

Catalytic Activity of Tin(II) Chloride in Esterification of Carboxylic Acids with Alcohols

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Esterification of carboxylic acids with alcohols has been recognized as a basic tool in synthetic organic chemistry.¹ Numerous esterification catalysts have been attempted for practical and substrates economical approaches² along with chemoselective processes.³ In connection with this report, several tin reagents such as organostannyl oxides, diorganotin dichlorides, 1,1'-dimethylstannocene, and distannoxane were reported as a catalyst for the esterification of carboxylic acids with alcohols.⁴ During the course of our ongoing studies on ruthenium-catalyzed organic synthesis,⁵⁻⁷ we have reported on the synthesis of indoles⁵ and quinolines⁶ by an alkyl group transfer from alkylamines to the nitrogen atom of anilines (amine exchange reaction) and it was found that the addition of tin(II) chloride dihydrate allows such a heteroannulation. Prompted by these findings and intrigued by the actual role of SnCl₂·2H₂O, we have directed our attention to the discovery of additive activity of tin(II) halides in organic reactions. Thus, we recently found that the addition of SnCl₂·2H₂O resulted in selective formation of *N*-monoalkylanilines for ruthenium-catalyzed *N*-alkylation of anilines with tetraalkylammonium halides⁸ and SnCl₂ catalyzed the cyclization of 2-aminophenols with carboxylic acids leading to 2-substituted benzoxazoles.⁹ Herein we report catalytic activity of SnCl₂ in esterification of carboxylic acids with alcohols.

The results of several attempted esterifications of benzoic acid (**1**) with propanol (**2**) are listed in Table 1. Typically, **1** was subjected to react with excess **2** in the presence of SnCl₂ to afford propyl benzoate (**3**). The yield of **3** increases with the increase of reaction temperature up to 100 °C for 20 h (runs 1-3). When the reaction was carried out in the presence of a catalytic amount of SnCl₂ (5-10 mol% based on **1**), **3** was produced in the range of 51-80% yields and the yield of **3** was improved by a longer reaction time (runs 4-6). Performing the reaction in the absence of SnCl₂ produced **3** in only 7% yield with incomplete conversion of **1** (run 7). Similar observation has already been made by Chattopadhyay *et al.* in the diorganotin-catalyzed esterification of carboxylic acids with alcohols.^{4c} However, treatment of equimolar amounts of **1** and **2** in dioxane resulted in lower yields of **3** (runs 8 and 9).

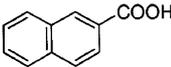
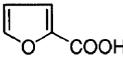
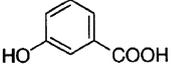
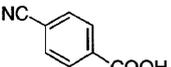
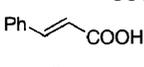
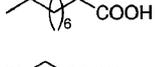
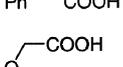
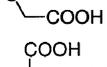
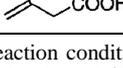
Given these results, the reactions of various carboxylic acids with **2** were screened using two sets of reaction conditions (SnCl₂ = 0.2 mmol, for 40 h; SnCl₂ = 1 mmol, for

Table 1. SnCl₂-catalyzed esterification of **1** with **2**^a

Run	PhCOOH 1	+ PrOH 2	Temp (°C)	Time (h)	Yield (%) ^b
1	1	1	100	20	94
2	1	1	80	20	61
3	1	1	60	20	25
4	0.1	1	100	20	51
5	0.2	1	100	20	61
6	0.2	1	100	40	80
7	—	1	100	40	7
8 ^c	1	1	100	20	13
9 ^c	0.2	1	100	40	10

^aAll reactions were carried out with **1** (2 mmol) and **2** (2 mL) unless otherwise stated. ^bIsolated yield based on **1**. ^c**2** (2 mmol) in dioxane (2 mL).

Table 2. SnCl₂-catalyzed esterification of carboxylic acids with **2**^a

Carboxylic acids	SnCl ₂ (mmol)	Time (h)	Yield (%) ^b
PhCOOH	0.2	40	80
	1	20	94
	1	20	67 ^c
	0.2	40	67
	1	20	87
	0.2	40	69
	1	20	84
	0.2	40	96
	1	20	99
	0.2	40	54
	1	20	87
	0.2	40	96
	1	20	95
	0.2	40	89
	1	20	91
	0.2	40	97
	1	20	98
	0.4	40	83
	2	20	89
	2	20	79

^aReaction conditions: Carboxylic acid (2 mmol), **2** (2 mL), at 100 °C.

^bIsolated yield. ^cIsopropyl alcohol was used.

20 h). The results are summarized in Table 2. Aryl and heteroaryl carboxylic acids were readily esterified with **2**. When isopropyl alcohol was used in place of **2**, the corresponding ester was also produced. 4-Cyanobenzoic acid was also esterified with **2** with the tolerance of cyano group.¹⁰ α,β -Unsaturated carboxylic acid, cinnamic acid was readily esterified with **2** irrespective of the used amounts of SnCl₂. In the cases of alkyl carboxylic acids, the reaction also proceeded well and the corresponding esters were produced in the range of 89-98% yields. With dicarboxylic acids, diglycolic acid and itaconic acid, the corresponding diesters were also formed in similar yields and no double bond migration was observed.¹¹

Typical experimental procedure is as follows. **1** (2 mmol), **2** (2 mL), and SnCl₂ (0.2-1 mmol) were placed in a 5-mL screw-capped vial. The reaction mixture was allowed to react at 100 °C for 20-40 h. After the excess alcohol was removed under reduced pressure, the crude mixture was separated by column chromatography (silica gel, ethyl acetate/hexane) to give **3** (61-94%).

In conclusion, we have shown that a convenient esterification of carboxylic acids with alcohols was achieved by the use of readily available SnCl₂. More practical esterification method by the use of equimolar amounts of both substrates in the presence of a catalytic amount of SnCl₂ and application of other metal halides are currently investigated.

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- IR spectrum of the product showed C=N stretching band (2232 cm⁻¹).
- Dipropyl itaconate: colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 0.93 (t, *J* = 7.5 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 3H), 1.60-1.74 (m, 4H), 3.35 (s, 2H), 4.06 (t, *J* = 6.8 Hz, 2H), 4.12 (t, *J* = 6.8 Hz, 2H), 5.69 (s, 1H), 6.33 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 10.35, 10.43, 21.93, 21.96, 37.85, 66.51, 66.61, 128.13, 134.17, 166.27, 170.82.