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METAL-CATALYZED SYNTHESIS OF CARBOXYLIC ESTERS UTILIZING (E)-PHENYL 2-PYRIDYL KETONE O-ACYLOXIMES (PPAO)

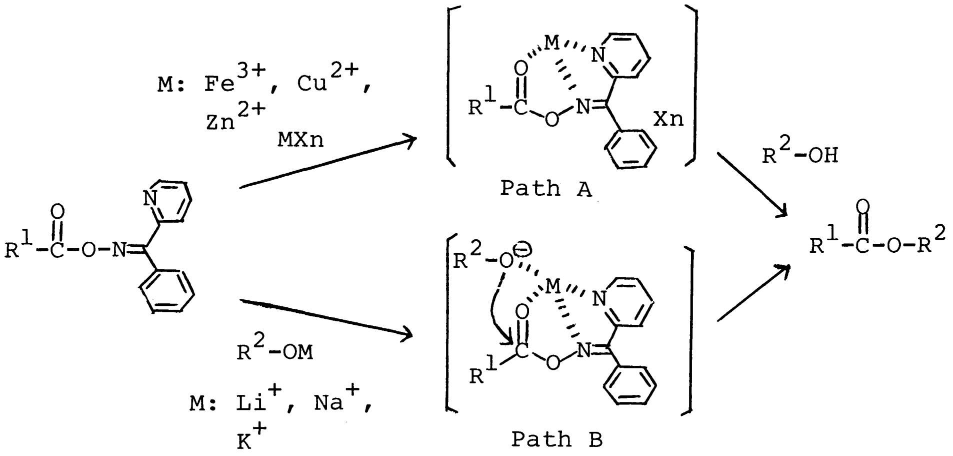
Tadayo MIYASAKA,* Hidehiro ISHIZU, Akihiro SAWADA,
Akiko FUJIMOTO, and Shunsaku NOGUCHI
Faculty of Pharmacy & Pharmaceutical Science, Fukuyama University,
985 Higashimura-Cho, Fukuyama, Hiroshima 729-02

(E)-phenyl 2-pyridyl ketone O-acyloximes (PPAO) could be highly activated by metal ions such as Fe^{3+}, Cu^{2+}, and Zn^{2+}, and the most effective catalyst for the synthesis of carboxylic esters was found to be Zn^{2+}. Furthermore, sterically hindered carboxylic esters were easily obtained utilizing PPAOs and alcoholates in high yields.

The synthesis of carboxylic esters is one of the most important and fundamental reaction in organic synthesis and many methods have been reported.1) Recently, several excellent methods, such as transition-state-stabilized macrolide ring closures2) and models for metalloenzymes,3-6) have been reported to investigate the role of metal ions in the enzyme systems. However, relatively little works have been reported on the synthetic methods utilizing metal chelating agents as functional leaving groups or chelation control reagents.

Recently, we reported the highly chemoselective synthesis of carboxamides7) and ketones8) utilizing (E)-phenyl 2-pyridyl ketone O-acyloximes (PPAO). During these studies, we attributed the high chemoselectivity of these reactions to the binding between cationic species of nucleophiles and PPAOs.9) We now wish to report here metal-catalyzed synthesis of carboxylic esters utilizing PPAOs, as a synthetic model reaction of metalloenzymes. Synthetic sequence is shown in Scheme 1.

These reactions were based on the following considerations. Path A: Since PPAOs were highly activated by metal ions, the reaction of PPAOs with alcohols which were inactive without metal ions (see entry 1 in Table 1) was catalyzed by metal ions to afford the corresponding carboxylic esters. Path B: Since counter cations of

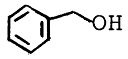
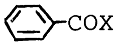
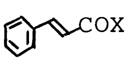
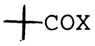
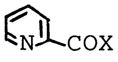
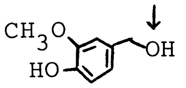


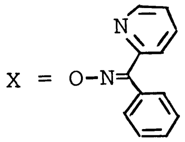
Scheme 1.

alcoholates were captured by PPAOs, and rather reactive free[10,11)] alcoholate anions attacked PPAOs, even sterically hindered carboxylic esters were easily obtained.

We first examined the catalytic effect of some metal ions in CH_2Cl_2 or CH_2Cl_2-CH_3CN. The results were summarized in Table 1. It was found that the most effective catalytic system for the synthesis of carboxylic esters was Zn^{2+}-CH_2Cl_2-

Table 1. Metal-catalyzed synthesis of carboxilic esters

Entry	PPAO[a)]	Alcohol	Metal MXn	Solvent	Time/h	Isolated[b)] yield/%
1	$C_{15}H_{31}COX$		-	CH_2Cl_2	24	0
2	〃	〃	$FeCl_3$	〃	18	76
3	〃	〃	〃	CH_2Cl_2-CH_3CN	18	73
4	〃	〃	$CuCl_2$	CH_2Cl_2	5	70
5	〃	〃	〃	CH_2Cl_2-CH_3CN	18	90
6	〃	〃	$ZnCl_2$	〃	18	92
7		〃	〃	〃	18	96
8		〃	〃	〃	18	92
9		〃	〃	〃	48	69
10		〃	〃	〃	18	76
11	$C_{15}H_{31}COX$	 c)	〃	〃	24	89

a) 

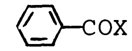
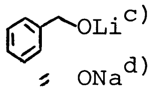
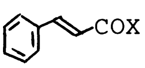
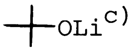
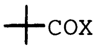
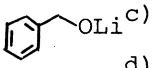
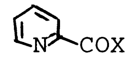
b) All the products gave satisfactory NMR and IR spectra.

c) 1.1 mmol of vanillyl alcohol was used. The arrow mark indicates the reaction point.

CH_3CN. Interestingly, primary alcohol of vanillyl alcohol was chemoselectively esterified in good yield, and phenol group was inactive in the present method.

Next, the reactions of PPAOs with alcoholates and the effect of counter cations such as Li^+, Na^+, and K^+ were investigated. The results were summarized in Table 2. It was found that the reaction rapidly proceeded to afford the corresponding carboxylic esters in high yields and the rate of esterification, $Li^+ > Na^+ > K^+$ (see entries 6-10 in Table 2), was directly proportional to the heat of hydration of these cationes.[12] These results show that alcoholate anions react with PPAOs in the form of free ions[10,11] rather than ion pairs, and cations strongly bind with PPAOs. Furthermore, it was found that the present reaction was applicable to the preparation of esters from sterically hindered carboxylic acids or alcohols. Though tertiary alcohols are generally esterified in very low yields by the most common acid-catalyzed condensation between carboxylic acid and alcohol, t-butyl cinnamate and benzyl pivalate were easily obtained in high yields (see entries 6-10 in Table 2).

Table 2. The preparation of carboxylic esters from PPAOs and alcoholates

Entry	PPAO	Alcoholate	Time/min[a]	Isolated yield/%[b]
1		 [c]	<5	97
2	〃	〃 ONa[d]	<5	94
3	〃	〃 OK[e]	20	98
4	$C_{15}H_{31}COX$	〃 ONa[d]	<5	96
5		〃 ONa[d]	<5	98
6	〃	 [c]	<5	95
7	〃	〃 OK	25	93
8		 [c]	<5	97
9	〃	〃 ONa[d]	15	97
10	〃	〃 OK[e]	35	90
11		〃 ONa[d]	<5	73

a) Checked by TLC, 5 min interval. b) All the products gave satisfactory NMR and IR spectra. c) 1.1 mmol of alcohol and n-BuLi were used. d) 1.1 mmol of benzyl alcohol and NaH were used. e) 1.1 mmol of potassium t-butoxide and 2 mmol of benzyl alcohol were used. t-Butyl benzoate and pivalate were not obtained.

A typical procedure for carboxylic ester synthesis is as follows. Path A: $ZnCl_2$ (159 mg, 1.1 mmol) was added to a solution of O-benzoyloxime (302 mg, 1 mmol) in CH_2Cl_2 (5 ml). After stirring for 10 min at room temperature under N_2 atmosphere, a solution of benzyl alcohol (162 mg, 1.5 mmol) in CH_3CN (5 ml) was added to the reaction mixture. After stirring for 18 h, the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography to afford benzyl benzoate (203 mg, 96%).

Path B: To a solution of t-butyl alcohol (82 mg, 1.1 mmol) in dry THF (5 ml) was added a solution of n-BuLi (1.53 mol/l) in hexane (0.72 ml) at 0 °C under N_2 atmosphere. After stirring for 10 min, O-cinnamoyloxime (328 mg, 1 mmol) was added to the reaction mixture, and stirred until O-cinnamoyloxime disappeared (checked by TLC) at room temperature under N_2 atmosphere. After evaporation of the solvent, the residue was purified by silica gel column chromatography to afford t-butyl cinnamate (193 mg, 95%).

References

1) T. Mukaiyama, Angew. Chem., Int. Ed. Engl., 18, 707 (1979); E. Haslam, Tetrahedron, 36, 2409 (1980) and references cited therein.
2) W. H. Rastetter and D. P. Phillion, J. Org. Chem., 45, 1535 (1980).
3) R. Breslow and L. E. Overman, J. Am. Chem. Soc., 92, 1075 (1970).
4) G. J. Lloyd and B. S. Cooperman, J. Am. Chem. Soc., 93, 4883 (1971).
5) D. S. Sigman, G. M. Wahl, and D. J. Creighton, Biochemistry, 12, 2236 (1972).
6) R. Breslow, R. Fairweather, and J. Keana, J. Am. Chem. Soc., 89, 2135 (1967).
7) T. Miyasaka and S. Noguchi, Chem. Lett., 1985, 701.
8) T. Miyasaka, H. Monobe, and S. Noguchi, Chem. Lett., 1986, 449.
9) See T. Miyasaka, H. Monobe, M. Masuhara, Y. Tsuruta, S. Noguchi, T. Taga. K. Kajiwara, T. Ohbatake, and K. Fuji, 12th Symposium on Progress in Organic Reaction and Synthesis, Nagoya, November 1985, Symposium Papers p. 73.
10) Y. Ishii, Kagaku, 18, 392 (1963).
11) J. H. Shroder and S. F. Acree, J. Chem. Soc., 1914, 2582 ; H. C. Robertson and S. F. Acree, J. Am. Chem. Soc., 37, 1902 (1915).
12) "Kagakubinran Kisohen (II) (in Japanese)," ed by The Chemical Society of Japan, Maruzen Inc., Tokyo (1975), p. 945.

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