

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

$X \backslash Y$	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 study¹¹ of the pyridinolysis.

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References

- S. D. Yoh, J. Kang and S. H. Kim, *Tetrahedron*, **44**, 2167 (1988).
- P. R. Wells, "Linear Free Energy Relationships", Academic Press, London, New York, 32, 1968.
- S. D. Yoh, Ph. D. Dissertation, Osaka Univ., 1973.
- Y. Tsuno, M. Fujio, S. D. Yoh, M. Sawada and Y. Yukawa, "Abstracts of the 25th Conference on Organic Reaction Mechanism", The Chemical Society of Japan, Tokyo, 199, 1974.
- S. D. Yoh, Y. Tsuno and Y. Yukawa, *J. Korean Chem. Soc.*, **28**(6), 443 (1984).
- S. D. Yoh, Y. Tsuno, M. Fujio, M. Sawada and Y. Yukawa, *J. Chem. Soc., Perkin Trans 2*, 7, 1989.

Chemoselective Reduction of Carboxylic Acid Esters with Potassium Triethylborohydride

Nung Min Yoon*, Ho Seok Yang, and Young Soo Hwang

Department of Chemistry, Sogang University, Seoul 121-742. Received October 17, 1988

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 (BH₃SMe₂) (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
	<i>N,N</i> -dimethylhexaneamide	<i>N,N</i> -dimethylhexaneamide	98.6
5	ethyl benzoate	benzyl alcohol	95
	capronitrile	capronitrile	94.9
6	isopropyl benzoate ^c	benzyl alcohol	93
	capronitrile	isopropyl benzoate capronitrile	7 95
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 benzyl alcohol isopropyl benzoate	14 12 83
		hexanol	95
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 effect. 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).

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References

1. N. G. Gaylord, *Reduction with Complex Metal Hydride*, Wiley-Interscience, New York, 1956.
2. (a) E. Winterfeldt, *Synthesis*, **617** (1975); (b) N. M. Yoon and Y. S. Gyoung, *J. Org. Chem.*, **50**, 2443 (1985).
3. H. C. Brown, S. C. Kim and S. Krishnamurthy, *J. Org. Chem.*, **45**, 1 (1980).
4. N. M. Yoon and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 2927 (1968).
5. H. C. Brown, Y. M. Choi and S. Narasimhan, *J. Org. Chem.*, **47**, 3153 (1982).
6. H. C. Brown and S. Narasimhan, *J. Org. Chem.*, **47**, 1604 (1982).
7. K. Soai and A. Ookawa, *J. Org. Chem.*, **51**, 4000 (1986).
8. N. M. Yoon, H. S. Yang and Y. S. Hwang, *Bull. Korean Chem. Soc.*, **8**, 285 (1987).

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

Mu Shik Jhon

Department of Chemistry, Korea Advanced Institute of Science and Technology,
Seoul 131. Received October 19, 1988

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-