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Kinetic Studies of Solvolysis. XIV. The Solvolysis of Optically Active α-Phenylethyl Chloride in Binary Mixtures of Methanol and Phenol —The S_N1 Methanolysis with the Retention of the Configuration—

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The competitive S_N1 methanolysis and S_N1 phenolysis of optically-active α-phenylethyl chloride in the presence of added triethylamine give α-phenylethyl methyl ether and α-phenylethyl phenyl ether, both with a net inverted configuration, in 50 wt% methanolic phenol, whereas in 85—95 wt% methanolic phenol both the methyl and the phenyl ether have been obtained with a net retained configuration. In the intermediate solvent range (*e.g.*, 75 wt% methanolic phenol), the methyl ether possesses a net inverted configuration, while the phenyl ether has a net retained configuration. Over the entire solvent range examined, the *o*- and *p*-α-phenylethylphenols (the *C*-alkylation products) possess net inverted configurations. This heretofore unusual retained steric course of the methanolysis is explained by the S_Ni-like four-center attack of a methanol molecule from the retentive side of the S_N1 ion-pair intermediate. Much as in the retentive hydrolysis in the aqueous phenols, the specific solvation of the phenol molecules to the S_N1 ion-pair intermediate may be suggested as a factor which assists the retentive attack of the methanol molecule.

In previous papers of this series[1] we have reported on the retentive hydrolysis of optically-active α-phenylethyl chloride in aqueous phenol solvents (75—95 wt% phenol). As an extention of those experiments, we designed competitive methanolysis and phenolysis in binary mixtures of phenol and methanol; we will report in this paper that a further example of the retentive solvolyses[1,2] is found in the methanolysis of optically-active α-phenylethyl chloride in 85—95 wt% methanolic phenols. In addition, the factors which affect the retentive course of this methanolysis will be briefly discussed.

1) a) Part XIII: K. Okamoto, M. Hayashi, K. Komatsu and H. Shingu, This Bulletin, **40**, 624 (1967); b) Preliminary communication of Part XIII: K. Okamoto, M. Hayashi and H. Shingu, *ibid.*, **39**, 408 (1966).

2) K. Okamoto, K. Komatsu and H. Shingu, This Bulletin, **39**, 2785 (1966).

Results

The solvolysis in methanolic phenols was conducted on optically-active α-phenylethyl chloride in the presence of added triethylamine at 50.0°C. After ten-half lives, the four solvolysis products, *i.e.*, α-phenylethyl methyl ether, α-phenylethyl phenyl ether, *o*-α-phenylethylphenol, and *p*-α-phenylethylphenol, were separated by elution chromatography using an elution column packed with basic alumina in the upper part and silica gel in the lower part of the column. After purification by distillation *in vacuo*, the rotations of these products were measured, and the configurations and the optical purities were determined.[3] The extents (α%) of the retention (or the inversion) of the configuration are plotted against the concentrations of phenol in the methanolic phenols in Fig. 1.

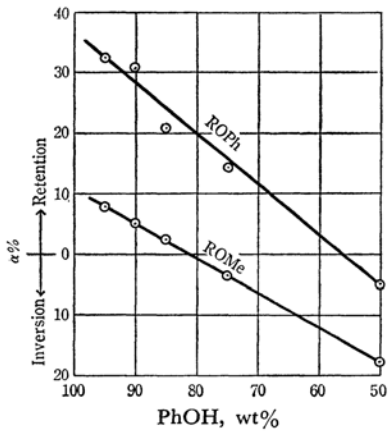

Fig. 1. The extents of the retention of the optical purities for the products of the competitive methanolysis and phenolysis of optically-active α-phenylethyl chloride in the binary mixtures of phenol and methanol at 50°C.

The solvolysis in 50 wt% methanolic phenol gives both the methyl and the phenyl ether with a net inverted configuration; this is a standard result for the S_N1 solvolysis of simple secondary alkyl derivatives.[4] In contrast, in the solvent range from 85 to 95 wt% methanolic phenol, both the ethers have a retained configuration, accompanied by a predominant racemization. In the intermediate solvent range (*e.g.*, 75 wt% methanolic phenol), the solvolysis gives the methyl ether with a net inverted configuration, whereas the phenyl ether so obtained has a net retained configuration. The extents of the retention of the optical purities for both the ethers vary somewhat linearly from the region of inversion to that of retention as the phenol concentration in the methanolic phenols becomes higher; this is shown in Fig. 1.

Over the entire solvent range examined, the solvolysis gave *o*- and *p*-α-phenylethylphenol with a net inverted configuration; this is similar to the results found with the aqueous phenols[1a] and also in the phenolyses in binary mixtures of phenol and nonhydroxylic co-solvents.[5] These results are shown in Table 1, along with the S_N1 rate constants measured titrimetrically in 50 and 75 wt% methanolic phenol.

Discussion

In previous papers[1] we suggested two possible factors to which the retained steric course of the hydrolysis in aqueous phenols could be ascribed: a) the S_Ni-like four-center attack of a water molecule from the retentive side of the S_N1 ion-pair intermediate; b) a specific solvation of the intermediate by phenol molecules, thus assisting the retentive attack of the water molecule.

In the case of methanolysis in methanolic phenols, if the b factor mentioned above were predominant in the steric course, we could expect an increasingly retentive α% of the methyl ether with an increase in the phenol concentration in the methanolic phenols; this is indeed the case in the solvent range from 85 to 95 wt% methanolic phenol. As has been said of the b factor in a previous paper,[1a] we do not yet have any definitive support for considering the "back-side shielding"[6] of a phenol molecule as the predominant characteristic of this retentive specific solvation of the phenol molecules. This problem must be left for future study.

It was previously found, in the case of aqueous phenol solvents,[1] that the retentive α% of the hydrolysis product, *i.e.*, α-phenylethyl alcohol, showed a tendency to decrease at higher phenol concentrations. Contrary to this observation, the above-mentioned specific (retentive) solvation of the phenol molecules predicts a tendency for the retentive α% of α-phenylethyl alcohol in aqueous phenols to increase with higher phenol concentrations. Therefore, we may consider this tendency to de-

3) The maximum rotations (neat, 1 dm) taken for the estimation of the optical purities are as follows: R-α-phenylethyl chloride, +125° (H. M. R. Hoffman and E. D. Hughes, *J. Chem. Soc.*, **1964**, 1244); R-α-phenylethyl phenyl ether, −46.6° (Ref. 5); R-α-phenylethyl methyl eter, +120° (Ref. 9); *o*-R-α-phenylethylphenol, +27.85° (Ref. 5); *p*-R-α-phenylethylphenol, −10.26° ($[\alpha]_D$ in benzene, Ref. 5).

4) See Ref. 1a and also A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., New York (1962), pp. 59, 73.

5) K. Okamoto, H. Yamada, I. Nitta and H. Shingu, This Bulletin, **39**, 299 (1966).

6) a) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956); b) A. Streitwieser, Jr., and W. D. Schaeffer, *J. Am. Chem. Soc.*, **79**, 6233 (1957); c) A. Streitwiser, Jr., and S. Andreades, *ibid.*, **80**, 6533 (1958); d) H. Weiner and R. A. Sneen, *ibid.*, **87**, 287, 292 (1965); e) N. Kornblum and D. E. Hardies, *ibid.*, **88**, 1707 (1966).

Table 1. The extents of retention of the optical purity for the products of the competitive solvolyses of α-phenylethyl chloride in the mixture of phenol and methanol at 50°C[a]

Run No.	Solvent PhOH wt%	Solvent MeOH wt%	α_D, neat, 0.5 dm.[b] RCl[d]	ROMe[d]	ROPh[d]	RPhOH[d] (o-)	RPhOH[d,e] (p-)	α%[c] ROMe	ROPh	RPhOH (o-)	RPhOH (p-)	10^4k_1[f] sec^{-1}
1	50	50	+27.06°	−4.51°	+0.50°	−1.93°	+0.22°	17.4 inv.	5.0 inv.	32.0 inv.	5 inv.	4.42
2	75	25	+23.24°	−0.77°	−1.48°	−2.22°	+0.51°	3.5 inv.	17.1 ret.	42.8 inv.	13 inv.	35.5
3	85	15	−24.17°	−0.59°	+1.88°	+0.505°	−0.92°	2.5 ret.	20.9 ret.	9.4 inv.	23 inv.	—
4	90	10	−24.17°	−1.11°	+2.80°	−0.72°	−0.54°	4.78 ret.	31.0 ret.	13.4 inv.	14 inv.	—
5	95	5	−23.86°	−1.78°	+2.90°	+0.54°	−2.7°	7.77 ret.	32.5 ret.	10.2 inv.	69 inv.	—

a) At 50.1—50.5°C; Initial concentration of α-phenylethyl chloride and triethylamine were 0.105 and 0.109—0.116 M, respectively.
b) Taken at 17—22°C.
c) The extent of retention of optical purity.
d) R=α-Phenylethyl; RPhOH=α-Phenylethylphenol.
e) $[\alpha]_D$, taken in benzene.
f) The rate constants for the racemic chloride.

Table 2. The yields of the products of the solvolyses of optically-active α-phenylethyl chloride in the mixtures of phenol and methanol

Run. No.	Solvent PhOH	Solvent MeOH	Reaction temp. °C	Initial concn. RCl M	Initial concn. Et_3N M	Yields[a] % ROMe[b]	ROPh[b]	RPhOH[b] (o-)	RPhOH[b] (p-)	Reaction time hr
1	50	50	50.4	0.105	0.109	51.1	11.1	3.8	2.9	4.3
2	75	25	50.5	0.105	0.115	23.6	48.7	5.9	2.9	0.7
3	85	15	50.1	0.105	0.116	13.8	32.0	11.1	7.3	0.5
4	90	10	50.4	0.105	0.116	8.5	55.5	5.9	4.5	0.4
5	95	5	50.1	0.105	0.112	4.2	66.8	5.9	8.4	0.3

a) Based on the starting chloride.
b) R=α-Phenylethyl.

crease in aqueous phenols to be due to a factor other than the specific solvation, probably the insertion of the concurrent inversive S_N2 hydrolysis. In the slightly-methanolic phenols, in which no tendency for the α% of the methyl ether to decrease was found with an increase in the phenol concentrations (Fig. 1), such insertion would be difficult because of the lower S_N2 reactivity of the methanol molecule.

As has been previously mentioned in connection with similar results in aqueous phenols[1a] and also in binary mixtures of phenol and non-hydroxylic cosolvents,[5] the inversive steric course of the α-phenylethylphenols, found in the methanolic phenols, may be ascribed to the inversive S_N2-like attack of the phenoxide (or of a phenol molecule) on the S_N1 ion-pair intermediate.

Experimental[7]

The Solvolysis of Optically-active α-Phenylethyl Chloride in Binary Mixtures of Phenol and Methanol at 50.0°C. The results of solvolyses in various mixtures of phenol and methanol are illustrated in Table 1; the yields of the products for each run are given in Table 2. The details of the procedures are illustrated by the following description of a representative run in 95 wt% methanolic phenol.

A mixture of 2.09 g (0.0149 mol) of optically-active α-phenylethyl chloride (bp 53—55°C/5 mmHg; α_D^{16} −23.86°, 0.5 dm, neat)[8] and 140 cc of a solution of triethylamine (0.112 N) in 95 wt% methanolic phenol (phenol: methanol, 95: 5 by weight) was kept for 20

7) The infrared spectra were obtained from a Shimadzu model IR-27 spectrometer. For the measurement of the optical rotations a " Zeiss-Winckel, Kreispolarimeter, 0.01° " was used.
8) The chloride was prepared by a previously-reported method.[1a]

minutes at 50.1±0.1°C in a glass-stoppered, 500-cc Erlenmeyer flask. After 300 cc of ether had then been added to the reaction mixture, the mixture was washed with three 80-cc portions of 10% aqueous sodium chloride, ten 100-cc portions of 10% aqueous sodium hydroxide, and then seven 100-cc portions of 10% aqueous sodium chloride until the washings became neutral to litmus. The ether solution was then dried with magnesium sulfate and distilled under reduced pressure to give 2.54 g of an oily material, which was chromatographed using an elution column packed with 29 g silica gel (Nakarai, No. II-A. 100—200 mesh) in the lower part and 30 g of basic alumina (Nakarai, 200—300 mesh) in the upper part. The column was eluted successively with *n*-hexane - benzene (1 : 1 by volume) and with ether and ethanol-ether (5 : 95 by volume) in 25-cc portions. The fraction 3, using *n*-hexane - benzene (1 : 1 by volume), gave 3.0 mg of styrene (with the same infrared spectrum as an authentic sample). Fractions 4—9, using *n*-hexane - benzene, gave 1.73 g of α-phenylethyl phenyl ether (bp 84.0—86.5°C/0.45 mmHg; 58.8% yield; n_D^{30} 1.5612, n_D^{25} 1.5634; with the same infrared spectrum as an authentic sample; α_D^{21} +2.90±0.05°, 0.5 dm, neat). The fraction 12, using ether, gave 0.086 g of α-phenylethyl methyl ether (bp 93—98°C/30 mmHg; 4.2% yield; n_D^{25} 1.4906 (lit. n_D^{25} 1.4905[9]; with the same infrared spectrum as an authentic sample; α_D^{20} −1.78 ±0.11°, 0.5 dm, neat). Fractions 15 and 16, using ethanol-ether (5 : 95 by volume), gave 0.163 g of *o*-α-phenylethylphenol (bp 130—135°C/3 mmHg; 5.6% yield; the infrared spectrum was identical with that of an authentic sample; $\alpha_D^{16.5}$ +0.54±0.06°, 0.5 dm, neat). The fraction 17 gave 0.019 g of an oily mixture of *o*- and *p*-α-phenylethylphenol (about 1 : 1 by weight; 0.6% yield). Fractions 18—34, using ethanol-ether (5 : 95 by volume), gave 0.238 g of *p*-α-phenylethylphenol (mp 56—56.7°C (uncorr.) (lit. mp 56—56.3°C[10]); 8.1% yield; with the same infrared spectrum as an authentic sample; $[\alpha]_D^{19}$ −2.71±1.16° (*c* 30, benzene)).

Kinetic Measurements. The reaction rates were followed by pipetting 1-cc aliquots into about 10 cc of acetic acid and by then titrating the solution with standard perchloric acid (0.05 N) in acetic acid, using crystal violet in acetic acid as the indicator. Infinity titers were determined after at least ten-half lives; they gave reproducible results. All the rate data were treated graphically by a plot of $\log a/(a-x)$ against the time. In each case the reaction was followed to at least a 80% reaction; a smooth linear relationship was obtained. The remaining reaction mixtures were used for the product analysis. The rate data are shown in Table 1.

9) K. Mislow, *J. Am. Chem. Soc.*, **73**, 4043 (1951).

10) H. Hart, *Anal. Chem.*, **24**, 1500 (1952).