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A FACILE SYNTHESIS OF CARBOXYLIC ESTERS AND CARBOXAMIDES BY THE USE OF 1,1'-DIMETHYLSTANNOCENE AS A CONDENSING REAGENT

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Various carboxylic esters or carboxamides are prepared in good yields under nearly neutral conditions from equimolar amounts of free carboxylic acids and alcohols or amines, respectively, by the use of 1,1'-dimethylstannocene as a condensing reagent.

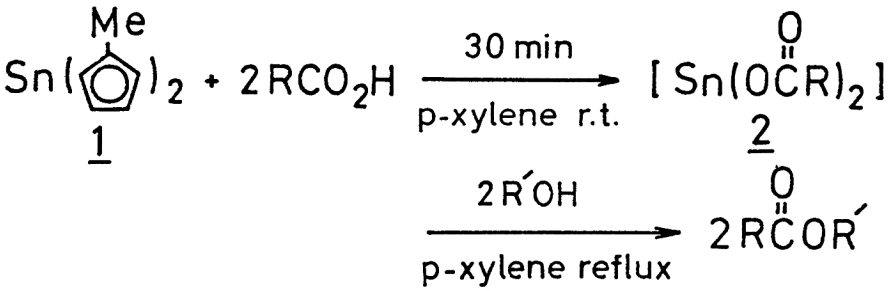
In the previous communication, we have demonstrated that acylation of alcohols and amides proceeds under mild conditions by the use of 1,1'-dimethylstannocene and acyl chlorides to afford the acylated products in good to excellent yields.[1] These results show that 1,1'-dimethylstannocene behaves as an efficient hydrogen chloride captor. As it became apparent that 1,1'-dimethylstannocene has unique characteristics as a synthetic reagent, we have further studied the application of these properties to new synthetic reactions.

In this communication, we wish to report a facile method for the synthesis of carboxylic esters or carboxamides from equimolar amounts of free carboxylic acids and alcohols or amines, respectively, under nearly neutral conditions by the use of 1,1'-dimethylstannocene as a condensing reagent. Usually, the preparation of carboxylic esters or carboxamides from free carboxylic acids and alcohols or amines requires excess amounts of one of the starting materials and removal of water formed in the reaction, except when N,N'-dicyclohexylcarbodiimide[2] and 2-halopyridinium salts[3] are employed as condensing reagents.

In the first place, a condensation of benzoic acid and 3-phenylpropanol was carried out as a model experiment. 3-Phenylpropanol (1 mmol) was treated with 1,1'-dimethylstannocene (1 mmol) at room temperature in toluene for 30 min, and then benzoic acid (1 mmol) was added to the reaction mixture. Although the reaction did not proceed at room temperature, the corresponding ester, 3-phenylpropyl benzoate was obtained in 49% yield after being refluxed for 5 h, followed by usual work-up. On the other hand, in the absence of 1,1'-dimethylstannocene or in the presence of stannous chloride in place of 1,1'-dimethylstannocene, the above reaction hardly took place. These observations show that 1,1'-dimethylstannocene acts as an efficient dehydrating reagent.

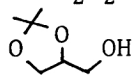
After examination on the reaction conditions, that is, the solvent, the reaction temperature and time, and, the molar ratio and the order of the addition of the reagents, the optimum yield was given in the following procedure. Benzoic acid and 3-phenylpropanol were successively added to 0.5 molar amounts of 1,1'-

dimethylstannocene, and the reaction was carried out in p-xylene under reflux for 3 h to afford the corresponding ester in 81% yield and 13% of 3-phenylpropanol was recovered. It should be further noted that the corresponding acid anhydride or ether was not detected when either a carboxylic acid or an alcohol was respectively treated with 1,1'-dimethylstannocene in p-xylene under reflux. Based on these observations, the reaction would proceed as shown in the following equation.



As illustrated in the equation, a free carboxylic acid initially reacts with 1,1'-dimethylstannocene (1) to give the tin(II) carboxylate (2),[4] which in turn reacts with an alcohol to yield a carboxylic ester.

Table I Synthesis of Carboxylic Esters[a]

Entry	RCOOH	R'OH	Time(h)	Yield(%)[b]
1	$Ph(CH_2)_3COOH$	$Ph(CH_2)_3OH$	3	86
2	$PhCH(C_2H_5)COOH$		3	85
3	$(CH_3)_3CCOOH$		6	80
4	$Ph(CH_2)_3COOH$	$Ph(CH_2)_2CH(CH_3)OH$	6	80
5	$PhCH(C_2H_5)COOH$		9	79
6	PhCOOH	$Ph(CH_2)_3OH$	3	81
7	$CHCl_2COOH$		3	74
8	$CH_3CO(CH_2)_2COOH$		3	74
9	$CH_3OCO(CH_2)_2COOH$		3	74
10	$CH_3CH=CHCH=CHCOOH$		3	76
11	$Cl(CH_2)_2COOH$		4	78
12	$Ph(CH_2)_3COOH$	$Cl(CH_2)_2OH$	3	75
13			4	75

a) Molar ratio of RCOOH:R'OH:1 = 1:1:0.5.

b) Isolated yield. All samples gave satisfactory NMR and IR spectra.

A typical experimental procedure is described for the reaction of benzoic acid and 3-phenylpropanol; to a p-xylene (3 ml) solution of 1,1'-dimethylstannocene (119 mg, 0.430 mmol) was added benzoic acid (105 mg, 0.860 mmol) in p-xylene (2 ml) at room temperature under an argon atmosphere. After the mixture was stirred for 30 min, 3-phenylpropanol (117 mg, 0.860 mmol) in p-xylene (1.5 ml) was added. After the resulting mixture was refluxed for 3 h, white precipitate appeared and then pH 7 phosphate buffer was added. The aqueous phase was extracted with ether three times and the combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the resulting crude product was purified by silica-gel thin layer chromatography to afford 3-phenylpropyl benzoate (167 mg, 81%).

In a similar manner, various esters were prepared in good yields as summarized in Table I. It should be noted that the present method is applicable to the preparation of esters from equimolar amounts of free carboxylic acids and alcohols having bulky alkyl group or functional group sensitive toward acid or base.

Next, the synthesis of carboxamides was examined taking advantage of the efficient dehydrating ability of 1,1'-dimethylstannocene. After 4-phenylbutylic acid (1 mmol) was treated with 1,1'-dimethylstannocene (1 mmol) in p-xylene at room temperature, a p-xylene solution of 2-phenylethylamine (1 mmol) was added. The reaction mixture had been refluxed for 3 h to afford the corresponding carboxamide in 86% yield. According to this procedure, various carboxamides were prepared in good yields (see Table II).

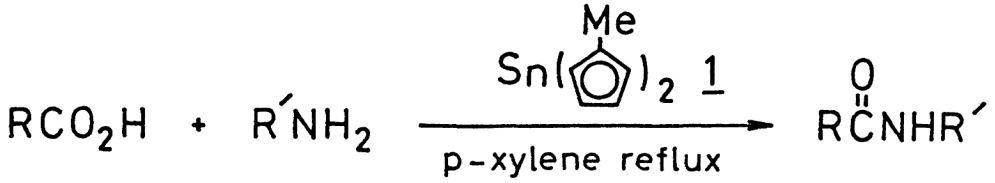


Table II Synthsis of Carboxamides[a)]

Entry	RCOOH	R'NH_2	Time(h)	Yield(%)[b)]
1	$Ph(CH_2)_3COOH$	$Ph(CH_2)_2NH_2$	3	86
2	$PhCH(C_2H_5)COOH$		3	82
3	$(CH_3)_3CCOOH$		9	74
4	PhCOOH		3	72
5	$Ph(CH_2)_3COOH$	$PhCH(CH_3)NH_2$	6	81
6		$PhCH_2C(CH_3)_2NH_2$	9	52
7		$PhNH_2$	3	80
8		$(C_4H_9)_2NH$	9	62

a) Molar ratio of RCOOH:R'NH_2:1 = 1:1:1.

b) Isolated yield. All samples gave satisfactory NMR and IR spectra.

It is noted that the present reaction provides a convenient method for the preparation of various carboxylic esters or carboxamides including sterically hindered ones and functionalized ones in good yields from equimolar amounts of free carboxylic acids and alcohols or amines under nearly neutral conditions. Further investigation on application to new synthetic reactions using 1,1'-dimethylstannocene as a dehydrating reagent is now in progress.

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