Kinetic Studies on Solvolysis. VII. On the Kinetic Resolution at the First Stage of the S_N1-type Solvolysis of α-Phenethyl Chloride in Optically Active Carboxylic Acid Solvents

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(Received November 21, 1960)

In the previous paper[1] we have demonstrated that the acetolysis of *tert*-butyl bromide proceeds with some linear rate acceleration in the presence of *p*-nitrophenol and some other *p*-substituted phenols, while the presence of *o*-substituted phenols in which the hydroxyl groups are fixed by intramolecular hydrogen-bridge does not cause any catalytic acceleration. From this it was concluded that the free hydroxyl group was distinctly the center of the reaction in those hydroxylic molecules including alcohols, phenols, carboxylic acids and water. It is, therefore, clear that they play a rôle not only as a general solvent but also as a kind of reactant molecule in the first ionization stage of the S_N1-type solvolysis.

Thus it may be anticipated that, when the S_N1-type solvolysis of a racemic halide is carried out in an optically active solvent, there would be observed a kinetic resolution in the first stage of the solvolysis with the result that the unchanged asymmetric halide may have some optical activity. This possibility of asymmetric solvolysis of S_N1-type was examined in the case of the solvolysis of (±)-α-phenethyl chloride in (+)-α-methyl hydrogen camphorate and in (−)-pinonic acid. This paper presents evidence in support of the existence of such kinetic resolution in those optically active solvents.

S_N2-type Kinetic Resolution of (±)-α-Phenethyl Chloride in Dioxane.—The rate studies on the S_N1-type solvolysis in these optically active solvents in the presence of 0.1 M of triethylamine showed that both of the reactions were of the first order in α-phenethyl chloride and of zero order in the added base, this being illustrated in Figs. 1 and 2. Although these results indicate that the reactions proceed predominantly by S_N1 mechanism, they do not exclude a slight, presumably less than 1%, concurrency of S_N2 mechanism[2].

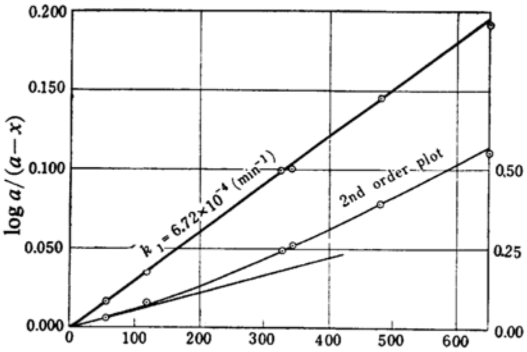

Fig. 1. Solvolysis rate of (±)-α-phenethyl chloride in (−)-pinonic acid, $[\alpha]_D^{20}$ −51.5°, in the presence of 0.116 M of triethylamine at 80.0±0.1°C. The initial concentration of the chloride, 0.116 M.

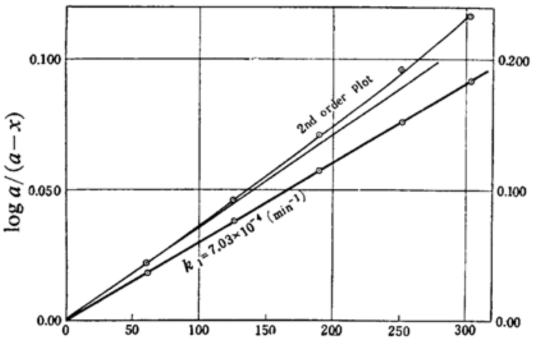

Fig. 2. Solvolysis rate of (±)-α-phenethyl chloride in α-methyl hydrogen camphorate, $[\alpha]_D^{15}$ 58.0°, in the presence of 0.123 M of triethylamine at 98.0±0.1°C. The initial concentration of the chloride, 0.123 M.

As a control experiment, thererfore, the extent and direction of the S_N2-type kinetic resolution of α-phenethyl chloride was examined under the reaction conditions comparable to those of the S_N1-type resolution. For this purpose the S_N2-reaction of α-phenethyl chloride and triethylammonium salt of the optically active carboxylic acid was carried out in dioxane, which is a favorable solvent for the

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[1] K. Okamoto and H. Shingu, This Bulletin, 34, 1131 (1961).

[2] H. Shingu and K. Okamoto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), 78, 547 (1957).

TABLE I. SUMMARY OF OPTICAL PURITIES OF THE RECOVERED α-PHENETHYL CHLORIDE AND OF α-PHENETHYL ALCOHOL IN THE S_N1-TYPE SOLVOLYSIS OF (±)-α-PHENETHYL CHLORIDE

Solvent	Nucleophile	Temp. °C	Time[a] hr.	Optical purity, % α-Phenethyl chloride (recovered)	Optical purity, % α-Phenethyl alcohol[b]
(+)-α-Methyl hydrogen camphorate $[\alpha]^{15}_D$ 58.0°	Triethylammonium (+)-α-methyl camphorate	98~100	7.5	L[c] 0.54±0.13	L 2.24±0.28
		98		L 0.58±0.09	L 2.95±0.74
		100		(L 2.82±0.01[d])	(D[c] 10.6 ±0.09)
(−)-Pinonic acid $[\alpha]^{18}_D$ −10.9°	Triethylammonium	70	15	D 0.27±0.08	D 0.57±0.07
$[\alpha]^{20}_D$ −51.5°		70~80	15.5	D 0.20±0.05	D 1.04±0.25
$[\alpha]^{18}_D$ −76.1°		70	15	D 0.13±0.02	L 1.56±0.39
Acetonitrile	Anilinium (+)-α-methyl camphorate[e]	85	4.85	0.00±0.02	—
	Anilinium (−)-pinonate[f]	85	4.35	0.00±0.03	L 3.22±1.38
Dioxane[g]	Triethylammonium (+)-α-methyl camphorate[e]	100	9[h]	L 0.08±0.01	(L)[i]
	Triethylammonium (−)-pinonate[f]	70	16[h]	L 0.15±0.01	(L)[i]

a) Approximately the half life time for each reaction.
b) The alcohol obtained from α-phenethyl ester.
c) Configuration.
d) The run with L-(+)-α-phenethyl chloride; $[\alpha]^{15}_D$ 30.4°, optical purity 28.7%.
e) The acid, $[\alpha]^{15}_D$ 58.0°, chloroform.
f) The acid, $[\alpha]^{20}_D$ −75.0°, chloroform.
g) The reaction under S_N2 mechanism.
h) The reaction time for the stage of 5% conversion of the chloride.
i) Deduced from the principle that the inversion of configuration occurs in the S_N2-type reaction.

S_N2 mechanism. In the reaction with triethylammonium (−)-pinonate (the acid $[\alpha]^{20}_D$ −75°), about 5% of (±)-α-phenethyl chloride was consumed in 16 hr. at 70°C and the unchanged chloride of 0.15% optical purity (L configuration) was obtained (cf. Table I). A similar reaction was carried out with triethylammonium (+)-α-methyl camphorate (the acid $[\alpha]^{15}_D$ +58°) and the unchanged α-phenethyl chloride showed 0.08% of optical purity (L configuration) after 9 hr. at 100°C at the stage of about 5% conversion. These values would indicate the extent of the kinetic resolution caused by the supposedly co-existing S_N2 mechanism in the S_N1-type reactions in these optically active carboxylic acid solvents.

Possibility of the Induced Resolution Caused by Kinetic Resolution at the Second Stage of S_N1-type Solvolysis. — The slight resolution observed in the S_N2 condition would indicate another mechanism for interpretation of the results of the S_N1-type resolution. Since the intermediate in the S_N1-type solvolysis is converted to the product by a process quite similar to the S_N2 mechanism, the starting chloride which is in equilibrium with the intermediate may also become optically active, even if the intermediate was kinetically resolved by an optically active nucleophile at the second stage of solvolysis, instead of being resolved at the first ionizing stage.

In order to examine this possibility, another control experiment was carried out under conditions that should cause kinetic resolution only at the second stage, i. e., the product forming stage. For this purpose acetonitrile, which does not react with the intermediate, was used as a solvent for the solvolysis of α-phenethyl chloride. As is expected from the S_N1 mechanism, the solvolysis rates optically active nucleophiles (anilinium (−)-pinonate and (+)-α-methyl camphorate) were found to obey good first order kinetics at 85°C, this being shown in Figs. 3 and 4. Half way through the reactions the recovered α-phenethyl chloride did not give any optical activity for either

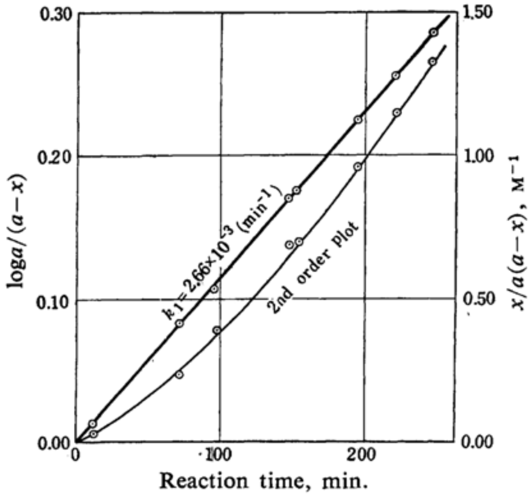

Fig. 3. Solvolysis rate of (±)-α-phenethyl chloride in acetonitrile in the presence of 0.675 N anilinium (−)-pinonate at 85.0±0.1°C. The initial concentration of the chloride, 0.675 M.

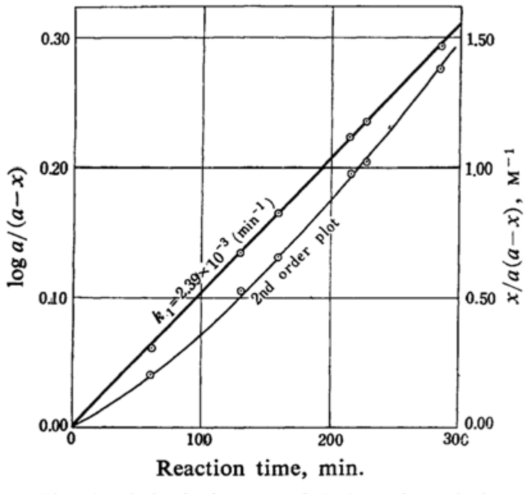

Fig. 4. Solvolysis rate of (±)-α-phenethyl chloride in acetonitrile in the presence of 0.682 N anilinium (+)-α-methyl camphorate at 85.0±0.1°C. The initial concentration of the chloride, 0.682 M.

of the nucleophiles within the experimental error, while the small amount of α-phenethyl alcohol obtained after hydrolysis of α-phenethyl pinonate showed about 5% of optical purity (D-configuration) (cf. Table I). This eliminates the possibility that the kinetic resolution at the second stage of the S_N1-type solvolysis can induce any preceptible resolution at the first ionization stage.

Kinetic Resolution at the Ionization Stage of the S_N1-type Solvolysis.—With these considerations in mind, we first carried out the S_N1-type solvolysis in (+)-α-methyl hydrogen camphorate in the presence of triethylamine at 98∼100°C for 7.5 hr. until about 50% of α-phenethyl chloride was consumed, and the unchanged chloride had 0.54±0.13% of optical purity (L-configuration) (cf. Table I). In a similar experiment at 98°C for 9.5 hr., α-phenethyl chloride of 0.58±0.09% of optical purity (L-configuration) was recovered. Although the direction of the rotation of the recovered chlorides was the same as in the above mentioned reaction of the S_N2 mechanism in dioxane, the degree of optical purity, i. e., the extent of the kinetic resolution, is obviously greater than the one expected in the S_N2-type reaction under the corresponding reaction conditions, even after the correction of optical purity for the difference of the reaction percentage in both of the mechanisms. Hence it is evident that the optical rotation in the recovered chloride was predominantly caused by the kinetic resolution at the first ionization stage of the S_N1-type solvolysis in (+)-α-methyl hydrogen camphorate.

In a similar manner analogous experiments on the S_N1-type solvolysis of α-phenethyl chloride in the other optically active solvent was carried out in the presence of triethylamine in (−)-pinonic acids of various optical rotations for 15 hr. at about 70°C. In pinonic acid of optical rotations, $[\alpha]^{18}_{D}$ −10.9°, $[\alpha]^{20}_{D}$ −51.5° and $[\alpha]^{18}_{D}$ −76.1°, the unreacted chlorides showed 0.27±0.08, 0.20±0.05 and 0.13±0.02% of optical purity (D-configuration), respectively.

As above mentioned, in the resolution of the S_N2 mechanism with triethylammonium (−)-pinonate in dioxane the direction of rotation of the unreacted chloride was that of L-configuration, and this is just opposite to the one (D-configuration) observed in the reactions carried out in (−)-pinonic acid. This result clearly indicates that the kinetic resolution occurred at the first ionization stage of the S_N1-type solvolysis in this optically active solvent.

Finally, the kinetic resolution at the ionization stage of these S_N1-type solvolyses may be considered as a further evidence for the solvent molecule playing a rôle as a kind of reactant in this stage[1).

Configuration of the Optically Active α-Phenethyl Alcohol Derived from α-Phenethyl Esters of Optically Active Carboxylic Acids.—In the reactions in (+)-α-methyl hydrogen camphorate the isolated β-(α-phenethyl) α-methyl camphorate was hydrolysed with alcoholic sodium hydroxide or reduced with lithium aluminum hydride, and the optical purity of the recovered α-phenethyl alcohol

TABLE II. RELATIONSHIP BETWEEN CONFIGURATIONS OF RECOVERED α-PHENETHYL CHLORIDE AND α-PHENETHYL ALCOHOL DERIVED FROM α-PHENETHYL ESTER OBTAINED IN THE $\mathrm{S_N}1$-TYPE SOLVOLYSIS OF (±)-α-PHENETHYL CHLORIDE IN OPTICALLY ACTIVE CARBOXYLIC ACIDS

Configuration of recovered α-phenethyl chloride	Resolution controlling stage for α-phenethyl alcohol	Configuration for α-phenethyl alcohol derived from α-phenethyl esters	Optically active carboxylic acids as a solvolytic solvent
L	first	L	(+)-α-Methyl hydrogen camphorate
	second*	L	——
D	first	D	(−)-Pinonic acid, $[\alpha]_{\mathrm{D}}$ −10.9° and −51.5°
	second*	L	(−)-Pinonic acid, $[\alpha]_{\mathrm{D}}$ −76.1°

* It is assumed that the resolution at the second stage gives the alcohol with L-configuration by the $\mathrm{S_N}2$ mechanism (see text).

amounted to 2.24±0.28 and 2.95±0.74% (L-configuration) for each run (cf. Table I), while α-phenethyl alcohols derived from α-phenethyl (−)-pinonate by alkaline hydrolyses showed optical purities of 0.57±0.07 (D-configuration), 1.04±0.25 (D-configuration) and 1.56± 0.39% (L-configuration) for the reactions in (−)-pinonic acid with optical rotations, $[\alpha]^{18}_{\mathrm{D}}$ −10.9°, $[\alpha]^{20}_{\mathrm{D}}$ −51.5° and $[\alpha]^{18}_{\mathrm{D}}$ −76.1°, respectively (cf. Table I).

In these reactions the directions of rotation for the α-phenethyl alcohols derived from the ester of the optically active carboxylic acids doubtless controlled, generally, by two factors, namely, the kinetic resolution caused by the attack of the optically active nucleophile at the second stage of the solvolysis and the resolution in the intermediate determined by the electrophilic attack by optically active solvent molecules at the first ionization stage.

The resolution at the first ionization stage has already been discussed in the previous section. For the discussion of the results of the resolution at the second stage the knowledge about the steric behavior of α-phenethyl chloride at this stage is required, since it is uncertain whether the configuration of the chloride would invert at the second stage of the $\mathrm{S_N}1$-type reaction in these optically active carboxylic acids. Thus, the solvolysis of originally optically active chloride, L-(+)-α-phenethyl chloride, was carried out in (+)-α-methyl hydrogen camphorate in the presence of triethylamine at 100°C. Half way through the reaction α-phenethyl alcohol of 37% inversion, 63% racemization of configuration was obtained after reductive hydrolysis of β-(α-phenethyl) α-methyl camphorate (cf. Table I)[3]. This indicates that at the second stage of this solvolysis the chloride reacted predominantly with inversion of the configuration. This is consistent with the results previously known in the reaction of this chloride in the other hydroxylic solvents[4].

Considering this inversion of configuration of α-phenethyl chloride at the second stage of the $\mathrm{S_N}1$-type solvolysis, we may expect that the direction of the second stage resolution would be the same as that of the resolution by the $\mathrm{S_N}2$-type mechanism. This is verified by the fact that the $\mathrm{S_N}1$-type resolution of (±)-α-phenethyl chloride with anilinium (−)-pinonate in acetonitrile, used as a solvent in which the resolution occurs only at the second stage, gives alcohol with L-configuration which is the same type obtainable in the $\mathrm{S_N}2$-type resolution, e. g., in dioxane (cf. Table I).

Assuming that the direction of second stage resolution in the $\mathrm{S_N}1$-type solvolysis in the optically active carboxylic acids would be the same as in acetonitrile, we can determine the resolution controlling stage, first or second, for the α-phenethyl alcohol derived from the esters by comparing the direction of resolution for the recovered chloride with those of the alcohol obtained, this being indicated in Table II.

In Table II it is shown that in (−)-pinonic acids, $[\alpha]_{\mathrm{D}}$ −10.9° and −51.5°, the configuration of the resolved α-phenethyl alcohol (cf. Table I) is predominantly determined at the first ionization stage, while in almost optically pure (−)-pinonic acid with $[\alpha]_{\mathrm{D}}$ −76.1° it is determined at the second stage of the reaction. In α-methyl hydrogen camphorate it seems likely that the configuration of α-phenethyl alcohol (cf. Table I) is predominantly controlled at the first ionization stage, since the

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[3] The recovered α-phenethyl chloride was mostly racemic and retained only 10% of the original optical purity, as is expected from the reversibility of the ionization process at the first stage of the $\mathrm{S_N}1$-type solvolysis.

[4] E. D. Hughes, C. K. Ingold and A. D. Scott, *J. Chem. Soc.*, **1937**, 1201.

resolution percentage of α-phenethyl chloride at the S_N2 condition, i. e., in dioxane, is considerably less than that observed at the S_N1-type reaction in this optically active solvent.

Experimental[5]

Specific Rotations in Chloroform for Optically Pure α-Phenethyl Alcohol and α-Phenethyl Chloride.—Because of the lack of previously reported data, specific rotations in chloroform for α-phenethyl alcohol of the rotations α_D, neat, −37.0° (at 15.0°C), +19.4° (at 24.4°C) and −40.1° (at 25.4°C), *l* 1 dm. for all, were measured, and the following results were obtained: $[\alpha]_D$ −47.5° (at 15.0°C, *c* 16.0), +24.8° (at 24.4°C, *c* 6.70) and −50.7° (at 25.4°C, *c* 6.70), respectively. From these values and the reported value[6] for neat rotation of optically pure α-phenethyl alcohol (α_D^{25} 43.7°, *l* 1 dm.), a specific rotation in chloroform for the optically pure alcohol was estimated to be 55.9° (at 15~25°C, *c* 6.70~16.0). In a similar manner, a specific rotation in chloroform for optically pure α-phenethyl chloride was estimated to be 105~107° (at 17~25°C, *c* 6.8~6.9) from the following data: reported value[7] for neat rotation of optically pure chloride, α_D^{25} 126~129°, *l* 1 dm.; observed specific rotations in chloroform for α-phenethyl chloride of neat rotations α_D −34.8° (at 17.0°C, *l* 1 dm.) and +17.8° (at 25.7°C, *l* 1 dm.): −28.9° (at 17.0°C, *c* 6.83) and +14.9° (at 25.7°C, *c* 6.90), respectively.

Reaction of (±)-α-Phenethyl Chloride and Triethylammonium (−)-Pinonate in (−)-Pinonic Acid.—(−)-Pinonic acid was prepared by potassium permanganate oxidation of α-pinene according to the previously reported method[8]. A mixture of pinonic acid (35.0 g., b. p. 152~156°C/4 mmHg, $[\alpha]_D^{18}$ −10.9°, *c* 10.9, chloroform), triethylamine (7.0 g., b. p. 88~89°C) and (±)-α-phenethyl chloride (10.45 g., b. p. 92.0°C/36 mmHg) was kept at 70°C for 15 hr. After addition of ether (50 cc.) the ethereal solution containing crystals of triethylammonium hydrochloride was washed successively with two 50 cc. portions of 10% aqueous sodium hydroxide and two 50 cc. portions of water, dried, and concentrated. The residue was fractionally distilled in vacuo, giving α-phenethyl chloride (6.9 g., b. p. 77.0~78.0°C/18 mmHg., n_D^{20} 1.5265, α_D^{18} −0.180±0.005°, $[\alpha]_D^{18}$ −0.287°, *l* 2 dm., *c* 31.4, chloroform, Found: C, 68.18; H, 6.27. Calcd. for C_8H_9Cl: C, 68.33; H, 6.45%). The residual mass was refluxed with a mixture of 20% aqueous sodium hydroxide (15 cc.) and ethanol (10 cc.) for 4 hr. and distilled with steam. The distillate (about 100 cc.) was extracted with two 50 cc. portions of ether. Concentration of the combined ether solutions afforded an oily material which was distilled in vacuo to give α-phenethyl alcohol (2.2 g., b. p. 80.0~81.0°C/7 mmHg, n_D^{20} 1.5245, α_D^{17} −0.040 ±0.005°, $[\alpha]_D^{17}$ −0.320°, *l* 2 dm., *c* 6.23, chloroform, Found: C, 78.62; H, 8.26. Calcd. for $C_8H_{10}O$: C, 78.65; H, 8.25%).

The second run carried out under similar conditions, 70~80°C, 15.5 hr., with pinonic acid (20.0 g., b. p. 152.0°C/7 mmHg, m. p. 70~80°C, $[\alpha]_D^{20}$ −51.5°, chloroform), triethylamine (5.0 g.) and (±)-α-phenethyl chloride (7.0 g.) afforded α-phenethyl chloride (3.3 g., b. p. 58.0°C/7.5 mmHg, α_D^{15} −0.100±0.025°, $[\alpha]_D^{15}$ −0.21°, *l* 2 dm., *c* 23.8, chloroform) and α-phenethyl alcohol (2.2 g., b. p. 80~82.0°C/9 mmHg, α_D^{18} −0.105±0.025°, $[\alpha]_D^{18}$ −0.58°, *l* 2 dm., *c* 9.1, chloroform, Found: C, 78.58; H, 8.06%).

Starting from pinonic acid (25.0 g., m. p. 65.0~75.0°C, $[\alpha]_D^{18}$ −76.1°, *c* 9.63, chloroform), triethylamine (5.0 g.) and α-phenethyl chloride (6.75 g.), the third run afforded at 70°C for 15 hr. α-phenethyl chloride (4.0 g., b. p. 58.0~59.0°C/9 mmHg, n_D^{20} 1.5230, α_D^{18} −0.040±0.005°, $[\alpha]_D^{18}$ −0.141°, *l* 2 dm., *c* 14.2, chloroform, Found: C, 68.38; H, 6.59%) and α-phenethyl alcohol (0.50 g., b. p. 68.0~69.0°C/3 mmHg, n_D^{20} 1.5210, α_D^{18} 0.020±0.005°, $[\alpha]_D^{18}$ 0.872°, *l* 2 dm., *c* 1.15, Found: C, 78.35; H, 8.44%).

Reaction of (±)-α-Phenethyl Chloride and Triethylammonium (+)-α-Methyl Camphorate in (+)-α-Methyl Hydrogen Camphorate. — α-Methyl hydrogen camphorate was obtained by esterification of camphoric acid according to the previously reported method[9]. To a mixture of α-methyl hydrogen camphorate (52.5 g., m. p. 56.0~57.0°C, $[\alpha]_D^{15}$ 58.0°, chloroform) and triethylamine (10.0 g.), (±)-α-phenethyl chloride (14.0 g.) was added. After being kept at 98~100°C for 7.5 hr., the reaction mixture was taken into ether (100 cc.), and washed successively with water (100 cc.), three 50 cc. portions of 10% aqueous sodium hydroxide, and two 50 cc. portions of water. The ethereal solution was dried with anhydrous sodium sulfate and concentrated. The oily material was fractionally distilled in vacuo, giving a fore-run (1.0 g.), containing styrene and a small amount of α-phenethyl chloride, α-phenethyl chloride (5.6 g., b. p. 53.0 ~ 55.0°C / 8.5 mmHg, n_D^{20} 1.5274, α_D^{13} 0.020±0.005°, $[\alpha]_D^{13}$ 0.57°, *l* 2 dm., *c* 1.71, chloroform, Found: C, 68.14; H, 6.58%) and β-(α-phenethyl) α-methyl camphorate (10.4 g., b. p. 165~168°C/2 mmHg, n_D^{20} 1.5052).

Found: C, 71.41; H, 8.11. Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23%.

β-(α-Phenethyl) α-methyl camphorate was reduced with lithium aluminum hydride. A mixture of lithium aluminum hydride (5.0 g.) and dry ether (250 cc.) was stirred for 1 hr. under a nitrogen atmosphere and treated with β-(α-phenethyl) α-methyl camphorate (10.0 g.) dissolved in ether (50 cc.) over a period of 5 min. After being stirred for 5 hr. and being kept overnight at 15°C, the mixture was treated with water (10 cc.) which was added over a period of half an hour. The precipitated material was filtered and washed with ether (100 cc.), and the combined ether solution was concentrated. The residue was distilled under reduced pressure to give α-phenethyl alcohol (2.6 g., b. p. 70.0~71.0°C/7 mmHg, n_D^{20} 1.5260, α_D^{17}

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[5] Microanalyses by Microanalytical Center, Kyoto University. Melting points are not corrected. For the measurement of optical rotations "Zeiss Winckel, Kreispolarimeter, 0.01°" was used.

[6] E. Downer and J. Kenyon, *J. Chem. Soc.*, **1939**, 1156.

[7] R. L. Burwell, Jr., A. D. Shields and H. Hart. *J. Am. Chem. Soc.*, **76**, 908 (1954).

[8] G. Dupont and G. Brus, *Ann. Chim.*, **19**, 186 (1923).

[9] J. Walker, *J. Chem. Soc.*, **61**, 1088 (1892).

0.400+0.005°, $[\alpha]_D^{17}$ 1.25°, *l* 2 dm., *c* 16.0, chloroform. Found: C, 78.75; H, 8.36%).

The second run carried out at 98°C for 9.5 hr. with α-methyl hydrogen camphorate (23.0 g.), triethylamine (5.0 g.), and (±)-α-phenethyl chloride (7.0 g.), afforded α-phenethyl chloride (1.9 g., b. p. 49.0~51.0°C/6 mmHg, α_D^{15} 0.13±0.02°, $[\alpha]_D^{15}$ 0.62°, *l* 2 dm., *c* 10.5, chloroform) and after alkaline hydrolysis of the ester α-phenethyl alcohol (0.15 g., b. p. 80.0°C/9 mmHg, α_D^{15} 0.04±0.01°, $[\alpha]_D^{15}$ 1.65°, *l* 2 dm., *c* 1.21, chloroform) was obtained.

Reaction of (+)-α-Phenethyl Chloride and Triethylammonium α-Methyl Camphorate in (+)-α-Methyl Hydrogen Camphorate.—(±)-α-Phenethyl alcohol was resolved according to the published method⁶⁾ and the first crop of brucine salt of α-phenethyl hydrogen phthalate gave (−)-α-phenethyl alcohol, $[\alpha]_D^{15}$ −47.5°, *c* 16.0, chloroform, From the first mother liquors (+)-α-phenethyl alcohol ($[\alpha]_D^{13}$ 37.0°, *c* 15.4, chloroform) was obtained. From this (+)-alcohol (+)-α-phenethyl chloride ($[\alpha]_D^{15}$ 30.4°, *c* 7.15, chloroform) was prepared by chlorination with thionyl chloride according to the previously reported method³⁾. The reaction was carried out with (+)-α-methyl hydrogen camphorate (50.0 g.), triethylamine (4.5 g.) and (+)-α-phenenethyl chloride (5.6 g., $[\alpha]_D^{15}$ 30.4°) at 100°C for 8 hr. After treatment similar to the previous experiment with (±)-α-phenethyl chloride, α-phenethyl chloride (2.4 g., b. p. 51.0~52.0°C/6 mmHg, n_D^{20} 1.5268, α_D^{15} 0.450±0.01°, $[\alpha]_D^{15}$ 2.98°, *l* 2 dm., *c* 7.55, chloroform, Found: C, 68.40; H, 6.37%) was recovered.

After reduction with lithium aluminum hydride, β-(α-phenethyl) α-methyl camphorate (4.6 g., b. p. 173°C/2 mmHg, n_D^{20} 1.5034, Found: C, 71.88; H, 8.31%.) afforded α-phenethyl alcohol (0.9 g., b. p. 63.0~67.0°C/3 mmHg, n_D^{20} 1.5169, α_D^{15} −0.580±0.005°, $[\alpha]_D^{15}$ −5.93°, *l* 2 dm., *c* 4.90, chloroform, Found: C, 78.48; H, 8.43%).

Reaction of (±)-α-Phenethyl Chloride and Triethylammonium (+)-α-Methyl Camphorate in Dioxane. — Triethylammonium (+)-α-methyl camphorate was prepared by mixing the equivalent amounts of triethylamine and (+)-α-methyl hydrogen camphorate in dioxane. A mixture of triethylamine (5.0 g.), (+)-α-methyl hydrogen camphorate (10.6 g.), dry dioxane (24.5 g.) and (±)-α-phenethyl chloride (7.0 g.) was kept at 100°C for 9 hr. The reaction percentage of the chloride was estimated to be about 5% from the aliquot titration of unchanged triethylammonium α-methyl camphorate with acetic acid solution of perchloric acid. After addition of ether (100 cc.) the mixture was washed with four 100 cc. portions of water, dried with anhydrous sodium sulfate, and concentrated. The residue was fractionally distilled under reduced pressure to give α-phenethyl chloride (5.8 g., b. p. 89.0°C/38 mmHg, n_D^{20} 1.5264, α_D^{20} 0.055±0.005°, $[\alpha]_D^{20}$ 0.086°, *l* 2 dm., *c* 31.8, chloroform, Found: C, 68.58; H, 6.52%).

Reaction of (±)-α-Phenethyl Chloride and Triethylammonium (−)-Pinonate in Dioxane. — A mixture of triethylamine (5.0 g.), (−)-pinonic acid (9.2 g., $[\alpha]_D^{20}$ −75.0°, chloroform), dry dioxane (25 cc.) and (±)-α-phenethyl chloride (7.0 g.) was kept at 70°C for 16 hr. The reaction percentage of the chloride was estimated to be about 5% from the titration of unchanged triethylammonium pinonate. After addition of ether (100 cc.) the mixture was treated in a manner similar to the reaction with triethyl ammonium α-methyl camphorate. The recovered α-phenethyl chloride gave the following constants; b. p. 89.0°C/37 mmHg, n_D^{20} 1.5272, α_D^{20} 0.09±0.005°, $[\alpha]_D^{20}$ 0.16°, *l* 2 dm., *c* 28.0, chloroform, Found: C, 68.58; H, 6.52%.

Reaction of (±)-α-Phenethyl Chloride and Anilinium (+)-α-Methyl Camphorate in Acetonitrile. — Anilinium α-methyl camphorate solution (0.750 N) was prepared from equivalent amounts of aniline and (+)-α-methyl hydrogen camphorate ($[\alpha]_D^{15}$ 58.0°) in acetonitrile. (±)-α-Phenethyl chloride (4.92 g.) was dissolved in the anilinium salt solution and diluted to a volume of 50 cc. with the solution. The mixture was kept in a sealed tube for 291 min. (half life time of the reaction) at 85.0°C. Ether (100 cc.) was added to the cooled reaction mixture, and the mixture washed with water (50 cc.). After evaporation of ether the residual oily mass gave α-phenethyl chloride (2.3 g., b. p. 55.0~56.0°C/6 mmHg, n_D^{20} 1.5251, α_D^{21} 0.00±0.02°, *l* 1 dm., neat). In the distillation residue no ester was found.

Reaction (±)-α-Phenethyl Chloride and Anilinium (−)-Pinonate in Acetonitrile.—In a manner similar to the reaction with anilinium (+)-α-methyl camphorate (±)-α-phenethyl chloride (5.81 g.) was kept with 0.750 N anilinium (−)-pinonate (the acid $[\alpha]_D^{20}$ −75.0) solution for 261 min. (half life time of the reaction) at 85.0°C. The recovered chloride (2.22 g.) gave the following constants; b. p. 53.0°C/2 mmHg, n_D^{20} 1.5239, α_D^{21} 0.00±0.03°, *l* 1 dm., neat, Found: C, 68.63; H, 6.60%. The higher boiling fraction (5.24 g., 137~140°C/0.8 mmHg) was hydrolysed with 20% aqueous sodium hydroxide (15 cc.) and ethanol (10 cc.) for 4 hr., and distilled with steam. The recovered α-phenethyl alcohol (0.05 g.) gave slight optical activity (α_D^{20} 0.07±0.03°, $[\alpha]_D^{20}$ 1.8°, *l* 1 dm. *c* about 4, chloroform).

Kinetic Measurement.—The reactions in (+)-α-methyl hydrogen camphorate ($[\alpha]_D^{15}$ 58°) and (−)-pinonic acid ($[\alpha]_D^{20}$ −51.5°) were carried out in a 15 cc. measuring flask placed in a thermostat. To a weighed amount of α-phenethyl chloride in the flask the optically active carboxylic acid solution of triethylamine was added to the volume of 15 cc. at the reaction temperature. After various periods of time, aliquot portions (1.000 cc.) were pipetted into 5 cc. of cold acetic acid and the solutions were titrated with 0.0672 N perchloric acid in acetic acid with crystal violet indicator. The rates in acetonitlile were measured by a sealed-ampoule technique. Each sample (1.000 cc.) was titrated with 0.245 N perchloric acid in acetic acid. The rate constants were calculated from the first order rate equation by a graphical method.

Summary

1) In S_N2 displacement reactions of (±)-α-phenethyl chloride with triethylammonium (+)-α-methyl camphorate and with triethylammonium (−)-pinonate in dioxane, α-phenethyl chloride of 0.08% of optical purity (L-

configuration) and of 0.15% of optical purity (L-configuration) were recovered at the stage of about 5% conversion, respectively.

2) In S_N1-type solvolysis of (±)-α-phenethyl chloride with anilinium (+)-α-methyl camphorate and (−)-pinonate in acetonitrile, the recovered α-phenethyl chlorides showed no perceptible optical activity on the half way for each of the reactions. From this, the possibility of the induced resolution caused at the first stage by kinetic resolution at the second stage of the S_N1-type solvolysis was eliminated.

3) In S_N1-type solvolysis of (±)-α-phenethyl chloride in (+)-α-methyl hydrogen camphorate and in (−)-pinonate, about half of the chloride was converted to the ester at the similar reaction conditions (temperature and time) to the S_N2 displacement reactions carried out in dioxane. The recovered chloride in the reaction in hydrogen camphorate showed optical purity of 0.54∼0.58% (L-configuration). In pinonic acids with various optical activities the recovered chlorides possessed optical purity of 0.13∼0.27% (D-configuration).

4) In comparing the configurations and optical purities in S_N1- and S_N2-conditions, it is concluded that optically active solvent molecules, like (+)-α-methyl hydrogen camphorate and (−)-pinonic acid, can cause kinetic resolution in the first ionization stage of the S_N1-type solvolysis and therefore they obviously play a rôle as a kind of reactant molecule which controls the steric course of the solvation reaction in the first stage of this solvolysis.

5) In the S_N1-type solvolysis of optically active α-phenethyl chloride in presence of triethylamine in (+)-α-methyl hydrogen camphorate, optically active β-(α-phenethyl)-α-methyl camphorate gave optically active α-phenethyl alcohol of 37% inversion, 63% racemization of configuration. From this it was concluded that S_N2-like spatial orientation predominates at the second stage of this solvolysis.

6) For each of the resolution results of α-phenethyl chloride under S_N1- and S_N2-conditions, the relationship between the configuration of the resolved alcohol and the resolution-controlling stage was predicted on the basis of the observed inversion at the second stage of the solvolysis. The configurations observed for the α-phenethyl alcohols were found to be consistent with the predictions.

The authors wish to thank Mr. Ryôichi Kanô for his assistance in preparation of (−)-pinonic acid.

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