

Table 1. Second-Order Rate Constants for the Pyridinolysis of Substituted Phenyl Acetates at 60°C in Acetonitrile (k_{XY}/k_{HH} value)

$\begin{matrix} X \\ Y \end{matrix}$	4-NO ₂	4-Cl	H	3-CH ₃	4-CH ₃
4-NH ₂	2.50	1.77	1.76	1.75	1.71
3,4-(CH ₃) ₂	1.73	1.39	1.21	1.20	1.20
H	1.39	1.11	1.00*	0.99	0.98
3-COCH ₃	0.87	0.71	0.64	0.63	0.63
3-Cl	0.80	0.63	0.59	0.59	0.58

* $k_{HH} = 3.40 \times 10^{-4} \text{ l mol}^{-1} \text{ sec}^{-1}$.**Table 2. Reaction Constants (ρ_X , ρ_Y) for Pyridinolysis of Phenyl Acetates**(a) ρ_Y values

σ_X	4-NO ₂	4-Cl	H	3-CH ₃	4-CH ₃
ρ_Y	-0.469	-0.460	-0.447	-0.445	-0.441
	*($r = 0.991$)	(0.988)	(0.993)	(0.993)	(0.992)

(b) ρ_X values

σ_Y	4-NH ₂	3,4-(CH ₃) ₂	H	3-COCH ₃	3-Cl
ρ_X	0.180	0.175	0.165	0.153	0.148
	*($r = 0.997$)	(0.990)	(0.994)	(0.992)	(0.988)

* r : Correlation coefficient.

The plot of $|\rho_Y|$ vs σ_X and ρ_X vs σ_Y are well correlated with $\rho_Y^{(X)} = -0.03 \sigma_X - 0.447$, ($r = 0.965$), and $\rho_X^{(Y)} = -0.03 \sigma_Y + 0.165$, ($r = 0.966$), respectively.

Therefore, the rate constants are varied with substituents X and Y and it correlated with $\log k_{XY} - \log k_{HH} = 0.165 \sigma_X - 0.03 \sigma_X \sigma_Y - 0.447 \sigma_Y$. The most important facts are that the coefficient of the interaction term, $\rho_{XY} \sigma_X \sigma_Y$, is the same small value of -0.03 , which is derived from either ρ_X or ρ_Y , and its value indicates that the degree of interactions between nucleophile and leaving group are same but interactions between X and Y are small. •

The results are interpreted in terms of concerted mechanism in which involving a metastable tetrahedral intermediate. These are in accord with the mechanism of previously reported our study¹⁾ of the pyridinolysis.

Acknowledgement. We are grateful to the Korean Science and Engineering Foundation (KOSEF) for financial support of this work.

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Chemoselective Reduction of Carboxylic Acid Esters with Potassium Triethylborohydride

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The reduction of carboxylic acid esters to the corresponding alcohols can be achieved readily with various metal hydrides such as lithium aluminum hydride¹ (LiAlH₄), diisobutylaluminum hydride² (i-Bu₂AlH), and lithium triethylborohydride³ (LiEt₃BH), however, little chemoselectivity could be expected from these strong reducing agents. On the other hand, aluminum hydride⁴ (AlH₃), borane-dimethyl sulfide⁵ (BH₃·SMe₂) (at 65 °C), lithium borohydride (LiBH₄) with 9-methoxy-9-BBN catalyst⁶, and LiBH₄-MeOH-Et₂O⁷ system have been reported to reduce esters rapidly without attacking nitro and halogen substituents.

Recently we have studied the reducing properties of potassium triethylborohydride⁸ (KEt₃BH), and compared with those of lithium derivatives (LiEt₃BH). We found an interesting phenomenon. Thus the reducing power of potassium

derivative to ester is similar to LiEt₃BH which reduces esters in a few minutes, however, it reacts much slowly with other functional groups compared with LiEt₃BH. In this respect the replacement of Li⁺ with K⁺ resulted substantial decrease in reactivity for other functional groups such as epoxides, amides, nitriles *etc.* We now wish to report such chemoselectivity of KEt₃BH for the selective reduction of esters. Chemoselective reduction of esters with KEt₃BH was studied by competitive reaction. Thus an equimolar mixture of an ethyl ester and other substrate was reacted with 2.2 equivalents of KEt₃BH in THF. The reduction of ethyl caproate in the presence of cyclohexene oxide is representative. To an equimolar mixture of ethyl caproate (1 mmol) and cyclohexene oxide (1 mmol) containing 1 mmol of naphthalene as an internal standard in THF (1 ml) was added to 2.2 mmol of

Table 1. Chemoselective Reduction of Esters with KET_3BH in Tetrahydrofuran at 0°C ^a

entry	compounds	product	yield, ^a (%)
1	ethyl caproate	hexanol	99
	cyclohexene oxide	cyclohexene oxide	100
2	ethyl cyclohexanecarboxylate ^b	cyclohexylmethanol	94
	cyclohexene oxide	cyclohexene oxide	99
3	ethyl benzoate	benzyl alcohol	95
	cyclohexene oxide	cyclohexene oxide	94.9
4	ethyl benzoate	benzyl alcohol	96
	N,N-dimethylhexanamide	N,N-dimethylhexanamide	98.6
5	ethyl benzoate	benzyl alcohol	95
	capronitrile	capronitrile	94.9
6	isopropyl benzoate ^c	benzyl alcohol	93
	capronitrile	isopropyl benzoate	7
7	ethyl benzoate	benzyl alcohol	94
	quinoline	quinoline	98.6
8	ethyl benzoate	benzyl alcohol	100
	2-bromooctane	2-bromooctane	93
9	ethyl benzoate	benzyl alcohol	99.4
	bromocyclohexane	bromocyclohexane	98.6
10	ethyl benzoate	benzyl alcohol	100
	1-dodecene	1-dodecene	97
11	ethyl caproate ^d	hexanol	85
	isopropyl benzoate	ethyl caproate	14
		benzyl alcohol	12
		isopropyl benzoate	83
12	ethyl caproate ^d	hexanol	95
	<i>t</i> -butyl benzoate	<i>t</i> -butyl benzoate	95
13	ethyl benzoate ^d	benzyl alcohol	94
	<i>t</i> -butyl caproate	<i>t</i> -butyl caproate	100

^aA mixture of one mmol each of an ethyl ester and other substrate was reacted with 2.2 mmol KET_3BH at 0°C for 15 min. Yields were estimated by GLC, using naphthalene as an internal standard.

^bReaction for 3 h. ^cReaction for 6 h. ^dAt -15°C .

KET_3BH (1.37 ml) solution in THF at 0°C . After 15 min, the reaction mixture was quenched with 1 ml of water and oxidized with $\text{H}_2\text{O}_2\text{-NaOH}$ for 2 h at 30°C . After drying with

anhydrous K_2CO_3 , the GLC analysis of THF layer showed a 99% yield of hexanol and cyclohexene oxide (100%) intact. The results are summarized in Table 1. As shown in the Table, ethyl caproate, ethyl cyclohexanecarboxylate and ethyl benzoate can be reduced in the presence of cyclohexene oxide, N,N-dimethylcaproamide or capronitrile (entry 1-5) with excellent chemoselectivity. The reduction of ethyl cyclohexanecarboxylate is a little slower and completed in 3 h at 0°C (87% in 1 h). The reduction of isopropyl benzoate is also slow, however good selectivity is realized in 6 h (entry 6). KET_3BH is also able to reduce ester selectively leaving quinoline, 2-bromooctane, bromocyclohexane or 1-dodecene intact (entry 7-10). We do not expect these kinds of selectivity with AlH_3 , BMS (at 65°C), or LiBH_4 with a MeO-9-BBN catalyst. And KET_3BH is also susceptible to steric effects. Thus ethyl esters could be selectively reduced in the presence of *t*-butyl esters at -15°C (entry 12 and 13). When the competitive reduction of ethyl benzoate and *t*-butyl caproate was carried out at 0°C , the selectivity was not satisfactory. Thus benzyl alcohol was obtained in 83% yield at 0°C , but only 75% of *t*-butyl caproate remained unattacked. Even at -15°C , the chemoselectivity between ethyl caproate and isopropylbenzoate was less satisfactory giving the mixture of 85% hexanol and 12% benzyl alcohol together with unreacted esters (entry 11).

Acknowledgement. We are grateful to the Korea Science and Engineering Foundation for financial support of this work.

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Role of Water as Our Life Expectancy due to the Agings and Various Cancers

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In a series of my recent papers and lectures, we discussed the roles of water in modern diseases such as cancers, dia-

betes and AIDS (Acquired Immune Deficiency Syndrome)¹⁻³. According to our water environment theory, the local di-