5 dm, neat; 14.7% inversion of the configuration). Fractions 15—20, using benzene-ether, afforded 0.034 g of *p*-$\alpha$-phenylethylphenol (2.3% yield; bp 135° (bath temp.)/0.1—0.5 mmHg; mp 55.0—57.0°C; the same infrared spectrum as the authentic sample; $[\alpha]^{19}_{\mathrm{D}}$ $-1.60+0.96°$ (*c* 6.26, in benzene); 41% inversion of the configuration). Fraction 22, using ether, afforded 0.073 g of $\alpha$-phenylethyl alcohol (8.0% yield; bp 70°C (bath temp.)/ 3.5 mmHg; $n^{30}_{\mathrm{D}}$ 1.5211; the same infrared spectrum as the authentic sample; $[\alpha]^{20}_{\mathrm{D}}$ $-1.92 \pm 0.04°$, neat, 0.5 dm, calculated from the rotation of the diluted sample with the racemic alcohol; 22.8% retention of the configuration). None of the intermediate fractions gave any residual matter after the evaporation of the respective eluent.

**Kinetic Measurements.** All kinetics were measured at 14.4 or 29—30°C, using the racemic chloride in some cases. The reaction vessels were 100-cc glass-stoppered Erlenmeyer flasks, from which 1-cc aliquots were removed at intervals. The aliquots were poured into about 10 cc of cooled acetic acid and titrated with 0.05 N perchloric acid in acetic acid, using crystal violet as an indicator. Infinity titers were determined after at least ten half-lives. All the data were treated graphically by a plot of $\log a/(a-x)$ against the time. The results are shown in Table 2. In each run the reaction was followed to at least 80% completion, and a smooth linear relationship was obtained (for a representative run with the racemic chloride, see Fig. 2).