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Retentive Solvolysis. 16.[1] Reinvestigation of the Retentive Phenolysis of 1-Phenylethyl Chloride. The Mechanism and the Structure of Ion Pair Intermediate

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The effect of added aniline on the polarimetric (k_p) and titrimetric rate constants (k_t) has been reexamined for the phenolysis of 1-phenylethyl chloride (RCl) in phenol–benzene (1:1 w/w). The k_p–k_t plot against the aniline concentrations exhibited the pattern C, instead of A which was the previous results in our laboratory. It has been revealed that the previous rate constants at the lower aniline concentrations, including the case of absence of aniline, were underestimated due to overlooking the reverse reaction caused by the liberated hydrogen chloride. The pattern C indicates that the first ion pair intermediate, not the second one, is nucleophilically attacked by solvent phenol molecule. The major products were the partially retained *o*-RC_6H_4OH, the partially inverted *p*-RC_6H_4OH, together with the partially retained ROPh. The same k_p–k_t pattern C has been observed for the competitive solvolysis of RCl in phenol–methanol (85:15 w/w), which produced the partially retained ROMe and ROPh, the partially inverted *o*- and *p*-RC_6H_4OH, and styrene. Such stereochemical outcomes for both solvolyses demonstrate that the major first ion pair intermediate should be a rear-side-shielded ion pair intermediate.

On the basis of the pattern of salt effect of added aniline on the polarimetric and titrimetric rate constants (k_p and k_t, respectively),[2] the retentive phenolysis of 1-phenylethyl chloride[2–5] (RCl), the first example of the retentive phenolysis, has been hitherto recognized to be one of a few solvolysis systems,[1,6–9,††] which exhibited the pattern A[1,6,9] in the k_p–k_t plot against the concentration of added salt.

However, there have been left two problems for the phenolysis of 1-phenylethyl chloride. First, the pattern of k_p–k_t diagram, previously reported for the phenolysis of RCl,[2] exhibited an "unusually" steep slope of the special salt effect[7,10,11] on k_t. Although such a steep slope has been often reported for S_N1 solvolyses in some solvents[11] other than phenol, it has not been known for the phenolyses examined so far.[1,6,8,9,12,13]

The steep increase in the k_t is characterized by the use of the parameters proposed by Winstein and his co-workers.[11a] The parameters are: $k^0_{t,ext}/k^0_t$=5.0 and $[salt]_{1/2}$=0.0036 M (1 M=1 mol dm^{-3}) for RCl, whereas 1.09—2.69 and 0.01—0.03 M, respectively, for the other systems.[1,6,8,9,12,13] The $k^0_{t,ext}$ designates the k_t value extrapolated at zero salt concentration from the linear part at higher salt concentrations, k^0_t is the actual k_t value at zero salt concentration, and $[salt]_{1/2}$ is the salt concentration corresponding to $\frac{1}{2}\cdot(k^0_{t,ext}+k^0_t)$.

Secondly, it has been known that the phenolysis accompanies the reverse reaction in the absence of an added base,[14,15] which results in retardation of the apparent rate (k_t)[14] and rearrangement of ROPh to *o*- and *p*- RC_6H_4OH by the liberated strong acid such as hydrogen chloride.[15] Such an effect of reverse reaction was sometimes overlooked.[16]

We have therefore reinvestigated the k_p–k_t pattern for the phenolysis of 1-phenylethyl chloride with suspicions on the pattern A,[1,6,9] under the conditions where the effect of reverse reaction is completely eliminated.

Although we briefly mentioned the results in the footnotes of the preceding papers,[1,6,13] we now report in details that the k_p–k_t diagram for the phenolysis of RCl in the presence of $PhNH_2$, Et_3N, and NaOPh does exhibit the pattern C,[1,6] which specifies Int-1, not Int-2, for the ion pair stage of product formation. Furthermore, adding the stereochemical outcomes for the reinvestigated methanol-perturbed phenolysis of RCl,[17] we also report that the structure of the major Int-1 should be a rear-side-shielded ion pair intermediate.

Results and Discussion

Reexamination of Phenolysis Rates. Optically active 1-phenylethyl chloride (RCl) has been subjected to the phenolysis under the identical conditions with those employed previously,[2] i.e., in phenol–benzene (1:1 w/w) at variable concentrations (0—0.391 M) of added aniline at 25 °C, except the concentration of RCl, 0.10 M instead of previous 0.55 M[2] for the k_p measurements. The phenolysis rate has been reexamined both titrimetrically and polarimetrically. Titrimetric rate measurements have been carried out by the use of 0.05 M aqueous HCl (or NaOH) solution as a titrating reagent, cold acetone (ca. −15 °C) as a stop solution, and lacmoid as an indicator, instead of previous 0.1 M $HClO_4$ (or NaOAc) acetic acid

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†† Although the acetolysis of 2-(*p*-methoxyphenyl)-propyl tosylate was previously reported to proceed via Int-2,[10] reexamination of the pattern of salt effect by us[6] has clarified that the product source is Int-1, not Int-2.

Table 1. The Titrimetric and Polarimetric Phenolysis Rates (k_t and k_p) of 1-Phenylethyl Chloride (RCl) in the Presence of a Base in Phenol–Benzene (1:1 w/w) at 25 °C

Added base/M		RCl / M	k_t / s^{-1} [a]	k_p / s^{-1} [b]
None	0.000	0.050	3.20×10^{-4} [c]	
	0.000	0.100		3.82×10^{-4}
	0.000 [d]	0.050	5.95×10^{-5}	
	0.000 [d]	0.100	6.85×10^{-5}	
	0.000 [d]	0.550		3.48×10^{-4}
Hind.Py. [e]	0.0539	0.0501	3.33×10^{-4}	
$PhNH_2$	0.0051	0.050	3.23×10^{-4}	
	0.0075	0.050	3.17×10^{-4}	
	0.106	0.101	3.25×10^{-4}	
	0.169	0.104	3.22×10^{-4}	
	0.198	0.102	3.19×10^{-4}	3.79×10^{-4}
	0.391	0.103		3.75×10^{-4}
	0.0049 [d]	0.0500	2.30×10^{-4}	
	0.0095 [d]	0.0500	2.82×10^{-4}	
	0.0200 [d]	0.0500	3.02×10^{-4}	
	0.0402 [d]	0.100	3.03×10^{-4}	
	0.0500 [d]	0.0500	3.03×10^{-4}	
	0.10 [d]	0.100	3.00×10^{-4} [c]	
	0.265 [d]	0.100	2.83×10^{-4}	
	0.470 [d]	0.550		3.20×10^{-4}
	0.513 [d]	0.50		3.20×10^{-4} [c]
	0.523 [d]	0.500		3.20×10^{-4}
Et_3N	0.101	0.099	3.17×10^{-4}	3.80×10^{-4}
	0.201	0.103	3.00×10^{-4}	3.73×10^{-4}
	0.302	0.105	3.02×10^{-4}	3.71×10^{-4}
NaOPh	0.051	0.050	3.95×10^{-4}	4.87×10^{-4}
	0.102	0.100	5.25×10^{-4}	5.97×10^{-4}
	0.153	0.103	6.17×10^{-4}	7.04×10^{-4}
$LiClO_4$ [f]	0.010	0.0497	3.33×10^{-4}	
	0.020	0.0502	3.50×10^{-4}	
	0.030	0.0499	3.57×10^{-4}	

a) Accurate to within ±2%. b) Accurate to within ±3%. c) An average value for duplicate measurements. d) Cited from Ref. 2. e) 2,6-Di-*t*-butyl-4-methylpyridine (see the text). f) In the presence of 0.055 M 2,6-di-*t*-butyl-4-methylpyridine.

solution, acetic acid (ca. 10 °C), and Crystal Violet, respectively.[2] All the rate data are summarized along with those in the presence of Et_3N, NaOPh, lithium perchlorate, and a hindered pyridine in Table 1 and they are plotted against the concentration of aniline in Fig. 1 together with the previously-reported data.[2]

In the absence of aniline, the k_t^0 value had a tendency to decrease as the reaction proceeded at 1—25% conversion. After ca. 25% conversion, the reaction retarded much more. This phenomenon can be ascribed to the occurrence of competing reverse reaction, i.e., the cleavage reaction of the aralkyl phenyl ether by the liberated hydrogen chloride to give the starting RCl.[14,15] The initial k_t^0 value at zero % reaction, therefore, has been extrapolated from k_t^0 values at 1—13% reaction. The new k_t^0 value coincides within experimental errors with a k_t value (Table 1) in the presence of a hindered amine, 2,6-di-*t*-butyl-4-methylpyridine, which plays only as a neutralizer for the liberated acid, not as a phenoxide donor. The new k_t^0 value is 5.0 (±0.4) times larger than the previously-reported value,[2] which had been measured at 12—27% reaction. An approximately identical value with the previous one[2] could be obtained at such 10—25% reaction. The k_p^0 value, k_p value in the absence of the base, exhibited a little acceleration with an increase in the reaction %, most probably due to the cleavage reaction of the aralkyl phenyl ether.[14,15] The initial k_p^0 value was determined, therefore, by the extrapolation method similar to that described above. The new k_p values are 1.1 times larger than the previous ones over the whole range of $PhNH_2$ concentration (Fig. 1). The discrepancy can be mainly ascribed to the difference of the phenol concentration

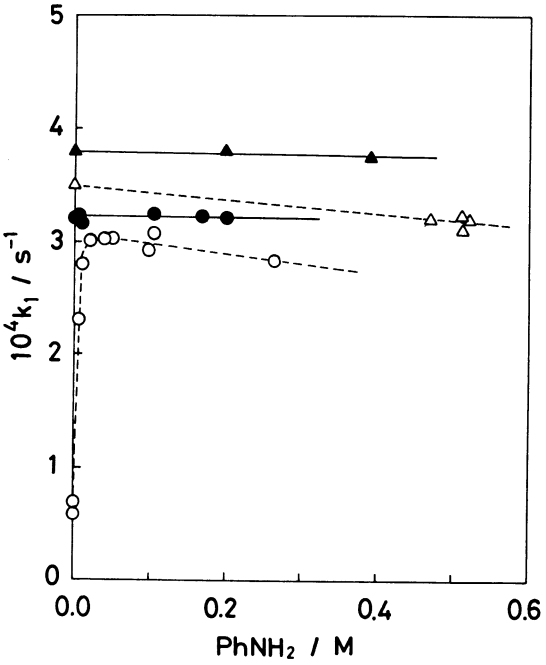


Fig. 1. Effect of added $PhNH_2$ concentration on the titrimetric and polarimetric rate constants (k_t and k_p) for the phenolysis of 1-phenylethyl chloride in phenol–benzene (1:1 w/w) at 25°C.
● k_t, ▲ k_p; this work. ○ k_t, △ k_p; cited from Ref. 2.

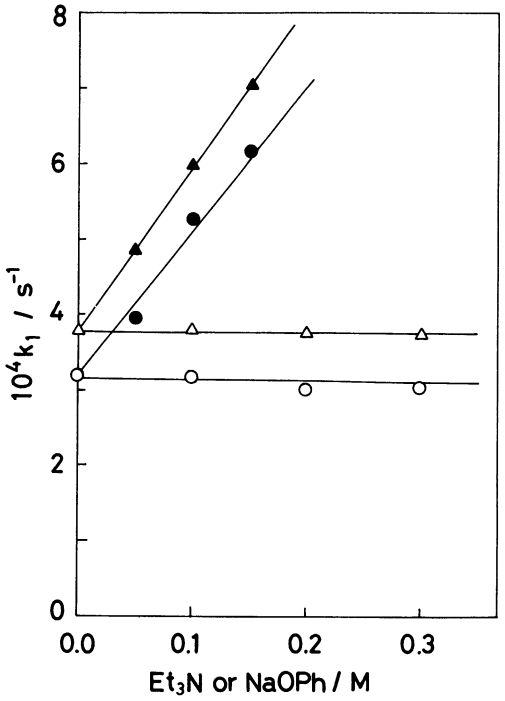


Fig. 2. Effect of added Et_3N and NaOPh concentration on the titrimetric and polarimetric rate constants (k_t and k_p) for the phenolysis of 1-phenylethyl chloride in phenol–benzene (1:1 w/w) at 25°C.
○ k_t, △ k_p; in the presence of Et_3N. ● k_t, ▲ k_p; in the presence of NaOPh.

in the respective solvents owing to that of the substrate concentrations between in this work (0.10 M) and in the previous work (0.55 M).[2]

The k_t value at 0.0050 M $PhNH_2$ (0.050 M RCl) was obtained from the data at 1—8% reactions. The new value is 1.4 times larger than the previously-reported value which had been estimated at 5.8% reaction.[2] For each run in the presence of 0.106—0.198 M $PhNH_2$, a smooth first-order linear relationship (correlation coefficient≥0.9997) has been obtained until at least 80% reaction and the new values are somewhat larger than the previous ones.[2] In view of the conditions and the accuracy of rate measurements, the new data are much more reliable than the previously-reported data.[2]

Reexamination of the k_p–k_t Pattern for Phenolysis. The new pattern of the salt effect of $PhNH_2$ on the k_p–k_t diagram exhibits no special salt effect on k_t, differently from the previous one[2] (Fig. 1). The k_p/k_t ratio is constant, 1.19, over the whole range of the concentration of $PhNH_2$. The analogous k_p–k_t patterns have been also observed in the presence of Et_3N and NaOPh (Fig. 2) instead of $PhNH_2$. Lithium perchlorate also exhibits no special salt effect on k_t[†††] (Table 1). Such patterns were classified as pattern C in one of our previous reports.[1,6]

Thus, the k_p–k_t patterns indicate that the first ion pair intermediate (Int-1), not the second one (Int-2), partially reacts with the solvent phenol molecule, partially returns to the substrate, and partially racemizes by itself,[1,6] whereas the previously-reported k_p–k_t profile[2] suggested that all the products derived from the reaction of Int-2 with the phenoxide at higher base concentrations.[1,6]

The same k_p–k_t pattern C[1,6] has been reported for the phenolyses of 1-phenylethyl,[8] 1-phenylpropyl,[9] 1-methyl-1-phenylpropyl,[9] 2-methyl-1-phenylpropyl,[9] and *p*-chlorobenzhydryl *p*-nitrobenzoates[9] in the presence of NaOPh or Et_3N, and 2,2-dimethyl-1-phenylpropyl *p*-nitrobenzoate in the presence of $(n\text{-}Bu)_4NClO_4$,[6] for the hydrolysis of RCl in 60% aqueous dioxane in the presence of $LiClO_4$,[18] and for the acetolysis of *exo*-2-norbornyl brosylate in the presence of KOAc.[19,§]

Product Distribution for the Phenolysis. Product distribution for the phenolysis of RCl was analyzed by the use of GLPC in the presence of $PhNH_2$ under the conditions identical with those employed in the

††† 2,6-Di-*t*-butyl-4-methylpyridine was added in order to neutralize the liberated acid which might cause the reverse reaction.

§ Although the rates for the acetolysis of *exo*-2-norbornyl brosylate were measured only at two concentrations of added KOAc,[19] the k_p–k_t pattern can be estimated to be the same as the corrected one for this system.[6]

Table 2. The Product Distribution for the Phenolysis of 1-Phenylethyl Chloride (RCl) in the Presence of Aniline in Phenol–Benzene (1:1 w/w) at 25 °C[a]

$PhNH_2$	Product distribution/%[b]						
	ROPh	o-RC_6H_4OH	p-RC_6H_4OH	RNHPh	o-$RC_6H_4NH_2$	p-$RC_6H_4NH_2$	Styrene
0.110	89.5	5.4	1.6	2.0	0.1	0.1	1.4
	(92.9)	(5.5)	(1.6)				
0.310	85.0	5.1	1.8	6.4	0.5	0.3	0.9
	(92.5)	(5.6)	(1.9)				
0.408[c]	69.0[d]	16.3[d]	14.7[d]	—	—	—	—

a) [RCl]=0.10 M. b) Determined by GLPC; (ROPh+o-RC_6H_4OH+p-RC_6H_4OH+RNHPh+o-$RC_6H_4NH_2$+p-$RC_6H_4NH_2$)%=100%: in parentheses; (ROPh+o-RC_6H_4OH+p-RC_6H_4OH)%=100%. c) In the presence of Et_3N instead of $PhNH_2$ at 40 °C; cited from Ref. 3. d) Isolated yield %.

kinetic measurements. Together with the usual phenolysis products, i.e., ROPh, o- and p-RC_6H_4OH, and styrene, the phenolysis produces minor amounts of RNHPh, o- and p-$RC_6H_4NH_2$ which were not previously detected[2] (Table 2). In the absence of aniline, no ROPh was obtained because of the rearrangement of ROPh to o- and p-RC_6H_4OH by the liberated acid.[15]

With an increase in the concentration of added $PhNH_2$, the yield% of the aniline derivatives increases, albeit still minor amounts. The yield% ratio of the phenol derivatives to the aniline ones in products can be regarded as approximately comparable with the composition of phenol and aniline in the solvolysis media. Furthermore, the ratio of ROPh to RC_6H_4OH (o- and p-) is almost invariable.[§§]

Such results of product analyses suggest that the added aniline in this system does not play a role of phenoxide donor, but roles of a scavenger of the liberated acid and of a competing nucleophile with an almost identical nucleophilicity with that of phenol. The effect of added $PhNH_2$ on the product distribution is compatible with the k_p–k_t profile.

Stereochemical Courses of the Phenolysis. All the substitution products for the phenolysis of optically active RCl in the presence of $PhNH_2$ (0.110 and 0.290 M) were isolated by MPLC and preparative TLC (silica gel), although ROPh alone had been isolated in the previous work.[2] The net stereochemical course was deduced for the formation of each substitution product from its optical rotation. The results are summarized along with the previously-reported ones[2] in Table 4. The absolute configurations and maximum rotations for the related 1-phenylethyl derivatives are shown in Table 3.

The configuration is partially retained for the ROPh formation and partially inverted for the p-RC_6H_4OH formation with predominant racemization, respectively, and highly inverted for the RNHPh[20] and o-$RC_6H_4NH_2$[21] formations with less racemization (Scheme 1).

Table 3. Maximum Rotations of 1-Phenylethyl Derivatives with (*R*)-Configuration Relevant to the Phenolysis

RX	$\alpha_{D,max}$ or $[\alpha]_{D,max}$/°
RCl	+125[a,b]
ROPh	−46.6[a,c]
o-RC_6H_4OH	+27.8[5][c,d]
p-RC_6H_4OH	−10.2[6][c,d]
RNHPh	−19.6,[e] −26.1,[f] −4.26,[a,g] −34.5[g,h]
o-$RC_6H_4NH_2$	−41.3[i]
ROMe	+135[a,j]
ROH	+45.7[a,k]

a) a) Neat, 1 dm. b) H. M. R. Hoffmann and E. D. Hughes, *J. Chem. Soc.*, **1964**, 1244. c) Ref. 3. d) In benzene. e) In methanol; the value extrapolated from data at 436, 546, and 578 nm by Wittig and Thiele (Ref. 20a) on the basis of the new value for maximum rotation of the starting RNH_2, 40.5° (A. P. Terent'ev, G. V. Pnova, G. N. Koval' and O. V. Toptygina, *Zh. Obshch. Khim.*, **40**, 1409 (1970)), from which RNHPh was synthesized. f) In ethanol; Ref. 20b. g) Ref. 20a. h) In cyclohexane. i) In chloroform; Ref. 21. j) Reported value, 120° (K. Mislow, *J. Am. Chem. Soc.*, **73**, 4043 (1951)), was recalculated on the basis of the above new value of maximum rotation for ROH, from which ROMe was synthesized. k) Ref. 8.

$$\begin{aligned}(R)\text{-}(+)\text{-RCl} + \text{PhOH} &\xrightarrow{PhNH_2} (R)\text{-}(-)\text{-ROPh} \\ &+ (R)\text{-}(+)\text{-}o\text{-}RC_6H_4OH \\ &+ (S)\text{-}(+)\text{-}p\text{-}RC_6H_4OH + (S)\text{-}(+)\text{-RNHPh} \\ &+ (S)\text{-}(+)\text{-}o\text{-}RC_6H_4NH_2 + (?)\text{-}p\text{-}RC_6H_4NH_2 \\ &+ PhCH{=}CH_2\end{aligned}$$

Scheme 1.

The retained ROPh formation (retentive phenolysis) has been confirmed in the presence of $PhNH_2$ in the phenolic solvent. For the retention % of ROPh formation, the previous[2] and new values coincide with each other within experimental errors. The retention % is somewhat smaller than that in the presence of Et_3N.[3] For 1-phenylethyl systems, some

[§§] Although the isolated yield % of each product changed for the phenolysis of RCl in pure phenol at 50 °C with an increase in the NaOPh concentration,[15] direct GLPC analysis has shown that the product distribution is invariable (ROPh: o-RC_6H_4OH:p-RC_6H_4OH (%)=73:14:13) within experimental errors at variable NaOPh concentrations (0.05—0.3 M).

Table 4. The Stereochemical Courses for Products of the Phenolysis of 1-Phenylethyl Chloride (RCl) in the Presence of Aniline in Phenol–Benzene (1:1 w/w)[a]

Added base/M		Temp	RCl	Net stereochemical course, α%, {$[\alpha]_D$/°}[c]				
		°C	M {α_D/°}[b]	ROPh	*o*-RC_6H_4OH	*p*-RC_6H_4OH	RNHPh	*o*-$RC_6H_4NH_2$
$PhNH_2$	0.110	25	0.100	17.2 Ret.	7.4 Ret.	11.8 Inv.	64.0 Inv.	55 Inv.
			{+24.2}	(±0.9)	(±0.7)	(±2.2)	(±3.6)	(±28)
				{−1.55}[b]	{+0.398}	{+0.235}	{+2.43}[d]	{+4.4}[e]
	0.291	25	0.0970	17.3 Ret.	8.8 Ret.	12.2 Inv.	60.9 Inv.	52 Inv.
			{+24.0}	(±1.8)	(±1.0)	(±2.4)	(±4.2)	(±17)
				{−1.55}[b]	{+0.468}	{+0.241}	{+2.29}[d]	{+4.1}[e]
	0.550[f]	25	0.050	17.6 Ret.	—	—	—	—
Et_3N[g]	0.408	40	0.072	23.7 Ret.	38.1 Inv.	41.2 Inv.	—	—

a) The maximum rotations for relevant compounds in this table are shown in Table 3. b) Neat, 1 dm. c) In benzene unless otherwise noted. d) In methanol. e) In $CHCl_3$. f) Cited from Ref. 2. g) Cited from Ref. 3.

retentive solvolyses have been reported in 90% aqueous acetone,[22] 2,2,2-trifluoroethanol,[23] 97% aqueous 2,2,2-trifluoroethanol,[23] trifluoroacetic acid[24] other than in phenol solvents, whereas many inversive results have been observed.[18,23,25]

The partial retention for *o*-RC_6H_4OH formation in the presence of $PhNH_2$ is in marked contrast to the partial inversion for that in the presence of Et_3N. The direct and retentive ortho-alkylation have not been known in the phenolysis[16] except those for 1-phenylethyldiazonium salt[4] and for 2,2-dimethyl-1-(*p*-methoxyphenyl)propyl *p*-nitrobenzoate.[13] The inversion % for *p*-RC_6H_4OH formation is much lower in the presence of $PhNH_2$ than that in the presence of Et_3N. The inversion % for RNHPh and *o*-$RC_6H_4NH_2$ formation is higher than that for *p*-RC_6H_4OH and is somewhat smaller than that (87.9±9.1%) for the anilinolysis of RCl in aniline, although the reaction conditions are different from each other.§§§

The stereochemical courses for all substitution products are approximately constant within experimental errors with an increase in the concentration of added aniline (Table 4), which is consistent with the salt effects on k_p–k_t diagram and on the product distribution.

The extent of racemization is variable for each product, from 36.0% (for RNHPh) to 92.6% (for *o*-RC_6H_4OH), which indicates that the racemization can not be attributed to a simple reason.

Methanol-Perturbed Phenolysis. The competitive solvolysis of RCl has been carried out at 25 °C in phenol–methanol (85:15 w/w) solvent, which was one of binary mixture solvents adopted in the previous work.[17] The solvolysis, i.e., methanol-perturbed phenolysis, has been followed both titrimetrically and polarimetrically in the presence of Et_3N (0—0.30 M) and NaOPh (0—0.25 M), although the solvolysis was not kinetically examined before.[17]

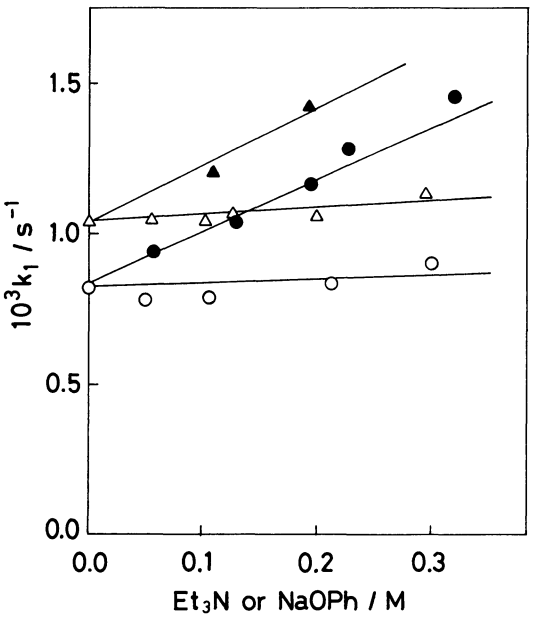


Fig. 3. Effect of added base concentration on the titrimetric and polarimetric rate constants (k_t and k_p) for the competitive solvolysis of 1-phenylethyl chloride in phenol–methanol (85:15 w/w) at 25 °C. ○ k_t, △ p_p; in the presence of Et_3N. ● k_t, ▲ k_p; in the presence of NaOPh.

The pattern of k_p–k_t diagram with k_p/k_t=1.24 (Fig. 3), analogous to that for the phenolysis in the phenol–benzene solvent (Figs. 1 and 2), indicates that all the products are derived from the reaction of Int-1 with solvent molecules, phenol and methanol, despite of the presence of the phenoxide.

The competitive solvolysis afforded ROMe together with the phenolysis products, ROPh, *o*- and *p*-R-C_6H_4OH, and styrene. The product distribution (Fig. 4) is similar to that at 50 ° C which was previously reported[17] and is invariable over the whole range of added base concentrations (0.05—0.3 M), which is consistent with the k_p–k_t profile.

§§§ Although the retentive nucleophilic substitution by aniline was recently mentioned for 1-phenylethyl benzenesulfonate in methanol,[26] the actual detailed data of stereochemical courses have not been reported.

The constancy of product distribution in the course of reaction (26.9—100%) has been confirmed at 0.110 M Et_3N concentration, showing that all the products were formed via a same reaction pathway.

Although RCl usually undergoes net inversion when solvolyzed in methanol-benzene[5] like in other common solvents,[18,23,25] the methanol-perturbation product, ROMe, and ROPh have the partially retained configurations, whereas *o*- and *p*-RC_6H_4OH's have the partially inverted ones (Table 5). These stereochemical results are approximately same as the previous results at 50 °C.[17] The stereochemical outcomes for the product formation in the presence of Et_3N (0.110 and 0.291 M) and NaOPh (0.13 M) are identical with each other within experimental errors.

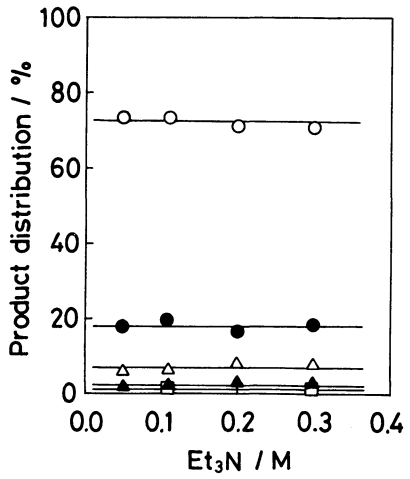


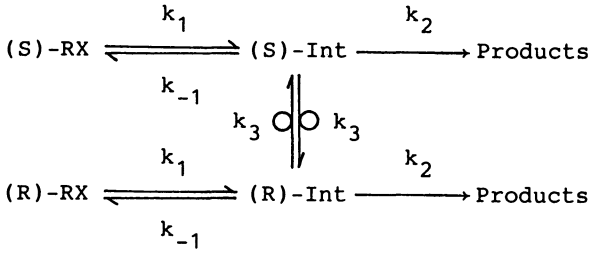
Fig. 4. Effect of added Et_3N concentration on the product distribution for the competitive solvolysis of 1-phenylethyl chloride in phenol-methanol (85:15 w/w) at 25 °C.
○ ROPh, ● ROMe, △ *o*-RC_6H_4OH, ▲ *p*-RC_6H_4OH, □ $C_6H_5CH{=}CH_2$.

That is consistent with the salt effect on the k_p–k_t diagram and on the product distribution.

For the formation of phenolysis products, ROPh, *o*- and *p*-RC_6H_4OH, the extents of racemization can be regarded as approximately identical with each other, suggesting that the phenolysis products might be derived from a single ion pair intermediate (Int-1).

Mechanism. The k_p–k_t profiles for the phenolysis and the methanol-perturbed phenolysis indicate that (i) all the products are derived from the first ion pair intermediate (Int-1), not from the second one (Int-2), (ii) the Int-1 is so reactive that it reacts with the solvent phenol or methanol molecule before it does with the added phenoxide, and (iii) the Int-1 partially returns to the substrate and partially racemizes by itself.[1,6] No contribution of phenoxide ion as a nucleophile has been confirmed by the constancy of product distribution for the phenol derivatives and that of the stereochemical course for each substitution product against an increase in added base concentration (vide supra).

These kinetic features can be expressed by the following reaction scheme, which contains a single ion pair intermediate.



Scheme 2.

According to Scheme 1, the total rate expressions for k_p and k_t can be derived as following Eqs. 1 and 2.[1]

Table 5. The Stereochemical Courses for Products of the Competitive Solvolysis of 1-Phenylethyl Chloride (RCl) in Phenol-Methanol (85:15 w/w) in the Presence of Et_3N and NaOPh at 25 °C[a]

Added base/M		Temp	RCl	Net stereochemical course, α%, {$[\alpha]_D$/°}[c]			
		°C	M {α_D/°}[b]	ROPh	*o*-RC_6H_4OH	*p*-RC_6H_4OH	ROMe
Et_3N	0.109	25	0.102 {+19.4}	21.4 Ret. (±2.3) {−1.55}[b]	16.2 Inv. (±2.9) {−0.700}	18.3 Inv. (±8.4) {+0.291}	4.5 Ret. (±0.7) {+0.95}[b]
	0.201	25	0.102 {+19.4}	16.6 Ret. (±2.9) {−1.20}[b]	16.9 Inv. (±1.6) {−0.729}	15.1 Inv. (±10.3) {+0.241}	4.5 Ret. (±0.5) {+0.950}[b]
	0.11[d]	50	0.11	20.9 Ret.	9.4 Inv.	23 Inv.	2.5 Ret.
NaOPh	0.135	25	0.104 {+19.4}	13.9 Ret. (±2.4) {−1.21}[b]	17.1 Inv. (±2.4) {−0.878}	17.5 Inv. (±10.3) {+0.331}	5.5 Ret. (±1.7) {+1.37}[b]

a) The maximum rotations for relevant compounds in this table are shown in Table 3. b) Neat, 1 dm. c) In benzene unless otherwise noted. d) Cited from Ref. 14.

$$k_p = \frac{k_1}{1 + \{k_{-1}/(k_2 + 2k_3)\}} \quad (1)$$

$$k_t = \frac{k_1}{1 + (k_{-1}/k_2)} \quad (2)$$

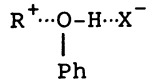
where $k_2 = k_2' + k_2''[\mathrm{PhOH}] + k_2'''[\mathrm{MeOH}]$.

Structure of the Ion Pair Intermediate. For the retentive ROPh formation in the solvolysis systems, solvent-separated ion pair model (a),[7,11,27] four-center ion pair model (b),[3,4,28] and rear-side-shielded ion pair model (c)[5,13,27i] could provide reasonable explanations as a key intermediate. Althogh they were all proposed for Int-2, not for Int-1, the models (b) and (c) are also applicable to Int-1. However, the model (a) might be inapplicable to Int-1, because it should be generated only via a contact ion pair (d)[7,11,27] as Int-1 (Scheme 3).

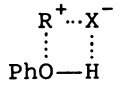
The stereochemical courses for all the other products in the phenolysis and in the methanol-perturbed phenolysis could be explained by the use of the model (b) and its analogues, i.e., six-center ion pair models (e),[4,17] or the model (c) and its analogues, i.e., ion pairs shielded by aniline molecule from the rear-side.

Models for ion pair intermediate structure:

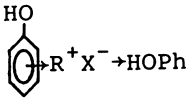
(a) solvent-separated ion pair model[7,11,27]



(b) four-center ion pair model[3,4,28]



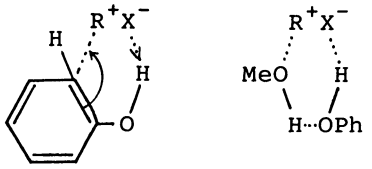
(c) rear-side-shielded ion pair model[5,13,27i]



and its analogues

(d) contact ion pair model[7,11,27] $R^+X^- \rightarrow HOPh$

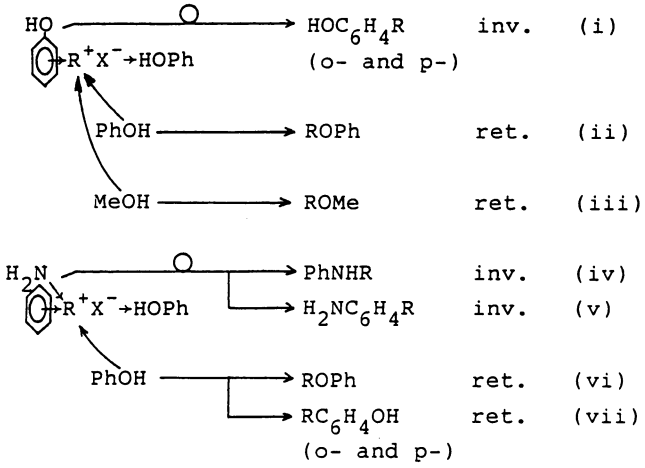
(e) six-center ion pair models[4,17]



Scheme 3.

In view of the rear-side attack of phenol molecule toward R^+ of Int-1 which is predominantly occupied by the C-alkylation in the presence of Et_3N or NaOPh, the Int-1 should have an ion pair structure shielded by a phenol molecule from the rear-side. It is probable that the retentive methanolysis proceeds via models (c) ((iii) in Scheme 4).

In the presence of $PhNH_2$, the inversive alkylations of $PhNH_2$ give an indication that model (c) shielded by $PhNH_2$ might coexist with another model (c) shielded by PhOH ((iv) and (v) in Scheme 4). The aniline-shielded ion pair (c) could produce the retained alkylphenols ((vii) in Scheme 4); the *o*-isomer might be more easily formed via a six-center conformation (cf. (e) in Scheme 3) than the *p*-isomer. The formation of retained *o*-alkylphenol in the presence of $PhNH_2$ (Table 4) could suggest that the aniline-shielded ion pair (c) might be predominant. These are consistent with the other fact that the inverted *p*-alkylphenol accompanies more racemization in the presence of $PhNH_2$ than in the presence of Et_3N (Table 4). From such rear-side-shielded ion pair models, predominant formation pathway for each product may be expressed in Scheme 4.



Scheme 4.

The Int-1 in this system, therefore, have an analogous ion pair structure to that for Int-2 in the phenolysis of 2,2-dimethyl-1-(*p*-methoxyphenyl)propyl *p*-nitrobenzoate.[13]

More racemization for ROMe than that for the other products suggests that a rear-side-open, not shielded, ion pair intermediate, e.g., a four-center ion pair (b) and/or a contact ion pair (d), might contribute as a minor Int-1 to the product formation.

In conclusion, (i) the reexamination of k_p–k_t profile for the phenolysis system has clarified that all the products are produced by the reaction of Int-1 with solvent phenol molecule, and (ii) the features of stereochemical outcomes for both solvolyses, the phenolysis in phenol–benzene (1:1 w/w) and the competitive solvolysis in phenol–methanol (85:15 w/w), indicate that the Int-1 might be composed of multiple ion pair intermediates with various types, not of a single one, but that the major Int-1 should be

a rear-side-shielded ion pair intermediate.

Experimental

^{13}C and ^{1}H NMR spectra were taken with a JEOL model JNM FX-100 25 MHz (FT) and Hitachi R-24 and R-600 (FT) 60 MHz instruments, respectively. IR spectra were recorded with a Hitachi model 215 spectrophotometer. Optical rotations were measured with a JASCO model DIP-SL polarimeter. GLPC was performed with a Hitachi model 163 instrument. MPLC was done with a chromatograph system composed of a FMI model RP-SY-2 pump system and a Merck silica gel 60 column. Melting points were measured on a Yamato model MP-21 apparatus.

Materials. Optically active 1-phenylethanol was obtained both by the resolution of the racemic alcohol according to the Pope-Peachey method[29] and by asymmetric reduction of acetophenone.[30] Optically active and racemic 1-phenylethyl chlorides were prepared by reactions of respective 1-phenylethanols with thionyl chloride as previously described.[2,3] Sodium phenoxide was prepared in the previously-reported manner.[31] 2,6-Di-*t*-butyl-4-methylpyridine was synthesized by a known method.[32] All the other organic reagents were of an analytical reagent grade, dried, and fractionated prior to use.

Titrimetric Rate Measurements. The usual aliquot technique[5] was employed, using cold acetone (ca. −15 °C) as a stop solution, 0.05 M NaOH (or HCl) solution as a titrating reagent, and lacmoid as an indicator. In the presence of a base, the reaction was followed to at least 80% reaction; smooth first-order linear relationships (correlation coefficient ≥0.9997) were obtained. In the absence of a base, the reaction was followed to ca. 30% completion; the initial rate constant was taken by extrapolation from rate constants at 1—13% reaction.

The rate data are shown along with polarimetric rate data in Table 1 and Figs. 1, 2, and 3.

Polarimetric Rate Measurements. (A) Phenolyses: The previous method[2] was followed. A reaction solution, prepared at the reaction temperature (25.0±0.1 °C), was immediately placed into a jacketed polarimeter tube (1 dm) maintained at 25 °C by circulation of water from a constant temperature bath kept at 25.0±0.1 °C. In each run, the reaction was followed to at least 80% conversion; a smooth first-order linear relationship was obtained (the correlation coefficients≥0.9997).

(B) Methanol-Perturbed Phenolyses: Each reaction solution ([RCl]=0.1 M, [Et_3N]=0—0.30 M; 10 ml) was kept at 25.0±0.1 °C. After a specified time, the solution was poured onto an ice-cooled mixture of 10% aq. NaOH solution (200 ml)–diethyl ether (400 ml) and immediately shaked. The ether layer was promptly separated, washed with cold 10% aq. NaCl solution, and dried. After subsequent removal of the solvent by rotary evaporation, the optical rotation of benzene solution (5 ml) of the concentrate was measured. Thus, the optical rotations at five or more specified times were graphically treated, and a smooth first-order linear relationship was obtained (the correlation coefficient≥ 0.9993).

The rate data are summarized in Table 1 and Figs. 1, 2, and 3 along with the titrimetric rate data.

Product Distribution Analysis. Product distributions for

Table 6. ^{13}C NMR Spectral Data for 1-Phenylethyl Derivatives (RX) Relevant to the Phenolysis[a]

RX	CH_3-	-C(I)-H	Ar-		
ROPh	24.42(q)	75.80(d)	115.83(d)	120.53(d)	143.13(s)
			125.41(d)	127.28(d)	157.87(s)
			128.46(d)	129.22(d)	
o-RC_6H_4OH	20.96(q)	38.41(d)	115.83(d)	120.71(d)	131.98(s)
			126.72(d)	127.33(d)	145.31(s)
			127.46(d)	127.81(d)	153.17(s)
			128.52(d)		
p-RC_6H_4OH	22.02(q)	43.86(d)	115.13(d)	125.88(d)	138.67(s)
			127.46(d)	128.22(d)	146.60(s)
			128.63(d)		153.35(s)
RNHPh	24.95(q)	53.37(d)	113.25(d)	117.13(d)	145.13(s)
			125.76(d)	126.75(d)	147.19(s)
			128.52(d)	128.98(d)	
o-$RC_6H_4NH_2$	21.72(q)	40.22(d)	116.13(d)	118.65(d)	129.69(s)
			126.28(d)	127.17(d)	144.25(s)
			127.34(d)	128.63(d)	145.54(s)
p-$RC_6H_4NH_2$	21.96(q)	43.86(d)	115.07(d)	118.42(d)	136.44(s)
			125.70(d)	127.40(d)	144.25(s)
			128.28(d)		147.01(s)
ROMe	23.78(q)	79.55(d)	126.05(d)	127.28(d)	143.37(s)
			128.28(d)		

a) δ; in $CDCl_3$.

the phenolyses were analyzed by GLPC in a manner similar to that reported earlier.[1,33]

The data are shown for the phenolysis in Table 2 and for the methanol-perturbed phenolysis in Fig. 4.

Isolation of Phenolysis Products. The previous procedures[5] were followed. All substitution products were separated by MPLC and preparative TLC (silica gel). As a representative run, isolation of the products in the phenolysis of RCl in the presence of $PhNH_2$ (0.110 M) is described in the following. A solution (350 ml) of (*R*)-(+)-RCl (5.021 g, 0.03571 mol; $\alpha_D^{23.5}$ +24.2±0.1° (neat, 1 dm)), in phenol–benzene (1 : 1 w/w) containing aniline (0.110 M) was kept at 25.0±0.1 °C for 6 h. After usual working-up,[5] (*R*)-(−)-ROPh (4.994 g, $\alpha_D^{21.5}$ −1.55±0.08° (neat, 1 dm)), (*R*)-(+)-*o*-RC_6H_4OH (0.318 g, $[\alpha]_D^{25.8}$ +0.398±0.035° (*c* 5.773, benzene)), and (*S*)-(+)-*p*-RC_6H_4OH (0.339 g, $[\alpha]_D^{26.0}$ +0.235±0.043° (*c* 4.673, benzene)), were obtained from the organic solution. Simultaneously, (*S*)-(+)-RNHPh[20](0.132 g; mp 46.8—47.9 °C (lit,[20b] 47.5—48.1 °C); $[\alpha]_D^{31.0}$ +2.43±0.13° (*c* 2.391, methanol)), (*S*)-(+)-*o*-$RC_6H_4NH_2$[21] (0.0249 g; mp 57.0—58.2 °C (lit, 57.5—58.5 °C,[20b] 58—59 °C,[34] 58.5—59.0 °C[35]); $[\alpha]_D^{24.9}$ +4.4±0.6° (*c* 0.32, benzene)), and *p*-$RC_6H_4NH_2$(0.0073 g) were isolated from an aqueous acidic solution used for washing the organic solution.

The stereochemical data for products are tabulated along with those at 0.29 M $PhNH_2$ and the previously-reported ones in Table 4. Those for the methanol-perturbed phenolysis are summarized in Table 5.

Each solvolysis product was identified on the basis of ^1H and ^{13}C NMR and IR spectral data and chromatographic data. ^{13}C NMR spectral data for all substitution products are shown in Table 6.

Anilinolysis of 1-Phenylethyl Chloride. An aniline solution (100 ml) of (*S*)-(−)-RCl (1.505 g, 0.0107 mol; $\alpha_D^{21.2}$ −51.90±0.08° (neat, 1 dm)) was maintained at 50.0±0.1 °C for 4.5 h (ca. $t_{1/2}$×10). After removing the solvent by distillation at a reduced pressure and a usual work-up, (*R*)-(−)-RNHPh[20](1.853 g, 87.8% yield; mp 46.7—47.8 °C; $[\alpha]_D^{19.4}$ −12.6±1.3° (*c* 0.150, cyclohexane)) was isolated by chromatographic separation and distillation in vacuo.

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