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FACILE METHOD FOR THE ACYLATION OF ALCOHOLS AND AMIDES BY THE USE OF 1,1'-DIMETHYLSTANNOCENE AND ACYL CHLORIDES

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Acylation of alcohols and amides was effected under mild conditions by the use of 1,1'-dimethylstannocene and acyl chlorides, giving the corresponding esters and imides in good to excellent yields.

Recently, divalent tin mediated aldol reactions[1,2] have been developed in our laboratory, and it became apparent that the characteristic properties of divalent tin species play important roles in these reactions. These results prompted us to investigate the reactivity of tin(II) alkoxides towards electrophiles such as acyl chlorides.

It has been known in the literature that various tin(II) compounds are readily available by treating active hydrogen compounds with 1,1'-dimethylstannocene (1).[3] However, few examples have been reported concerning their application to organic synthesis.

In this communication, we wish to report a facile method for the acylation of alcohols and amides by the use of 1,1'-dimethylstannocene (1) and acyl chlorides (molar ratio of 1 : alcohol : acyl chloride = 0.6 : 1 : 1.2; 1 : amide : acyl chloride = 1 : 1 : 2). In the first place, acylation of 3-phenylpropanol with benzoyl chloride was carried out as a model experiment. 3-Phenylpropanol (1 mmol) was treated with 1,1'-dimethylstannocene (1, 0.6 mmol) at room temperature in toluene for 30 min to prepare *in situ* the tin(II) alkoxide. Then benzoyl chloride (1.2 mmol) was added and the reaction mixture was kept stirring for 2 h at room temperature. After usual work-up, the acylated product, 3-phenylpropyl benzoate, was obtained in 59% yield. Concerning the solvent, the addition of hexamethylphosphoric triamide (17 vol%) proved to be very effective for the present reaction, and the yield of the above reaction was improved up to 90%. Under the above mentioned conditions, the reaction between various alcohols and acyl chlorides was studied, and the corresponding esters, even those having base sensitive functions, were obtained in good to excellent yields (see Table I).

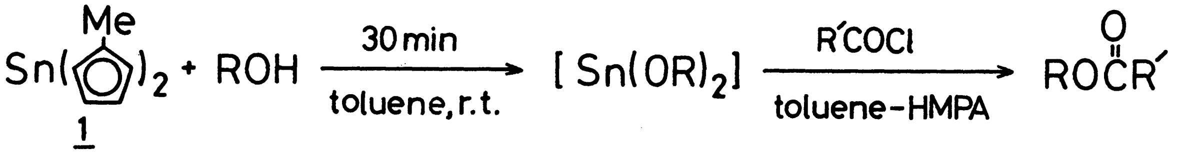
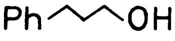
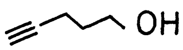
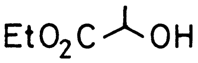
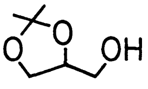
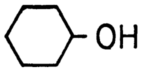
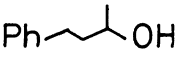
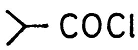
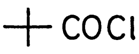
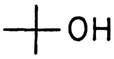
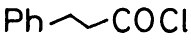
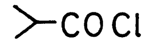
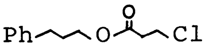
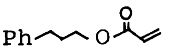
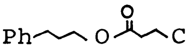
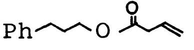
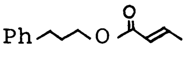


Table I. Acylation of alcohols

Entry	ROH	R'COCl	Temp.	Time(h)	Yield(%)[a]
1		PhCOCl	r.t.	2	90
2		$Me(CH_2)_{10}COCl$	r.t.	2	91
3			r.t.	2	90
4			r.t.	2	85[b]
5			r.t.	2	81[c]
6			r.t.	2	94
7	PhOH		r.t.	2	83
8			r.t.	2	94
9			r.t.	2	85
10			r.t.	15	83
11			r.t.	2	78
12			r.t.	8	85
13			r.t.	12	81
14			100°C	2.5	63
15			100°C	5	73
16			100°C	7	60

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

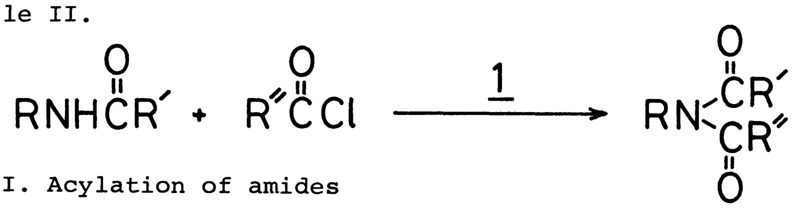
b) Acylation using Et_3N in place of 1 gave  (40%) and  (26%); acylation using pyridine gave  (88%).

c) Acylation using Et_3N in place of 1 gave only double bond isomerized product,  (90%); acylation using pyridine gave  (77%).

In the preparation of esters from alcohols and acyl chlorides, some kinds of metal alkoxides are generally used to enhance the nucleophilicity of alcohols.[4-8] However, most of the metal alkoxides have disadvantages in their preparations, for example, in the case of sodium,[4] lithium,[5] or halogenomagnesium[6] alkoxide, the reactions are usually carried out under strongly basic conditions. On the other hand, tin(II) alkoxides are prepared under nearly neutral conditions. Therefore, the present method is very effective for the preparation of esters from alcohols and acyl chlorides both of which have various substituents, such as chlorine atom (Entry 3, 4, 8), ester (Entry 6, 10), multiple bond (Entry 5, 9) and acetal (Entry 11).

A typical reaction procedure is described for the reaction of 3-phenylpropanol and benzoyl chloride; to a toluene (2 ml) solution of 1,1'-dimethylstannocene (1, 153 mg, 0.552 mmol) was added 3-phenylpropanol (125 mg, 0.921 mmol) in toluene (1.5 ml) at room temperature under an argon atmosphere. After the mixture was stirred for 30 min, hexamethylphosphoric triamide (1 ml) and benzoyl chloride (155 mg, 1.11 mmol) in toluene (1.5 ml) were successively added. The mixture was kept stirring for 2 h at room temperature and quenched with pH 7 phosphate buffer. 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, the resulting crude product was purified by silica-gel thin layer chromatography to afford 3-phenylpropyl benzoate (200 mg, 90%).

The results show that $Sn(OR)_2$ is reactive towards acyl chloride and also behaves as an efficient hydrogen chloride captor in the above reaction. Based on this observation, acylation of amides was examined. After N-benzylacetamide (1 mmol) was treated with 1,1'-dimethylstannocene (1, 1 mmol) in THF (3.5 ml) at room temperature, a THF (1.5 ml) solution of benzoyl chloride (2 mmol) and hexamethylphosphoric triamide (1 ml) were added. The reaction mixture was kept stirring at 60°C for 5 h to afford the corresponding imide in excellent yield. Usually in acylation of amide, an elevated temperature[9,10] or basic[9,11] or acidic condition[12] is required, while, the present reaction proceeded under mild conditions to give the acylated products in good to excellent yields. The results are summarized in Table II.



$$RNHCR' + R''CCl \xrightarrow{1} RN(COR')(COR'')$$

Table II. Acylation of amides

Entry	R	R'	R"	Solv.	Temp.	Time(h)	Yield(%)[a]
1	$PhCH_2$-	CH_3-	Ph-	THF-HMPA	60°C	5	93
2	$PhCH_2$-	CH_3-	CH_3CH_2-	THF-HMPA	60°C	5	86
3	$PhCH_2$-	CH_3-	$(CH_3)_2CH$-	THF-HMPA	60°C	3	82
4	$-(CH_2)_5-$		Ph-	THF	r.t.	5	quant.
5	$-(CH_2)_5-$		$PhCH_2CH_2$-	THF	r.t.	7	99

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

It is noted that various acylated products of alcohols or amides can be easily obtained under mild conditions in good to excellent yields by treating alcohols or amides with 1,1'-dimethylstannocene (1) and acyl chlorides. Further studies directed towards application to new synthetic reactions utilizing the unique charasteristics of 1,1'-dimethylstannocene (1) are now in progress.

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