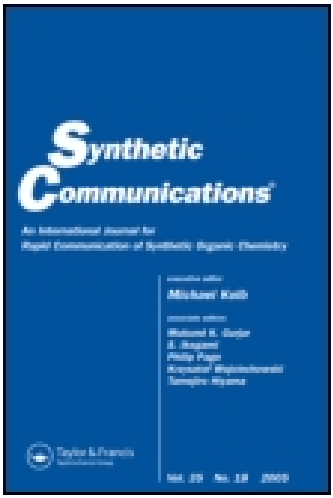

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Zinc Promoted Mild and Efficient Method for the Esterification of Acid Chlorides with Alcohols

J.S. Yadav [a] , Gondi SudershanReddy [a] , Dale Srinivas [a] & Konuru Himabindu [a]
[a] Indian Institute of Chemical Technology , Hyderabad, 500 007, India
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ZINC PROMOTED MILD AND EFFICIENT METHOD FOR THE ESTERIFICATION OF ACID CHLORIDES WITH ALCOHOLS

J.S. Yadav,* Gondi Sudershan Reddy, Dale Srinivas and Konuru Himabindu

Indian Institute of Chemical Technology, Hyderabad-500 007, India

Abstract : The esterification of variety of acid chlorides with alcohols in the presence of zinc is described. The easy formation of t-butyl and pivaloyl esters are the additional importance of this procedure.

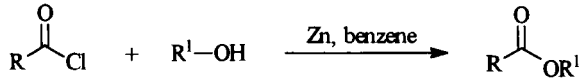
Esters are common intermediates in natural product chemistry due to their stability and accessibility for easy interconversion.[1] The traditional methods[2] use acid and alcohol in the presence of classic mineral acids which are corrosive in nature. Further modifications of methods have been made with alcohols and acid chlorides using zinc chloride,[3] magnesium[4] and inorganic solids such as alumina,[5] clay[6] and silica gel.[7] Since past decade, number of improved methods[8] have been developed using variety of catalysts. Some of these methods are also applicable for t-butyl esters, but most require heating, longer reaction times and tedious work up.

Recently, metal catalysted reactions[9] have gained wide popularity in organic synthesis because of their simple workup, activating or catalysing

* Address to whom correspondence should be made
IICT Communication No. 3785

nature and selectivity. Among the transition metals, zinc catalysis[10] has gained wide acceptance due to the unique property of surface coordination with polar groups. Herein we wish to report a zinc promoted rapid, convenient and general synthesis of esters, from acid chlorides and alcohols (Scheme).

Scheme



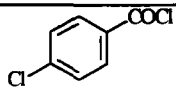
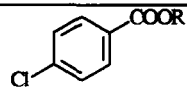
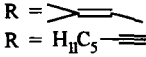
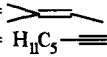
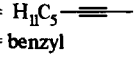
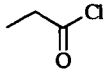
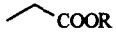
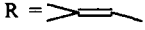
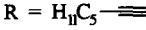
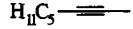
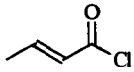
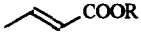
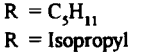
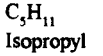
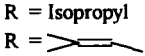
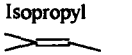
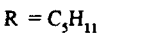
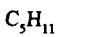
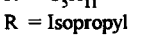
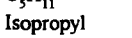
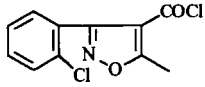
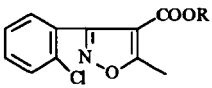
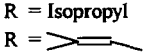
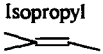
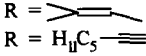
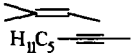
R = alky, aryl; R^1 = primary, secondary, tertiary, allyl, benzyl

The reaction of acid chlorides and alcohols is carried out in anhydrous benzene in the presence of zinc. The reaction is very fast and gives clean products in a few minutes.

Typical procedure; To a solution of acid chloride (10 mmol) in benzene (20 ml), activated zinc dust (10 mmol) was added and the suspension was stirred for 10 minutes. Then the benzene solution of alcohol (10 mmol in 20 ml) was added and stirring continued for given time (see table). The progress of the reaction was monitored by tlc. After completion of the reaction, the mixture is filtered and the solid washed with ether (100 ml). Combined organic layers were washed with $NaHCO_3$ solution (10%, 50 ml), water and dried over Na_2SO_4. Evaporation of the solvent gives esters in good yield and high purity. We have observed that the reaction can also be accomplished in toluene without loss of yields of esters.

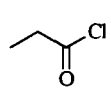
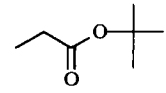
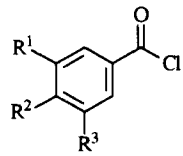
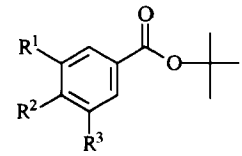
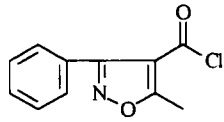
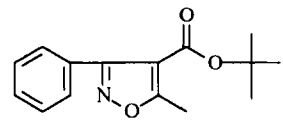
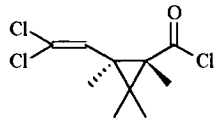
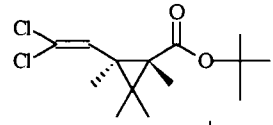
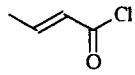
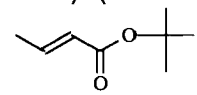
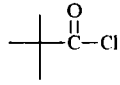
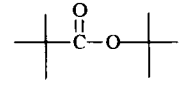
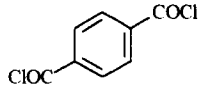
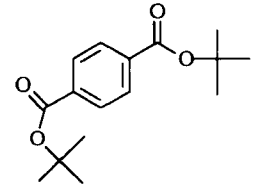
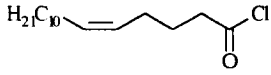
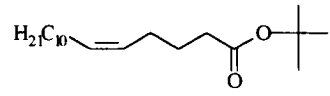
The efficiency of the reaction can be explained by the fact that the polar groups complex to the surface of zinc and increase the electrophilic character of the acyl groups.[11] The detailed mechanistic aspects of the reaction are under investigation. We have observed that the method has general application (see table) for the preparation of variety of esters. One of the remarkable features of the procedure is the formation of t-

Table-1 : Esterification of Acid Chlorides with Different Alcohols

Entry	Acid Chloride	Alcohols	Products	Time (min.)	Yield[a]
1.		ROH			
		a) R = C_5H_{11}	a) R = C_5H_{11}	8	92
		b) R = Isopropyl	b) R = Isopropyl	8	85
		c) R = 	c) R = 	6	84
		d) R = $H_{11}C_5$—	d) R = $H_{11}C_5$— 	9	89
		e) R = benzyl	e) R = benzyl	9	88
2.		ROH			
		a) R = C_5H_{11}	a) R = C_5H_{11}	6	90
		b) R = Isopropyl	b) R = Isopropyl	11	83
		c) R = 	c) R = 	7	85
		d) R = $H_{11}C_5$— 	d) R = $H_{11}C_5$— 	9	94
		e) R = benzyl	e) R = benzyl	10	85
3.		ROH			
		a) R = C_5H_{11}	a) R = C_5H_{11}	5	95
		b) R = Isopropyl	b) R = Isopropyl	8	90
		c) R = 	c) R = 	6	85
		d) R = $H_{11}C_5$— 	d) R = $H_{11}C_5$— 	5	88
		e) R = benzyl	e) R = benzyl	9	90
4.	t—C_4H_9COCl	ROH	t—C_4H_9COOR		
		a) R = C_5H_{11}	a) R = C_5H_{11}	9	90
		b) R = Isopropyl	b) R = Isopropyl	8	92
		c) R = 	c) R = 	10	85
		d) R = $H_{11}C_5$— 	d) R = $H_{11}C_5$— 	6	89
		e) R = benzyl	e) R = benzyl	10	82
5.		ROH			
		a) R = C_5H_{11}	a) R = C_5H_{11}	6	90
		b) R = Isopropyl	b) R = Isopropyl	9	88
		c) R = 	c) R = 	8	85
		d) R = $H_{11}C_5$— 	d) R = $H_{11}C_5$— 	8	92
		e) R = benzyl	e) R = benzyl	10	89

a : All the products exhibited physical and spectral (NMR, IR & Mass) properties in accord with the assigned structures.

Table-2 : Esterification of Acid Chlorides with t-Butanol

Entry	Acid Chloride	Product	Time (min.)	Yield[a]
1.			20	90
2.	 $R^1 = H, R^2 = Cl, R^3 = H$ $R^1 = R^2 = R^3 = H$ $R^1 = R^2 = R^3 = OCH_3$	 $R^1 = H, R^2 = Cl, R^3 = H$ $R^1 = R^2 = R^3 = H$ $R^1 = R^2 = R^3 = OCH_3$	20-30	85-90
3.			15	94
4.			12	93
5.			15	95
6.			15	85
7.			30	85
8.			18	89

a : All the products exhibited physical and spectral (NMR, IR & Mass) properties in accord with the assigned structures.

butyl and pivaloyl esters very rapidly.[8] This observation demonstrates the efficiency of the procedure. A double bond present elsewhere in the molecule remains unaffected whereas the reaction when carried out in the presence of bases such as triethylamine, pyridine require more time and can lead to double bond isomerized product.[12]

In conclusion, we have described a mild, highly efficient and convenient method for the esterification of wide variety of acid chlorides with a variety of alcohols such as primary, secondary, tertiary, allyl and benzyl. Further studies to determine the scope, limitation and application of zinc promoted protocol are under investigation and will be reported in due course.

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