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48. **Yukio Akahori**: Studies on Isotopic Acyl Exchange. II.[*1] Effects of Bases and Solvents on the Rate of Acyl Exchange between *p*-Nitrophenyl Acetate and Acetic Acid.

(*Shizuoka College of Pharmacy*[*2])

In the previous paper,[*1] isotopic acyl exchange between *p*-nitrophenyl acetate and acetic anhydride or acetic acid in pyridine was described, and the reaction mechanism was discussed by kinetic data. The exchange reaction consisted of the preliminary reaction and the true exchange step. The former was the reaction between the acid component and pyridine, and the resulting product participated in the exchange reaction to which the McKay's formula[1] was applied. The preliminary reaction was found to be slow when acetic anhydride was used, but the reaction was fast in the case of acetic acid. The role of pyridine, however, was not clear in the previous study, and the further studies were required. In order to elucidate the role of pyridine, it is necessary to study the effect of concentration of pyridine on the exchange rate. For the purpose, the exchange reaction should be undertaken in neutral organic solvents and it is expected that this experiment affords some informations concerning the reaction mechanism. Also the effect of structural changes of the base may be studied by means of this reaction system, and the result will afford some clues for the elucidation of the role of the base in this exchange reaction. Present paper deals with the study of effects of structural changes in base and solvent on the exchange reaction between *p*-nitrophenyl acetate and acetic acid.

Experimental

1) **Materials**——α-Picoline: Distilled α-picoline was dried over KOH and distilled through a column, b.p. 128° (lit. b.p. 128~128.6°,[2] 129.2~129.25°[3]). Picrate, m.p. 167.5° (lit. m.p. 168°).[4]

β-Picoline: Distilled β-picoline was purified by the method as described above, b.p. 142° (lit. b.p. 144.0°,[4] 144.15~144.2°[3]), picrate, m.p. 152~153° (lit. m.p. 153°,[4] 149~150°[5]).

γ-Picoline: Distilled γ-picoline was purified by the methed as described above, b.p. 143° (lit. b.p. 145.3°,[4] 145.45~145.5[3]), picrate, m.p. 166° (lit. m.p. 167°,[6] 168°[7]).

N,N-Dimethylaniline: Distilled N,N-dimethylaniline was purified by the method as described above, b.p. 191~191.5° (lit. b.p. 193.50°,[7] 194.15°[8]).

Benzene: Distilled thiophene-free benzene was dried over P_2O_5, then fractionally distilled. A fraction boiling at 80° was purified by fractional crystallization, b.p. 80°, m.p. 5° (lit. b.p. 80.103°, m.p. 5.533°).[9]

$CHCl_3$: Purified $CHCl_3$ was dried over $CaCl_2$, and redistilled through a column, b.p. 61° (lit. b.p. 61.152°).[9]

AcOH, Ac_2O, pyridine, toluene, and *p*-nitrophenyl acetate (carbonyl-^{14}C) were prepared by the method described in the previous paper.[*1]

2) **Analytical Procedure**——a) Counting was carried out by the method described in the previous

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[*1] Part I. Y. Akahori, S. Fukushima: This Bulletin, **12**, 166 (1964).
[*2] Oshika, Shizuoka (赤堀幸男).
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paper,[*1] using 0.42% PPO in toluene as scintillator solution.

b) Determination of kinetic rate was due to the method appeared in the previous paper.[*1]

c) Reaction procedure : The general method adopted in the previous paper[*1] was applied to this experiment. *p*-Nitrophenyl acetate (carbonyl-^{14}C) and stable acetic acid were dissolved in benzene or $CHCl_3$ containing the base, and the solution was divided into several small tubes and sealed rapidly, then the reaction was started in a thermostatically controlled bath. At appropriate time intervals, the sealed tubes were opened and the solutions were transferred into flasks, and the solvents were evaporated off *in vacuo*, followed by addition of ice-water. These treatments were carried out within few minutes. The resulting precipitates were recrystallized from dil. EtOH and dried *in vacuo*, yielding colorless prisms, m.p. 78~79°.

d) Examination of the isolation method : Chemical and radiochemical purities of the reaction products were confirmed by the methods described in the previous paper. The recovery of the reaction product was nearly quantitative. Treatment of the reaction-solution at time zero showed no separation-induced exchange.

e) The labeled position in the reaction product was determined by the method described in the previous paper, and the same result was obtained.

Results

1) Kinetic Order

The exchange reaction took place between *p*-nitrophenyl acetate (carbonyl-^{14}C) and acetic acid, in benzene or chloroform solution in the presence of pyridine. The linearity of log $(1-F)$ *vs.* t was observed as shown in Fig. 1, and the kinetic data were collected in Table I. The dependence of R on the concentration of pyridine was shown to be somewhat complicated. When pyridine was absent in this system, the exchange reaction did not take place. Increase of the concentration of pyridine promoted the exchange reaction, but it showed slight deviation from linearity between the exchange rate and the concentration of pyridine, as shown in Fig. 2. Assuming polarity changes in the reaction-solution by addition of pyridine, the deviations could be canceled. Consequently, the dependence of exchange rate R on the concentration of each component, could be expressed in the equation (1).

TABLE I. Rate of Exchange between *p*-Nitrophenyl Acetate and Acetic Acid in Solvents. at 37.0°

Solvent	N_1 (mole/L.)	N_2 (mole/L.)	N_3 (mole/L.)	$t_{1/2}$ (hr.)	$10^6 k$ (L./mole/sec.)	$10^6 k/N_3$ (L./mole/sec.)
Benzene	0.865	0.865	0	∞	0	—
	0.837	0.837	0.837	28.0	4.16	4.97
	0.797	0.797	1.594	15.5	7.33	4.60
	0.853	0.853	5.081	6.3	17.9	3.52
Chloroform	0.863	0.863	0	∞	0	—
	0.835	0.835	0.835	35.2	3.28	3.93
	0.780	0.780	1.560	22.0	5.62	3.60
	0.847	0.847	5.023	7.0	16.2	3.23
Pyridine[a)]	0.830	0.830	11.4	3.5	31.5	2.76

N_1: [Ester] N_2: [Acid] N_3: [Pyridine]
a) values taken from data in Part I.

$$R=k\cdot[\text{Ester}]\cdot[\text{Acid}]\cdot[\text{Base}] \qquad (1)$$

2) Effect of Preliminary Treatment of Acid-base Mixture

Acetic acid and pyridine were dissolved in benzene or chloroform and the solution was warmed in a thermostat for a period more than twice of the corresponding half-exchange time $t_{1/2}$ then *p*-nitrophenyl acetate (carbonyl-^{14}C) was added into the solution, followed by starting of the exchange reaction. The experiment showed no difference

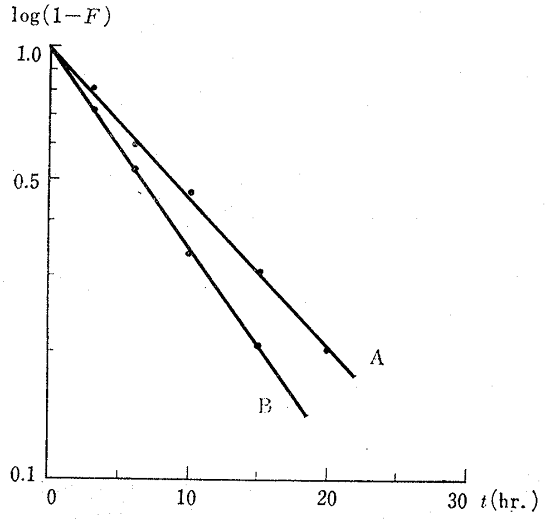
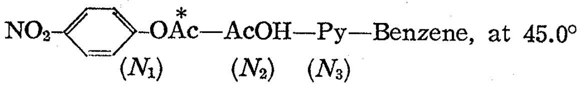


Fig. 1. Acyl Exchange Reaction in Benzene


$NO_2-C_6H_4-O\overset{*}{A}c—AcOH—Py—Benzene$, at 45.0°
(N_1) (N_2) (N_3)

	N_1 (mole/L.)	N_2 (mole/L.)	N_3 (mole/L.)
A	0.846	0.843	0.847
B	0.827	0.831	1.659

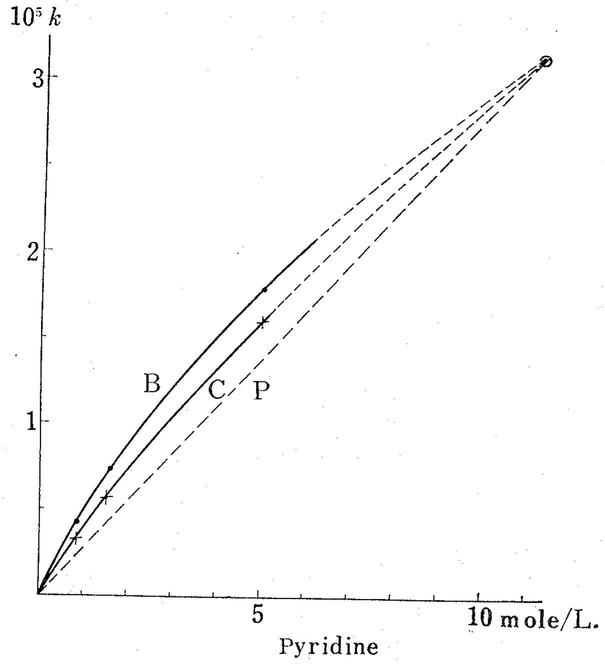
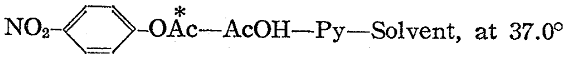


Fig. 2. Effect of Solvent and Concentration of Pyridine on the Exchange Rate


$NO_2-C_6H_4-O\overset{*}{A}c—AcOH—Py—Solvent$, at 37.0°

B : ●——●··· Benzene
C : ×——×··· Chloroform
P : – – – – – Pyridine

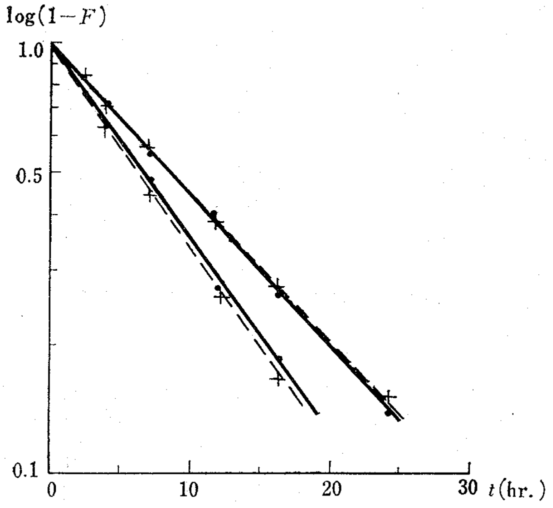
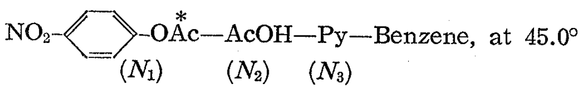


Fig. 3. Effect of Preliminary Heating


$NO_2-C_6H_4-O\overset{*}{A}c—AcOH—Py—Benzene$, at 45.0°
(N_1) (N_2) (N_3)

A, B : —●—●— without preliminary heating
A′, B′ : ···×···×··· with preliminary heating

from the run that had no preliminary heating, as shown in Fig. 3.

3) Solvent Effect

The exchange rates in benzene or chloroform in the presence of pyridine were determined, and it was found that the exchange reaction in benzene-solution was faster than that in chloroform-solution as shown in Fig. 2, where k is defined in the equation (2).*[1]

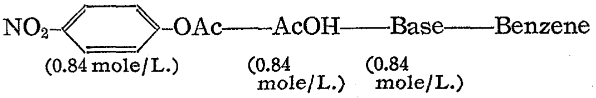
$$R = k \cdot [\text{Ester}] \cdot [\text{Acid}] \qquad (2)$$

The line B showed the relation in the exchange reaction undertaken in benzene and the line C showed that in chloroform. Fig. 2 showed the slight curvature for these two lines. The reason for the curvature will be described in discussion. To get more informations on this problem, the attempts were unsuccessfully undertaken using nitrobenzene and nitromethane as highly polar solvents. The isolation of the reaction product from nitrobenzene-solution was difficult because of less volatility of nitrobenzene at lower temperature, and the other trials of isolation were failed. The acidity of nitromethane was not neglected in this experiment, and it was concluded to be unfavorable.

4) Effects of Structural Changes of Bases

The exchange reaction between *p*-nitrophenyl acetate (carbonyl-^{14}C) and acetic acid in benzene-solution was studied in the presence of α-, β-, and γ-picolines and N,N-dimethyl aniline, and the results were collected in Table II and Fig. 4. Fig. 5 shows the temperature dependence of the reaction rates in these exchange reactions. These data showed the complicated effects which could be separated into steric effect and effect of base strength. Concerning their activation energies, there was found no remarkable difference, and their value were approximately identical with E_a value for the exchange reaction in pyridine.*[1]

Table II. Rate of Exchange Reaction between *p*-Nitrophenyl Acetate and Acetic Acid in Benzene. Structural Effect of Base on the Exchange Rate



$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{NO_2\text{-}C_6H_4\text{-}OAc}}$——$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{AcOH}}$——$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{Base}}$——Benzene

Base	$10^6\,k$ (L./mole/sec.)				E_a (Kcal./mole)
	65.0°	55.0°	45.0°	37.0°	
Pyridine	—	13.7	7.13	4.16	12.8
α-Picoline	2.91	1.74	1.03	—	11.7
β-Picoline	36.6	19.4	9.75	—	14.2
γ-Picoline	68.5	37.5	17.8	—	14.7
N,N-Dimethylaniline	0.777	0.475	—	—	—

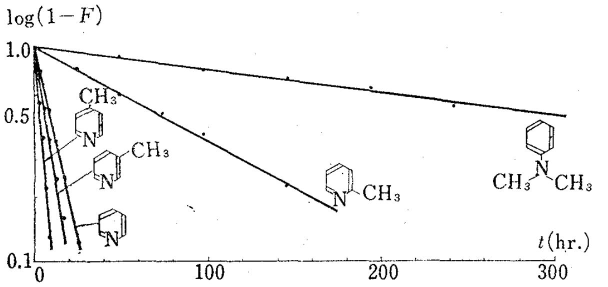
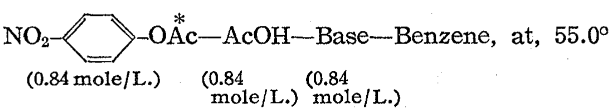


Fig. 4. Effect of Bases on the Exchange Rate



$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{NO_2\text{-}C_6H_4\text{-}O\overset{*}{A}c}}$—$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{AcOH}}$—$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{Base}}$—Benzene, at, 55.0°

Base	$t_{1/2}$(hr.)
Pyridine	8.5
α-Picoline	68
β-Picoline	6.0
γ-Picoline	3.2
N,N-Dimethylaniline	~280

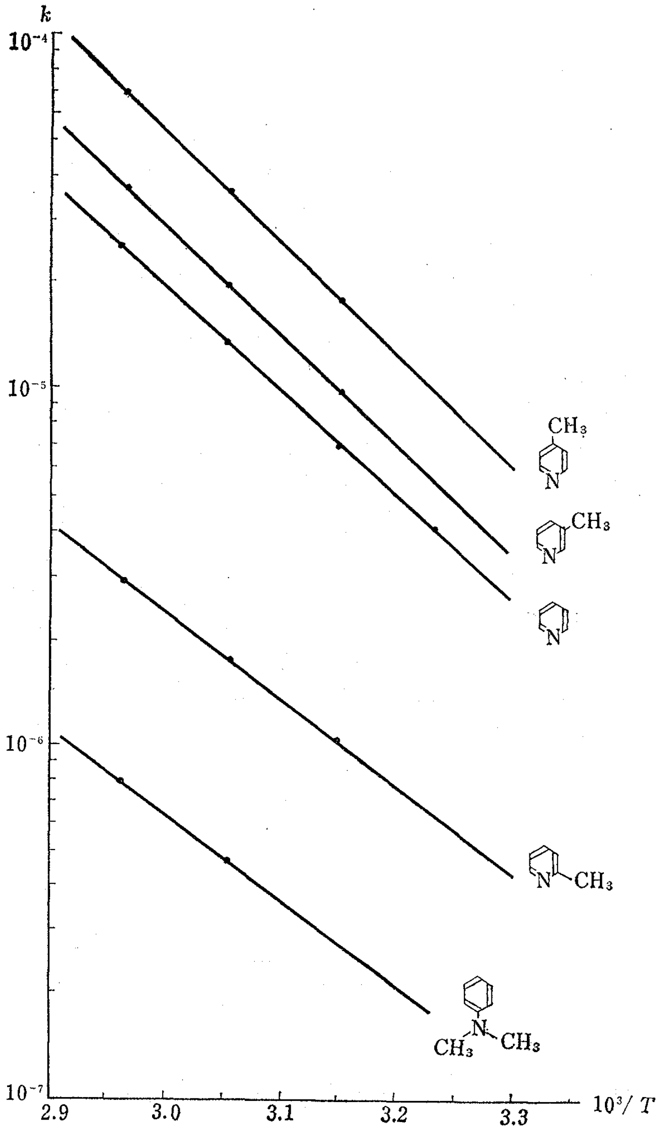
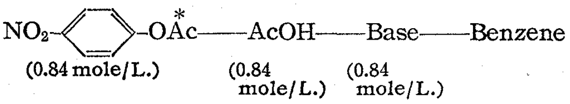


Fig. 5. Temperature Dependency of Exchange Rate



$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{NO_2\text{-}C_6H_4\text{-}O\overset{*}{A}c}}$——$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{AcOH}}$——$\underset{(0.84\,\mathrm{mole/L.})}{\mathrm{Base}}$——Benzene

Discussion

The solvent effect on the exchange

Table Ⅲ. Solvent Effect on the Exchange Rate

Solvent	Relative exchange rate[a)]	Dipole moment[b)] (D)
Benzene	1.80	0
Chloroform	1.42	1.06
Pyridine	1.00	2.20

a) Exchange reaction between *p*-nitrophenyl acetate and acetic acid in the presence of pyridine, at 37.0°. The concentration of each component is 0.84 mole/L.

b) M. Kotake, ed.: "Series of Comprehensive Organic Chemistry, Suppl. 2"; Y. Morino: "Electric Dipole Moments of Molecule," p. 500 (1963). Asakura Publishing Co.

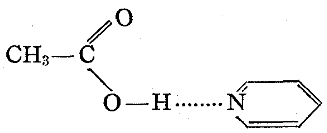
rate shown in Fig. 2 is explained by polarity of the solvents. According to Ingold,[10] polarity of solvent can be expressed by the molecular dipole moment and thickness of shielding of the dipole charges. For the present cases, pyridine, chloroform and benzene form a series of solvents in order of diminishing polarity, and their degrees are approximately represented by their dipole moments. Table Ⅲ shows the relation between the relative exchange rate and polarity of solvents, and it is concluded that low polarity of the reaction solution is favorable to the exchange reaction.

As shown in Fig. 2, the slight curvature in k *vs.* [Base] is observed in the cases of benzene and chloroform. The deviation from linearity which might be expected between the exchange rate and the concentration of pyridine may be due to the polarity change of the reaction mixture caused by addition of pyridine. Increase of the concentration of pyridine in the reaction-solution affords higher polarity of the reaction-solution, and it suppresses the rate of increase of the exchange rate.

Concerning activation energy, the E_a value for the reaction undertaken in benzene-solution shows no remarkable difference from E_a for the reaction in pyridine, as shown in Table Ⅱ. These evidences suggest the same reaction mechanism in these systems.

The dependence of the exchange rate R on the concentration of pyridine indicates participation of pyridine in the exchange reaction. As mentioned in the previous paper,[*1] the reaction of acetic acid with pyridine is considered as a preliminary step prior to the exchange reaction. No effect of preliminary heating of acid-base mixture upon the exchange rate indicates that the acid rapidly reacts with the base. And it is excluded by the kinetic data that the dissociated anion of the product in the acid-base reaction participates in the exchange reaction.

The reaction of acetic acid with pyridine has been known to be quite complicated.[11~14] According to Sunamori,[15] 1:1 hydrogen-bonding complex (I), 1:2 hydrogen-bonding complex (Ⅱ) and ion-pair complex (Ⅲ) exist in acetic acid-pyridine two component system. The cmplex (I) is formed in the mixture in which mole-fraction of acetic acid is lower, and the complex (Ⅲ) is favorable when mole-fraction of acetic acid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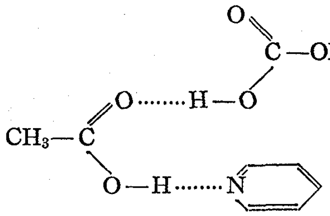
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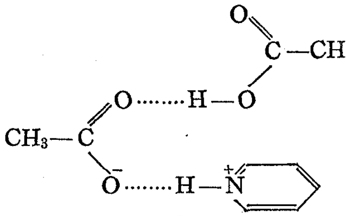
Ⅲ

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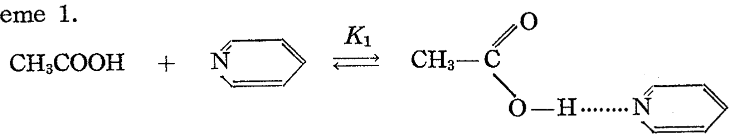
is higher, and the complex (II) lies in the intermediate stage. The mole-fraction in the exchange reaction undertaken in pyridine-solution corresponds to the stage forming I, and the mole-fraction in the exchange reaction carried out in benzene-solution lies in the range forming II and III. It was known for the formation of ion-pair complex (III) to require the aggregate of acetic acid,[15] and the ion-pair complex analogous to III may be formed in the exchange reaction when the ester is assumed to act as a role of the aggregate. Therefore, the following schemes are proposed for the preliminary reaction.

Scheme 1.



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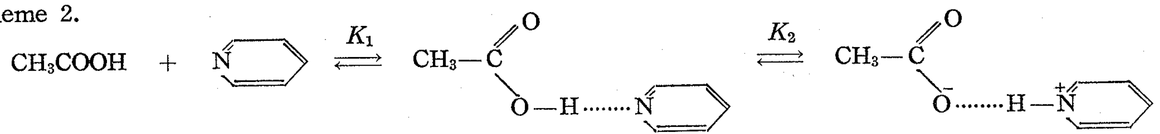
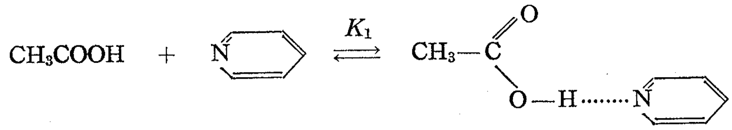
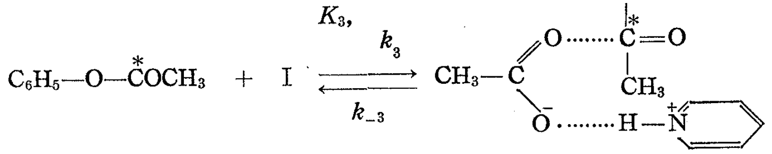
Scheme 2.



I IV



Scheme 3.



V

The equilibrium constants are expressed by the following equations.

$$K_1 = \frac{[\mathrm{AcOH}\cdots\mathrm{Py}]}{[\mathrm{AcOH}]\cdot[\mathrm{Py}]} \tag{3}$$

$$K_2 = \frac{[\mathrm{Ac\overset{-}{O}}\cdots\mathrm{\overset{+}{H}Py}]}{[\mathrm{AcOH}\cdots\mathrm{Py}]} \tag{4}$$

The concentrations of the products in the preliminary reactions are described as follows.

For the Scheme 1,

$$[\mathrm{AcOH}\cdots\mathrm{Py}] = K_1[\mathrm{AcOH}][\mathrm{Py}] \tag{5}$$

For the Scheme 2,

$$\begin{aligned}[\mathrm{Ac\overset{-}{O}}\cdots\mathrm{\overset{+}{H}Py}] &= K_2[\mathrm{AcOH}\cdots\mathrm{Py}] \\ &= K_1K_2[\mathrm{AcOH}][\mathrm{Py}] \end{aligned} \tag{6}$$

The product thus formed in these preliminary reactions reacts with the ester, and the true exchange reaction takes place. The true exchange reaction is slower than these equilibrium reactions, because the preliminary heating of the acid-base mixture affords no effect on the exchange rate. Accordingly, the rate determining step is involved in the true exchange reaction.

When the equation (5) or (6) is applied to the McKay's formula,[1] the exchange rate R is expressed by the equation (7).

$$R=\frac{KN_1N_2N_3}{N_1+KN_2N_3}\cdot\frac{\ln 2}{t_{1/2}} \tag{7}$$

N_1, N_2, and N_3 represent the concentration of the ester, the acid and the base, respectively. And K represents K_1 for Scheme (1) and K_1K_2 for Scheme (2). If the exchange rate R is expressed by the equation (8), the rate constant k_p is given by the equation (9).

$$R=k_pKN_1N_2N_3 \tag{8}$$

$$k_p=\frac{1}{N_1+KN_2N_3}\cdot\frac{\ln 2}{t_{1/2}} \tag{9}$$

It is also possible to assume that the formation of ion-pair complex takes place only by approaching of hydrogen-bonding complex (I) to the ester, as shown in Scheme (3), and resulting ion-pair complex (V) participates in the true exchange reaction. In this case, the concentration of the complex (V) is expressed by the equation (10), and the rate equation is expressed by the general equation (7), where K represents K_1K_3.

$$[\mathrm{V}]=K_3[\mathrm{Ester}]\cdot[\mathrm{I}]=K_1K_3\cdot N_1N_2N_3 \tag{10}$$

Consequently, the equation (9) can be applied for Scheme 3.

When the exchange reaction is carried out in pyridine as described in Part I,*[1] the value of N_3 is considered to be approximately constant. The equation (7) and (8) are transformed into the equation (11) and (12), respectively, when $KN_3=1$ is assumed in this case.

$$R=\frac{N_1N_2}{N_1+N_2}\cdot\frac{\ln 2}{t_{1/2}} \tag{11}$$

$$R=k_pN_1N_2 \tag{12}$$

Therefore, the equation (7) may be the general equation which includes the equation (11) as a special case.

In the exchange reactions undertaken in organic solvents, the K values may be sensitive to alteration of the mole-fractions in the reaction mixture and the values can not be estimated at present moment, and the equation (9) can not be applied to calculation of k_p. Accordingly, the equations (11) and (12) are tentatively applied to calculation of the exchange rate in the present cases, in order to compare the experimental results; and the tentative k values are obtained by the equation (13).

$$k=\frac{1}{N_1+N_2}\cdot\frac{\ln 2}{t_{1/2}} \tag{13}$$

When N_3 is changed under keeping N_1 and N_2 constant, the equation (9) indicates linear relation between $1/t_{1/2}$ and N_3, since k_p is constant for the same constitution of the reaction mixtures.

The ratio of the apparent rate constant to the theoretical one is expressed by the equation (14).

$$\frac{k}{k_p}=\frac{N_1+KN_2N_3}{N_1+N_2} \tag{14}$$

The equation (14) means linearity of k *vs.* k_p in the narrow range of K value. Assuming K and k_p are constant for the same compounds, k *vs.* N_3 must be linear. The increase of N_3, however, afforded curvature of k *vs.* N_3, as shown in Fig. 2. When N_3

is increased, the formation of the ion-pair complex may be retarded because of the decrease of the ratio N_2/N_3; and one of the reason for the curvature may be attributed to the change of K value. However, there is observed the solvent effect on the exchange rate, which may be due to the change of the exchange rate constant k_p. The change of k_p may exceed the change of K, as mentioned in the following discussion, and it is concluded that the curvature of k *vs.* N_3 may be mainly attributed to the change of k_p and partly to the change of K.

When the exchange reaction is carried out in the other kind of solvent under keeping N_1, N_2, and N_3 constant, change of K or k_p may be suggested by the equation (14). Assuming constancy of k_p under the change of solvent polarity, the increase of K must be accompanied by the decrease of solvent polarity because the exchange reaction is faster in the less polar solvent; this seems to be unfavorable. On the other hand, when N_1, N_2, and N_3 are constant and K is constant in the different kind of solvent, the equation (14) predicts the decrease of k_p caused by the increase of solvent polarity. If the transition state is assumed to be less polar than the reactants, the solvent effect on the exchange rate is explained by the change of k_p due to the change of solvent polarity; and the assumption is considered to be reasonable. Therefore, it is reasonable that the solvent effect is mainly due to the change of k_p and partly to the change of K.

When the kind of base is changed under keeping N_1, N_2, and N_3 constant, the ratio of their apparent rates is expressed by the equation (15).

$$\frac{k}{k'}=\frac{k_p}{k_p'}\cdot\frac{N_1+KN_2N_3}{N_1+K'N_2N_3} \tag{15}$$

Assuming k_p is constant for the variation of base, the ratio of the apparent rates represents the change of K values which may be affected by the structure of base. The rate of the exchange step may be rather independent on the structure of base, because the ester bond in the true exchange step may be so far located that the interaction between the bond and the base is weak. Therefore, the equilibrium constant K can be compared by the ratio of the apparent k values.

Scheme 1 is difficult to explain the solvent effect on the exchange rate, because the transition state in the exchange reaction might be more polar than the hydrogen-bonding complex (1) and accordingly the solvent effect may act in the reversed direction.[16] Scheme 2 and 3 are more favorable than Scheme 1, with respect to this problem. The mole-fraction of acetic acid in the exchange reaction undertaken in the pyridine-solution does not correspond to the stage forming the ion-pair complex (Ⅳ),[15] and accordinly, Scheme 2 is unfavorable for the exchange reaction in pyridine-solution unless some kinds of effects operate in this reaction-solution to promote the formation of the complex (Ⅳ). Therefore, Scheme 1 and 2 may be excluded, and Scheme 3 remains as the most probable one. However, the reasons which are used for exclusion of Scheme 1 and 2 are not so perfect, and there still remain the possibilities that Scheme 1 and/or 2 may be applied to the exchange reaction under some conditions or the exchange reaction proceeds competitively through these Schemes.

The structural changes of the base afford the changes of base strength and steric hindrance, and they are predicted to change equilibrium constants as described above. No remarkable difference of E_a values for the exchange reactions in the presence of several kinds of bases suggests that the rate determining step is not seriously affected by the structure of bases, and the effect on the exchange rate caused by structural changes of the base may be attributed to the effect on the preliminary step. Increase of base strength stabilizes the complexes, and it makes the equilibrium to incline

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[16] K. A. Cooper, M. L. Dhar, E. D. Hughes, C. K. Ingold, B. J. MacNulty, L. I. Woolf: J. Chem. Soc., **1948**, 2043.

toward the complex formation. Consequently, it is expected that the exchange rate R increases in accompanying with the increasing of base strength, and the relationship obtained in the present study is shown in Table IV. The fast exchange in the presence of γ-picoline is attributed to this relation; and in the case of α-picoline, steric hindrance of a methyl group at α-position makes the exchange rate slower. β-Picoline is an intermediate case between α- and γ-picoline with respect to the steric effect, and the rate of the exchange in the presence of β-picoline takes the value between those of α- and γ-picoline. The relation is shown in Fig. 6, and the same feature has been known in the case of base-catalyzed hydrolysis of acetic anhydride.[19,20] In N,N-dimethylaniline, the bulky groups attached on nitrogen atom strongly inhibit the complex-forming reaction and the exchange rate takes the fairly small value comparing with the rate of the exchange in the presence of pyridine, in spite of approximately equal base strength of these two bases.

TABLE IV. Relation between the Exchange Rate and the Base Strength

Base	Relative exchange rate, at 55.0°	log K at 25°	References
Pyridine	1.0	$\bar{9}.16$	17)
α-Picoline	0.14	$\bar{9}.94$	17)
β-Picoline	1.4	$\bar{9}.66$	17)
γ-Picoline	2.7	$\bar{8}.03$	17)
N,N-Dimethylaniline	0.031	$\bar{9}.06$	18)

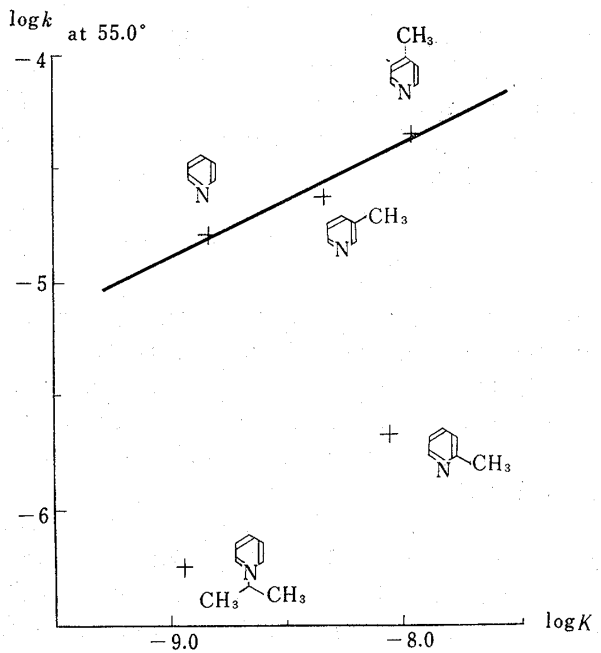

Fig. 6. Relationship between Exchange Rate and Dissociation Constant of Base

The existence of the complex-forming equilibrium was proved by the various experimental evidences as described above, but the problems concerning with the rate-determining step was not discussed. This will be discussed in the following papers. Moreover, the step which produces the ion-pair complex (V) may be the rate-determining step when the k_3 is extremely smaller than k_{-3}. This possibility, however, is denied by the other experimental evidences, and the details will be discussed in the next paper.

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19) V. Gold, E.G. Jefferson: J. Chem. Soc., **1953**, 1409.
20) J.E. Leffler, E. Grunwald: "Rates and Equilibria of Organic Reactions," p. 244 (1963), Wiley.

Summary

The isotopic acyl exchange between *p*-nitrophenyl acetate and acetic acid was studied in neutral organic solvents in the presence of several kinds of bases. The kinetics showed the first order dependency of the exchange rate on the base. The exchange reaction is shown to consist of the two steps. The preliminary step produced the pyridine-acetic acid complex which participated in the true exchange step. The effect on the exchange rate of structural changes of the base was attributed to changes in base strength and steric effect, and they affected the preliminary equilibrium. Solvent effect on the exchange rate and curvature of *k vs.* [Base] were due mainly to effect on the true exchange step and partly to effect on the preliminary step.

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49. **Yukio Akahori**: Studies on Isotopic Acyl Exchange. III.[*1]
Acyl Exchange Reaction of Substituted Phenyl Acetates; Effect of Nuclear Substituents on the Exchange Rate.

(*Shizuoka College of Pharmacy*[*2])

In Part I,[*1] isotopic acyl exchange between *p*-nitrophenyl acetate and acetic acid in pyridine was described, and the existence of a preliminary reaction between the acid and pyridine was suggested. The preliminary reaction was studied in Part II,[*1] and it was found that the preliminary reaction was the rapid equilibrium reaction and that the effect on the exchange rate of structural changes of the base was due to the change of the equilibrium constant. The main factor which governs the exchange rate, however, may be related to the rate-determining step which is closely connected with the ester employed in the exchange reaction. The structural changes of the acyl group in the ester may act on the exchange rate in dual manner; the one is the action on the preliminary equilibrium as acyl component, and the other is the direct effect on the rate-determining step. Therefore, the structural changes of acyl group in the ester may afford complicated effects on the exchange rate. Meanwhile, the effects on the exchange rate due to structural changes of the phenol group in the ester may act only on the rate determining step, and the study of the effects may be important to elucidate the reaction mechanism. Present paper deals with the study on the relation between the exchange rate and the structure of the phenol ring in the ester.

Experimental

1) **Materials**——Substituted phenyl acetates: Substituted phenols were acetylated by means of Ac_2O and conc. H_2SO_4 as described in Part I,[*1] and the resulting esters were recrystallized from suitable solvents. Phenyl acetate was prepared by the same method and purified by distillation. Their properties were collected in Table I.

[*1] Part I. Y. Akahori, S. Fukushima: This Bulletin, 12, 166 (1964); Part II. Y. Akahori: *Ibid.*, 13, 352 (1965).

[*2] Oshika, Shizuoka (赤堀幸男).