Kinetic Studies of Solvolysis. IX.[1] *The S_N1-type Cleavage of t-Butyl p-Substituted-phenyl Ethers and Optically-active α-Phenethyl Phenyl Ether by Hydrogen Halides in a Phenol-Dioxane Solvent**

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It has been well established experimentally that the mechanism for the cleavage of primary and secondary alkyl ethers by hydrogen halides is an S_N2-type displacement between a protonated ether (an oxonium ion-pair) and a hydrogen halide.[2] There have been, however, no publications concerning an unambiguous kinetic example of the S_N1-type cleavage for tertiary alkyl ethers, although the existence of such a cleavage has been suggested[3] on the basis of the rate sequence

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[1] Part VIII: K. Okamoto, K. Takeuchi and H. Shingu, This Bulletin, 35, 525 (1962).

* Presented at the 14th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1961.

[2] For a review see R. L. Burwell, Jr., *Chem. Revs.*, 54, 615 (1954).

[3] E. g., R. L. Burwell, Jr., ibid., 54, 626 (1954).

of alkyl ethers.[4] It is anticipated that, unlike the S_N2-type cleavage, which obeys third-order kinetics,[5] the S_N1-type mechanism would display second-order kinetics, for in this mechanism the oxonium ion-pair cleaves unimolecularly.

In this paper typical examples of the S_N1-type cleavage are presented for the cleavages of *t*-butyl *p*-substituted-phenyl ethers and of α-phenethyl phenyl ether by a hydrogen halide in a phenol-dioxane solvent. In addition, the steric course and the mechanism are discussed in detail for the S_N1-type cleavage of optically-active α-phenethyl phenyl ether.

The Molecularity of the Hydrogen Chloride Cleavage of *t*-Butyl Phenyl Ether. — The hydrogen chloride cleavage of *t*-butyl phenyl ether was followed titrimetrically from 20 to 60% of completion in 20 wt. % phenyl-80 wt. % dioxane at 70.0°C. Assuming the S_N1-type mechanism for this cleavage, we calculated the rate constants from the second-order rate equation:

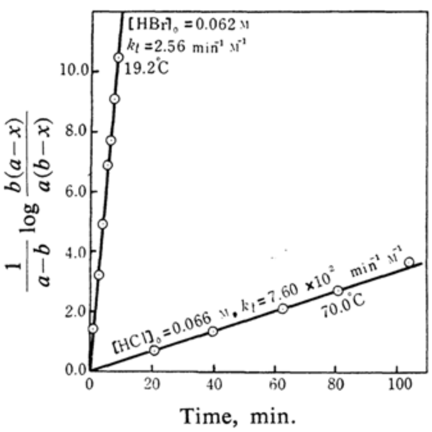

Fig. 1. Cleavage of *t*-butyl phenyl ether with hydrogen halides in 20 wt.% phenyl-dioxane.

TABLE I. SUMMARY OF RATES OF CLEAVAGE OF PHENYL ETHERS WITH HYDROGEN CHLORIDE IN PHENOL-DIOXANE

Compond	wt.% of phenol	Temp. °C	Initial concn. of the ether M	Initial concn. of HCl M	$10^2 k_t$ min.$^{-1}$ M^{-1}	$10^2 k_{t\text{corr}}$ min.$^{-1}$ M	Conversion % of the ether
t-Butyl	20.0	70.0	0.100	0.102	9.50	10.3	45
phenyl	20.0	70.0	0.100	0.0660	7.60	8.57	40
ether	20.0	70.0	0.100	0.0325	8.42	9.45	20
t-Butyl	20.0	70.0	0.100	0.103	8.40	9.26	55
p-tolyl	20.0	70.0	0.100	0.0650	6.91	7.79	35
ether	20.0	70.0	0.100	0.0309	7.08	7.60	18
t-Butyl	20.0	7.00	0.100	0.0487	2.04	2.26	4.1
p-chlorophenyl ether	20.0	70.0	0.100	0.0251	2.26	2.42	3.9
t-Butyl	20.0	70.0	0.100	0.0601	4.37	5.16	4.2
p-nitrophenyl ether	20.0	70.0	0.100	0.0280	4.15	4.53	4.1
t-Butyl	0.0	70.0	0.100	0.0620	0.93	—	9.0
phenyl ether	10.0	70.0	0.100	0.0593	2.5	—	25
t-Butyl	20.0	70.0	0.100	0.0570	15.8[a]	18.1	36
phenyl	20.0	70.0	0.100	0.0595	14.8[b]	16.5	39
ether	20.0	70.0	0.100	0.0595	12.7[c]	14.5	36
	20.0	70.0	0.100	0.0605	9.37	10.6	39
t-Butyl phenyl ether	20.0	19.2	0.100	0.0620[d]	256	—	53
α-Phenethyl	50.0	30.0	0.200	0.219	—	5.50[e]	60
phenyl ether	50.0	30.0	0.200	0.212	—	4.65	39

a, b and c) In the presence of 0.100, 0.0500, and 0.0250 M of *p*-nitrophenol, respectively

d) Concn. of HBr

e) The value of k_p (see text).

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4) B. W. Tronow and L. W. Ladigina, *Ber.*, **62**, 2844 (1929).

5) a) F. R. Mayo, W. B. Hardy and C. G. Shultz, *J. Am. Chem. Soc.*, **63**, 426 (1941); b) A. Y. Drummond and A. M. Eastham, ibid., **79**, 3689 (1957).

$$k_t = \frac{1}{t(a-b)} \ln \frac{b(a-x)}{a(b-x)} \quad (1)$$

where a is the initial concentration of the ether, b is the initial concentration of hydrogen chloride, and x is the concentration decrease in hydrogen chloride after the time lapse, t. Satisfactory second-order behavior was observed for each run; a representative run is illustrated in Fig. 1.

The values of the rate constants did not show any appreciable change between runs in various initial concentrations of hydrogen chloride, except for a slight increase probably due to the ionic strength effect of hydrogen chloride. These values are illustrated in Table I.

An examination of the extent of the completion of the reaction revealed that the consumption of hydrogen chloride did not exceed 91% of the starting ether after ten half-lives reaction time. This indicates that the major reaction is that of the cleavage, but also that there is, to a certain minor extent, a side reaction or a reverse reaction. Since the rate of the reverse reaction, i. e., the phenolysis rate of *t*-butyl chloride, was found to be negligibly small under these cleavage conditions, this incompleteness of hydrogen chloride comsumption may be ascribed to a concurrent side reaction. Although no attempt was made to clarify the characteristics of this side reaction, this seems to be rearrangement of the *t*-butyl group from ether-oxygen to the benzene-nucleus. This type of rearrangement has already been known in the hydrogen chloride cleavage of *t*-butyl phenyl ether in the absence of solvent at 20.0°C.[6]

In view of the fact that both the cleavage and the rearrangement proceed unimolecularly through the protonated ether, the ratio of the concentration decrease of hydrogen chloride to that of the ether at any reaction time should be equal to the ratio, r, of the concentration of the hydrogen chloride consumed by the ether at an infinite reaction time to the initial concentration of the ether. On the basis of this consideration, the ether concentration was expressed as $\{a-(x/r)\}$ instead of $(a-x)$ in Eq. 1, where a represents the initial concentration of the ether, and x represents the concentration decrease in hydrogen chloride after the time lapse, t. Thus, rate expression for the ether consumption:

$$-\mathrm{d}\{a-(x/r)\}/\mathrm{d}t = k_{t\mathrm{corr}}\{a-(x/r)\}(b-x) \quad (2)$$

gave a modified second-order kinetic equation:

$$k_{t\mathrm{corr}} = \frac{1}{(ar-b)} \ln \frac{b(ar-x)}{ar(b-x)} \quad (3)$$

The corrected second-order rate constants also gave good second-order behavior; these values are shown in Table I.

Hence, this cleavage is evidently a typical example of the S_N1-type ether cleavage, where an oxonium ion-pair, rapidly formed from the ether and hydrogen chloride, reacts intramolecularly by way of slow, unimolecular carbon-oxygen ionic fission.

Additional S_N1-type Characteristics of the Cleavage of *t*-Butyl Phenyl Ether.—The titrimetric rate constants (uncorrected), measured at 70.0°C in a series of solvents, i. e., dioxane 10 wt.% and 20 wt.% phenol-dioxane, increased with the phenol concentrations; this is illustrated in Fig. 2.

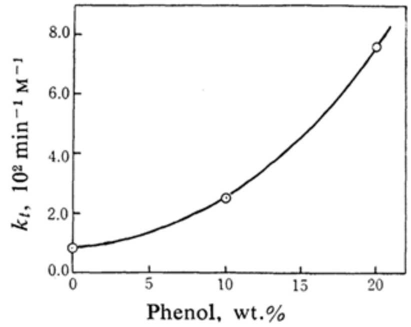

Fig. 2. Solvent effect in hydrogen chloride cleavage of *t*-butyl phenyl ether in phenol-dioxane.
$[\text{ether}]_0 = 0.100$ M
$[\text{HCl}]_0 = 0.059 \sim 0.066$ M, 70.0°C

Although the protonation of the ether might be promoted in the phenolic solvents by the relative decrease in dioxane concentration, it is more probable that the subsequent unimolecular cleavage would be greatly accelerated by an increase in phenol concentration. This kind of acceleration has already been found to be a normal pattern of the S_N1-type reaction in the phenolysis of *t*-butyl chloride.[6]

In addition, it was found that the titrimetric rate constants were markedly enhanced in the presence of added *p*-nitrophenol. This is illustrated in Fig. 3. This kind of phenomena has also been observed in the S_N1-type acetolysis of *t*-butyl bromide in acetic acid-carbon tetrachloride,[7] where it was interpreted as an acceleration of ionization due to hydrogen bonding. It may, therefore, be suggested that the similar acceleration by *p*-nitrophenol is effective in this cleavage.

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6) H. Shingu and K. Okamoto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 111 (1960).

7) K. Okamoto and H. Shigu, This Bulletin, **34**, 1131 (1961).

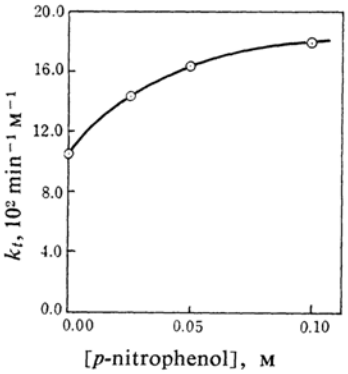

Fig. 3. Plot of k_t vs. [*p*-nitrophenol] for hydrogen chloride cleavage of *t*-butyl phenyl ether.

$[\text{ether}]_0 = 0.100$ M
$[\text{HCl}]_0 \fallingdotseq 0.06$ M, 70.0°C, 20 wt.% phenol

The Substituent Effect for the Hydrogen Chloride Cleavage of *t*-Butyl *p*-Substituted-phenyl Ether.—The cleavage of *p*-tolyl *t*-butyl ether, followed titrimetrically in 20 wt. % phenol-dioxane at 70.0°C, obeyed good second-order kinetics. The titrimetric rate constants for *p*-chlorophenyl and *p*-nitrophenyl *t*-butyl ether, especially for the run with higher concentrations of the *p*-nitrophenol ether, showed a tendency to drift upward in the plot for the second-order rate constant. In view of the acceleration of the cleavage of *t*-butyl phenyl ether by *p*-nitrophenol, this upward drift may probably be ascribed to autocatalytic acceleration by the *p*-chlorophenol or *p*-nitrophenol liberated during the cleavage. The second-order rate constants of these ethers were calculated from the initial rates. The rate constants are shown in Table I.

The percentages for the completion of the hydrogen chloride consumption of the *p*-methyl-, *p*-chloro- and *p*-nitro-phenyl ethers amounted to 92 (at about 40 half-lives), 95.5 (at about 11 half-lives) and 94.3% (at about 10 half-lives) respectively. Using these values for *r*, we calculated the corrected rate constants from Eq. 3; they are shown in Table I.

The plot of the corrected rate constants vs. Hammett's σ-constants shows that there are no linear free-energy relationships involving these constants, as Fig. 4 illustrates. Since the reaction proceeds through an oxonium ion-pair formation, these substituents might display a counter effect for the oxonium ion-pair formation and the subsequent unimolecular cleavage. The para-nitro group may accelerate the cleavave and retard the protonation because of its electron-attracting effect, and the para-methyl group may show converse tendencies in each of the processes. This seems to be the cause of the failure of Hammett's linear free-energy relationship for this reaction.

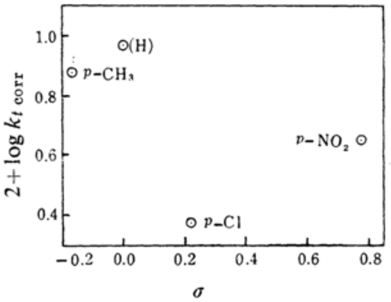

Fig. 4. Plot of $\log k_{t\,\text{corr}}$ vs. Hammett's σ constants for hydrogen chloride cleavage of *t*-butyl *p*-substituted-phenyl ether in 20 wt.% phenol-dioxane at 70.0±0.1°C.

The Hydrogen Bromide Cleavage of *t*-Butyl Phenyl Ether. — Satisfactory second-order behavior was observed for the hydrogen bromide cleavage of *t*-butyl phenyl ether in 20 wt. % phenol-dioxane at 19.2°C; this is illustrated in Fig. 1. Although no attempt was made to correct to a side reaction, this result indicates that the reaction is of the S_N1-type. The rate constant is definitely higher than that of the hydrogen chloride cleavage. In view of the fact that the protonated ether can exist along with the anion as an oxonium ion-pair, it is unlikely that the enhancement of the rate by hydrogen bromide is due only to the ease of formation of the protonated ether. It is more reasonable to assume that the predominant cause of the enhancement is acceleration by the nucleophilic attack of the bromine ion, for the bromine anion is more nucleophilic than the chlorine ion. From this consideration it follows that the unimolecular cleavage of the oxonium ion-pair is of the "intramolecular" nature and that it is mechanistically similar to the S_Ni-type reaction.

The Hydrogen Chloride Cleavage of Optically-Active α-Phenethyl Phenyl Ether.—To substantiate the intramolecular cleavage of the oxonium ion-pair, the hydrogen chloride cleavage of (+)-α-phenethyl phenyl ether was followed polarimetrically in 50 wt. % phenol-dioxane at 30°C. The optical rotation associated with the disappearance of the (+)-ether decreased, and at the completion of the reaction (at about 14 half-lives) it reached a minus value, having crossed the zero line. Since the (+)-ether has the same configuration as the (−)-chloride,[8a)] this result indicates that the configuration of the ether was retained after the cleavage. This is consistent with the previous

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8) a) H. Hart and H. S. Eleuterio, *J. Am. Chem. Soc.*, **76**, 518 (1954); a) H. Hart and H. S. Eleuterio, ibid., **76**, 1379 (1954); c) H. Hart and R. J. Elia, ibid., **83**, 985 (1961).

observation that optically-active α-phenethyl phenyl ether is cleaved by hydrogen chloride in benzene,[8b)] toluene,[8c)] 3-pentanone[8c)] and isobutanol;[8c)] also, the rotation of the α-phenethyl chloride so formed shows that the process involves retention of the configuration, accompanied by a slight racemization.[8)]

The polarimetric rate constant, k_p, was calculated from the rate equation 4:

$$\frac{-\mathrm{d(ether)}}{\mathrm{d}t}=k_p\ \mathrm{(ether)}\ \mathrm{(HCl)} \qquad (4)$$

by ploting d(ether)/dt, graphically calculated, against (ether) (HCl), where (ether) represents the ether concentration calculated from the polarimetric measurement and (HCl) represents the concentration of hydrogen chloride measured at a titrimetric run carried out under the same conditions. This is illustrated in Fig. 5.

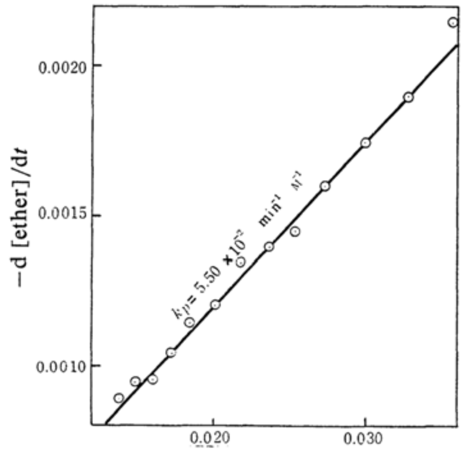


Fig. 5. Plot of $-\mathrm{d[ether]}/\mathrm{d}t$ vs. [ether] [HCl] for hydrogen chloride cleavage of (+)-α-phenethyl chloride in 50 wt.% phenol-dioxane at 30.0±0.1°C.

The titrimetric constant, $k_{t\ \mathrm{corr}}$, for this cleavage was also measured. The hydrogen chloride consumption at the completion of the reaction amounted to 75% of the starting ether. The rate of the reverse reaction was found to be negligibly small (2.3% of conversion at twenty half-lives of the cleavage). Evidently the incompleteness of hydrogen chloride consumption is due to a side reaction, probably a rearrangement of the oxonium ion-pair. Making a consideration analogous to the case of t-butyl phenyl ether, we estimated the concentration of the changed ether to be $x/0.75$, where x represents the concentration of the consumed hydrogen chloride at time t. The titrimetric rate constant was calculated from Eq. 5

$$k_{t\ \mathrm{corr}}=\frac{1}{(0.75a-b)}\ln\frac{b(0.75a-x)}{0.75a(b-x)} \qquad (5)$$

This was derived from the rate expression

$$\frac{-\mathrm{d}\{a-(x/0.75)\}}{\mathrm{d}t} =k_{t\ \mathrm{corr}}\{a-(x/0.75)\}\ (b-x) \qquad (6)$$

where a represents the initial concentration of α-phenethyl phenyl ether and b represents the initial concentration of hydrogen chloride.

A good second-order titrimetric rate constant was obtained by a plot of $(1/0.75a-b)\log b(0.75a-x)/0.75a(b-x)$ vs. t,; this is illustrated in Fig. 6.

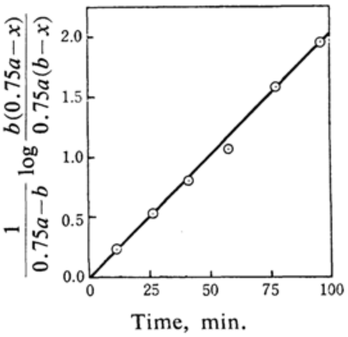


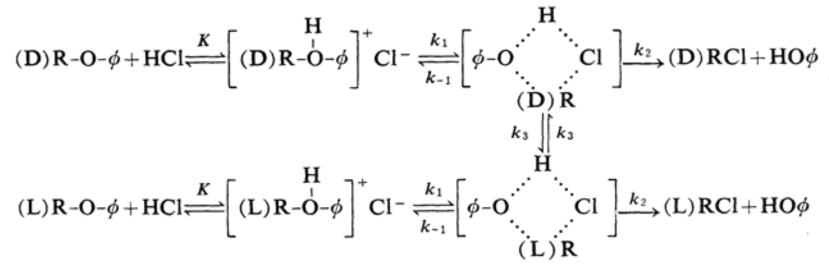
Fig. 6. Cleavage of α-phenethyl phenyl ether with hydrogen chloride in 50 wt.% phenol-dioxane at 30.0±0.1°C.
$[\mathrm{ether}]_0=0.200$ M
$[\mathrm{HCl}]_0=0.212$ M
$k_{t\ \mathrm{corr}}=4.65\times10^{-2}$ min^{-1} M^{-1}

As Table I shows, the polarimetric constant exceeds the titrimetric constant. This indicates kinetically that the racemization (or ionization) process of the oxonium ion-pair precedes the product-formation stage.

The Mechanism of the Hydrogen Halide Cleavage of *t*-Butyl and *α*-Phenethyl Phenyl Ether.—In the preceding sections the $\mathrm{S_N1}$-type characteristics of the protonated ether have been clearly indicated on the basis of the molecularity, the solvent effect, and the acceleration by phenolic compounds for the cleavage reaction.

The intramolecular, $\mathrm{S_N}i$-like nature for this cleavage has also been suggested from the rate enhancement by hydrogen bromide for the cleavage of t-butyl phenyl ether and from the steric course revealed for the cleavage of optically-active α-phenethyl phenyl ether.

Since the optically-active product was obtained at the cleavage of optically-active α-phenethyl phenyl ether, the intermediate should retain the optical activity. Therefore, we can postulate two " parallel " series of two-stage reactions of the " antipodal, " protonated ethers for the simplest expression of the ether



Scheme A

cleavage, as is depicted in Scheme A. The two parallel series of reactions of the antipodal substrates were previously postulated for the mechanism of the phenolysis of the optically-active α-phenethyl chloride.[1] In this mechanism the racemization is caused by way of interconversion between two antipodal intermediates. As a plausible structures for the intermediate; a quadrupolar type with a retained configuration; as has been suggested by Hart and Elia,[8b] may be assumed.

From Scheme A a quantitative explanation for the gap between the k_p and the k_t may be obtained by the following rate expressions:

$$k_p = Kk_1/(1+k_{-1}/(k_2+2k_3)) \qquad (7)$$

$$k_t = Kk_1/(1+k_{-1}/k_2)$$

In Eqs. 7 and 8, K, k_1, k_2 and k_3 represent the equilibrium constant for the protonated ether formation, the rate constant for the intermediate formation, the rate constant for the product formation, and the interconversion rate constant of the antipodal intermediates respectively,

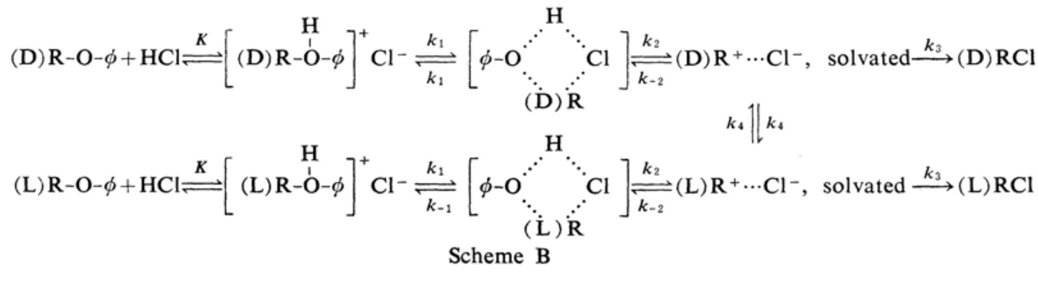
However, it would be possible to explain this cleavage mechanism, especially for the α-phenethyl system, by a more complicated mechanism. Since it was concluded in the previous paper[1] that the phenolysis of α-phenethyl chroride in a phenol-benzene solvent, i.e., the reverse reaction of the ether cleavage, proceeded under a " three-stage " mechanism of the S_N1-type with two kinds of intermediates, there is a possibility that the cleavage in phenol-dioxane goes back through the same " three-stages " as those of the phenolysis in a phenol-benzene solvent, This hypothesis seems reasonable judging from the principle of microscopic reversibility. Thus, the " three-stage " cleavage of the protonated ether is shown in Scheme B. In this mechanism the first intermediates would be a quadrupolar type intermediate consisting of an RCl and a phenol molecule, and the second ones, an ion-pair derived from RCl and surrounded by a solvation shell. If these intermediates are compared with those postulated for the phenolysis,[1] the first group may be considered to be non-racemizable and the second, racemizable (see Part VIII of this series[1]). The overall rate expressions for the k_t and k_p in this scheme are given in Eqs. 9 and 10 respectively:

$$k_p = Kk_1\Big/\left\{1+\frac{k_{-1}}{k_2}\left(1+\frac{k_{-2}}{k_3+2k_4}\right)\right\} \qquad (9)$$

$$k_t = Kk_1\Big/\left\{1+\frac{k_{-1}}{k_2}\left(1+\frac{k_{-2}}{k_3}\right)\right\} \qquad (10)$$

Discrimination between mechanisms A and B seems to be impossible on the basis of the kinetic examination of the trend of the gap between the k_t and the k_p. Namely, the change of solvent composition or the addition of a scavenger for the intermediates may cause an increase in the k_2 in Eqs. 7 to 10 or in the k_3 in Eqs. 9 and 10, but this will lessen the gap between the k_p and the k_t in " both " of Schemes A and B.

Thus, the experimental descrimination between Schemes A and B needs further study, although the principle of microscopic reversibility seems to favor Scheme B, especially for the α-phenethyl system.



Scheme B

Experimental[9]

Materials.—The preparation of *t*-butyl phenyl ether has been described previously[6] (b.p. 89.0°C/35.5 mm Hg, Found: C, 79.80; H, 9.04. Calcd, for $C_{10}H_{14}O$: C, 79.95; H, 9.39). *t*-Butyl *p*-tolyl ether and *t*-butyl *p*-chlorophenyl ether, prepared in the respective phenol by a method similar to that used for *t*-butyl phenyl ether,[6] had b.p.'s of 86~87°C/15.2 mmHg. (Found: C, 80,23; H, 9.71. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82%) and 84.0~85.5°C/9.0 mmHg respectively.

Found: C, 64.74; H, 6.89. Calcd. for $C_{10}H_{13}OCl$: C, 65.04; H, 7.09%.

t-Butyl *p*-nitrophenyl ether was obtained by means of the addition reaction of *p*-nitrophenol to isobutylene, To a mixture of 5.0 g of *p*-nitrophenol, 50 cc. of methylene chloride, and 0.55 cc. of 96% sulfuric acid, in a 200 cc., three-necked flask equipped with a thermometer, a cooled dropping funnel, and a drying tube, 12.0 g. of liquefied isobutylene were added in one portion at 0°C. After the mixture had stood for 20 hr. at 0~5°C, 40 cc. of 10% aqueous sodium carbonate was added to the reaction mixture to precipitate unchanged *p*-nitrophenol as the sodium salt. To the filtrate was added 10 cc. of ether, and the mixture was extracted with 10% aqueous sodium hydroxide, washed with water, dried and concentrated. The residue was fractionally distilled in vacuo, giving 1.91 g. (27.2% of theory) of *t*-butyl *p*-nitrophenyl ether; b.p. 103~110°C/2 mmHg.

Found: C, 62.02; H, 7.02. Calcd. for $C_{10}H_{13}NO_3$: C, 61,52; H, 6.71%.

(+)-α-Phenethyl phenyl ether was prepared from (+)-α-phenethyl chloride ($[\alpha]_D^{27°}$ 45.3°, homogeneous, 1 dm.) in the manner of Hart and Eleuterio[8a] (b.p. 106~110°/1 mmHg, $[\alpha]_D^{27°}10.11 \pm 0.05°$, homogeneous, 1 dm.). Aniline, phenol and dioxane (each of reagent grade) were dried and purified by fractional distillation; b.p. 42.0~43.0°C/1 mmHg, 178.5°C and 101.5°C respectively.

Kinetic Measurements.—The sealed ampoule technique was employed. The diminution of hydrogen chloride was followed by titration with standard sodium acetate in acetic acid, using crystal violet as an indicator. The polarimetric run was carried out in a manner similar to that previously described.[1]

Summany

1) Hydrogen chloride cleaves *t*-butyl phenyl ether at 70.0°C in 20 wt.% phenol-dioxane. The reaction is kinetically first-order in each reactant. The second-order rate constants show an increase with increasing phenol concentrations, and *p*-nitrophenol accelerates the reaction.

2) The hydrogen bromide cleavage of *t*-butyl phenyl ether at 19.2°C in 20 wt. % phenol-dioxane gives a second-order rate constant greater than that of hydrogen chloride.

3) The rate sequence of the hydrogen chloride cleavage of *t*-butyl *p*-substituted-phenyl ethers at 70.0°C in 20 wt.% phenol-dioxane is H>*p*-CH_3>*p*-NO_2>*p*-Cl, and there is no linear relationship between those rate constants and Hammett'σ constants.

4) The hydrogen chloride cleavage of (+)-α-phenethyl phenyl ether at 30.0°C in 50.0 wt.% phenol-dioxane obeys good second-order kinetics for both polarimetric and titrimetric runs. The value of the polarimetric rate constant exceeds that of the titrimetric constant, and from the final reading of the polarimetric run it has been concluded that the α-phenethyl chloride produced in the cleavage partly retained the configuration.

5) It has been concluded that the hydrogen halide cleavage of those phenyl ethers in phenol-dioxane proceeds through the protonated ether produced by a rapid equilibration between hydrogen halide and those ethers, and that the protonated ether reacts by an S_Ni-like mechanism. For the cleavage of the optically-active ethers, a detailed mechanism involving two parallel series of cleavage reactions of antipodal protonated ethers has been suggested wherein the partial racemization of the product is explained as resulting from the interconversion between the antipodal intermediates. For each series of S_Ni-type reactions, the possibility of a two-stage or three-stage mechanism has been discussed.

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[9] Microanalyses by Microanalytical Center, Kyoto University.