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 approaches[2] 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 indoles[5] and quinolines[6] 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 $SnCl_2{\cdot}2H_2O$, 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 $SnCl_2{\cdot}2H_2O$ resulted in selective formation of *N*-monoalkylanilines for ruthenium-catalyzed *N*-alkylation of anilines with tetraalkylammonium halides[8] and $SnCl_2$ catalyzed the cyclization of 2-aminophenols with carboxylic acids leading to 2-substituted benzoxazoles.[9] Herein we report catalytic activity of $SnCl_2$ 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 $SnCl_2$ 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 $SnCl_2$ (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 $SnCl_2$ 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).

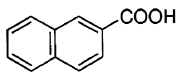
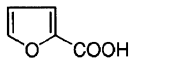
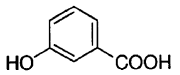
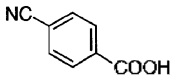
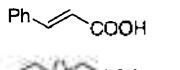
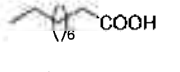
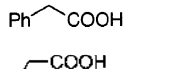
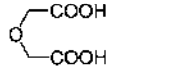
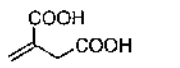
Given these results, the reactions of various carboxylic acids with **2** were screened using two sets of reaction conditions ($SnCl_2$ = 0.2 mmol, for 40 h; $SnCl_2$ = 1 mmol, for

Table 1. $SnCl_2$-catalyzed esterification of **1** with **2**[a]

Run	$SnCl_2$ (mmol)	Temp (°C)	Time (h)	Yield (%)[b]
1	1	100	20	94
2	1	80	20	61
3	1	60	20	25
4	0.1	100	20	51
5	0.2	100	20	61
6	0.2	100	40	80
7	–	100	40	7
8[c]	1	100	20	13
9[c]	0.2	100	40	10

[a]All reactions were carried out with **1** (2 mmol) and **2** (2 mL) unless otherwise stated. [b]Isolated yield based on **1**. [c]**2** (2 mmol) in dioxane (2 mL).

Table 2. $SnCl_2$-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

[a]Reaction conditions: Carboxylic acid (2 mmol), **2** (2 mL), at 100 °C. [b]Isolated yield. [c]Isopropyl alcohol was used.

20 h). The results are summarized in Table 2. Aryl and heteroaryl carboxylic acids were readly 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 $SnCl_2$. In the cases of alkyl carboxylic acids, the reaction also prodeeded 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 $SnCl_2$ (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 $SnCl_2$. More practical esterification method by the use of equimolar amounts of both substrates in the presence of a catalytic amount of $SnCl_2$ and application of other metal halides are currently investigated.

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10. IR spectrum of the product showed C=N stretching band (2232 cm^{-1}).
11. Dipropyl itaconate: colorless oil; ^1H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.35, 10.43, 21.93, 21.96, 37.85, 66.51, 66.61, 128.13, 134.17, 166.27, 170.82.