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The Esterification Reaction between Silyl Derivatives of Carboxylic Acids and Alcohols by the Promotion of a Catalytic Amount of Lewis Acid

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Various carboxylic esters are prepared in good to excellent yields by the reaction of equimolar amounts of silyl derivatives of carboxylic acids and alcohols by using a catalytic amount of active Lewis acid in hexamethyldisiloxane, a solvent.

Though a number of esterification procedures have been reported up to now, there have been known a few methods for the effective preparation of esters from equimolar amounts of carboxylic acids and alcohols under mild conditions.[1, 2)] Recently, it was found that the catalytic esterification reactions via mixed anhydrides were successfully accomplished by using an active Lewis acid catalyst.[1)] In the above reactions, an equimolar amount of *p*-trifluoromethylbenzoic anhydride was essentially needed in order to generate an active mixed anhydride, which in turn smoothly reacted with silyl derivatives of alcohol to form the corresponding esters. Then, we planned to decrease the amount of *p*-trifluoromethylbenzoic anhydride in the above reactions or to complete the reaction in the absence of the anhydride by the promotion of a catalytic amount of active Lewis acid.

First, 20 mol% of $TiCl_2(OTf)_2$ was used as a catalyst in the reactions of equimolar amounts of silyl derivatives of 3-phenylpropionic acid and 3-phenylpropanol in various solvents in the absence of *p*-trifluoromethylbenzoic anhydride. The reaction did not proceed at all at room temperature, while the reaction proceeded at 60 °C in non polar solvents such as 1,2-dichloroethane and toluene and the desired ester was obtained in 62% and 76% yields, respectively. In the polar solvents, tetrahydrofuran and acetonitrile, the above reaction proceeded slowly under the same conditions to give the desired ester in 22% and 29% yields, respectively. On the other hand, hexamethyldisiloxane, in which silyl derivatives were very stable, was quite effective as a solvent for the present catalytic esterification reaction to afford the desired ester in 82% yield under the same conditions.

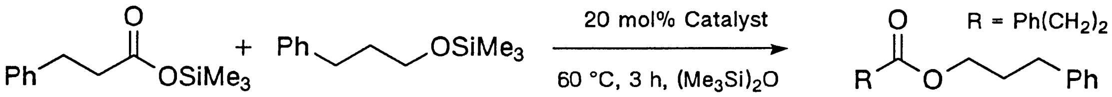
Next, several active Lewis Acids were examined by taking the above reaction as a model and it was shown that a catalyst generated from $SiCl_4$ and silver triflate gave a good result (Table 1, entry 3). This result was different from that obtained in the previously reported mixed anhydride method where titanium (IV) or tin (II) was very effective catalyst.[1)]

Several examples of the present esterification reaction are demonstrated in Table 2. In all cases, the corresponding esters were obtained in good to excellent yields, especially in entry 3, the use of only 2 mol% of the catalyst gave the desired ester in nearly quantitative yield. It is noted that the respective reactions of silyl derivatives of α-mono- or disubstituted carboxylic acid and benzoic acid with a silyl derivative of alcohol also proceed smoothly to give the desired esters in good yields (entries 5-7).

A typical experimental procedure is described: to a suspension of AgOTf (0.064 mmol) in hexamethyldisiloxane (1.0 ml), were added a solution of $SiCl_4$ (0.032 mmol) in toluene (0.1 ml) and a mixture of trimethylsilyl 3-phenylpropionate (0.17 mmol) and 3-phenyl-1-propyl trimethylsilyl ether (0.17 mmol) in hexamethyldisiloxane (1.0 ml). The reaction mixture was stirred for 3h at 60 °C, and then quenched with aq. sat. $NaHCO_3$. After usual work up, the crude product was purified by preparative TLC on silica gel to afford 3-phenylpropyl 3-phenylpropionate (96% yield). Other yields in Tables 1 and 2 are also isolated yields.

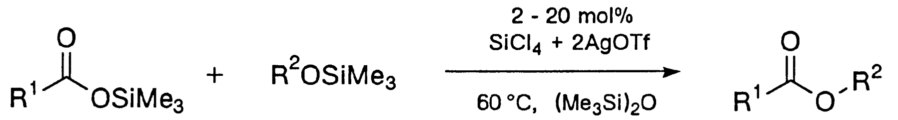
Further investigation of catalytic esterification of silyl derivatives of carboxylic acids and alcohols is now in progress.

Table 1. Effect of Catalyst



Entry	Catalyst	Yield / %	Entry	Catalyst	Yield / %
1	$TiCl_2(OTf)_2$	82	5	$Sn(OTf)_2$	37
2	$TiCl_4$ + $2AgSbF_6$	7	6	$AlCl_3$ + 2AgOTf	71
3	$SiCl_4$ + 2AgOTf	96	7	$GaCl_3$ + 2AgOTf	62
4	$SnCl_4$ + 2AgOTf	88	8	$ZrCl_4$ + 2AgOTf	73

Table 2. Synthesis of Carboxylic Esters



Entry	R^1	R^2	Cat. / mol%	Time / h	Yield / %
1	$Ph(CH_2)_2$	$Ph(CH_2)_3$	20	3	96
2	$Ph(CH_2)_2$	$Ph(CH_2)_3$	10	6	94
3	$Ph(CH_2)_2$	$Ph(CH_2)_3$	2	20	97
4	$Ph(CH_2)_2$	$Ph(CH_2)_2CH(CH_3)$	20	20	83
5	$c\text{-}C_6H_{11}$	$Ph(CH_2)_3$	15	15	94
6	^{t}Bu	$Ph(CH_2)_3$	20	15	78
7	Ph	$Ph(CH_2)_3$	20	15	79

References

1) T. Mukaiyama, I. Shiina, and M. Miyashita, *Chem. Lett.*, **1992**, 625, and references cited therein; T. Mukaiyama, M. Miyashita, and I. Shiina, *ibid.*, **1992**, 1747.

2) Tritylation of silyl derivatives of carboxylic acids by using a catalytic amount of trimethylsilyltriflate was reported; S. Murata and R. Noyori, *Tetrahedron Lett.*, **22**, 2107 (1981).

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