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A Simple Method for the Esterification of Carboxylic Acids Using Chlorosilanes

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Synopsis. Various carboxylic esters, including some with bulky substituents, are prepared in good yields from carboxylic acids and alcohols under mild conditions by the use of trimethylchlorosilane, dimethyldichlorosilane, methyltrichlorosilane, or tetrachlorosilane.

The esterification of carboxylic acids with alcohols is one of the most important reactions in organic synthesis, and quite a number of methods have been investigated. Among them, 2-halopyridinium salts,[1] (chloromethylene)dimethylammonium chloride,[2] 1-(sulfonyloxy)benzotriazoles[3] and graphite bisulfate[4] have been used successfully as coupling reagents for the reaction. In the course of the study of the reaction of acetoxytrimethylsilane with alcohols in the presence of hydrogen chloride,[5] we found that trimethylchlorosilane was a convenient reagent for the esterification of carboxylic acids with alcohols.

In this note, we wish to report some results of the esterification carried out by the use of chlorosilanes. The esterification was performed under the following standard conditions: $(CH_3)_3SiCl$ (1.7 mmol) was added to a mixture of RCOOH (3.3 mmol) and R'OH (5.0 mmol) in 2-methyltetrahydrofuran. After the reaction mixture had been allowed to stand for 15 min at room temperature, the products were analysed by GLPC. In a neat reaction, the starting homogeneous reaction mixture progressively separates into two layers as the reaction proceeds. Therefore, the solvent was chosen so as to be keep the reaction mixture homogeneous and to be favorable for GLPC analysis.

The results obtained with various carboxylic acids and alcohols by the use of trimethylchlorosilane are given in Table 1. In all cases, the production of hexamethyldisiloxane was confirmed. Although the esterification with secondary alcohols is slower than that with primary alcohols, the yields of all the esters, including sterically hinderd isobutyl pivalate, are very high. Therefore, trimethylchlorosilane can be said to be a very efficient and convenient reagent for the esterification of carboxylic acids with primary and secondary alcohols at room temperature. When, however, *t*-butyl alcohol and phenol were subjected to a reaction with acetic acid in the presence of trimethylchlorosilane, the reaction products were complicated and the yields of *t*-butyl acetate and phenyl acetate were only 9 and 19% respectively.

The rate of esterification decreases with the decrease in the amount of trimethylchlorosilane added. However, it must be emphasized that 1 mol of trimethylchlorosilane serves to produce more than 1 mol of the ester. This indicates that trimethylchlorosilane does not participate only as a hydrogen chloride source and/or a dehydrating agent in the reaction. When methoxytrimethylsilane, which is expected to be formed by the reaction of trimethylchlorosilane and methanol, was allowed to react with acetic acid in the presence of hydrogen chloride, methyl acetate was obtained in a 93% yield, along with the production of hexamethyldisiloxane. Therefore, the following scheme seems to be most probable for the esterification with trimethylchlorosilane:

$$\mathrm{(CH_3)_3SiCl + R'OH \longrightarrow (CH_3)_3SiOR' + HCl} \qquad (1)$$

$$\mathrm{RCOOH + (CH_3)_3SiOR' \xrightarrow{HCl} RCOOR' + (CH_3)_3SiOH} \qquad (2)$$

$$\mathrm{(CH_3)_3SiOH + R'OH \xrightarrow{H^+} (CH_3)_3SiOR' + H_2O} \qquad (3)$$

$$\mathrm{2(CH_3)_3SiOH \longrightarrow (CH_3)_3SiOSi(CH_3)_3 + H_2O} \qquad (4)$$

TABLE 1. ESTERIFICATION OF VARIOUS CARBOXYLIC ACIDS WITH ALCOHOLS USING $(CH_3)_3SiCl$[a] $\mathrm{RCOOH+R'OH \xrightarrow{(CH_3)_3SiCl} RCOOR'}$

R	R'	$\frac{[(CH_3)_3SiCl]}{[RCOOH]}$	Solvent	Reaction time	Yield of ester/%
CH_3	CH_3	0.13	2-Me–THF	30 min	72
CH_3	CH_3	0.13	2-Me–THF	110 min	87
CH_3	CH_3	0.5	2-Me–THF	15 min	97
C_2H_5	CH_3	0.5	2-Me–THF	15 min	95
$(CH_3)_2CH$	CH_3	0.5	THF	15 min	98
C_2H_5	CH_3	0.5	2-Me–THF	100 h	93
$(CH_3)_3C$	CH_3	0.5	THF	15 min	91
$(CH_3)_3C$	$(CH_3)_2CHCH_2$	0.5	2-Me–THF	15 min	90
CH_3	C_2H_5	0.5	2-Me–THF	15 min	92
CH_3	$CH_2{=}CHCH_2$	0.6	2-Me–THF	15 min	92
CH_3	$(CH_3)_2CH$	0.5	2-Me–THF	15 min	37
CH_3	$(CH_3)_2CH$	0.5	2-Me–THF	24 h	93
CH_3	$C_2H_5(CH_3)CH$	0.5	2-Me–THF	48 h	95
CH_3	c-C_6H_{11}	0.5	n-$C_{11}H_{24}$	48 h	81

a) Reactions were performed at room temperature.

In the initial stage of the reaction where alcohol remains in a large quantity, Eq. 3[6] may be faster than Eq. 4. However, in the final stage, Eq. 4 may become favorable. During the reaction, the alkoxytrimethylsilane produced in Eq. 3 participates repeatedly in the esterification of carboxylic acid *via* Eq. 2.

Other chlorosilanes can be used in this esterification as well as trimethylchlorosilane. By using dimethyldichlorosilane ($[(CH_3)_2SiCl_2]/[CH_3COOH]=0.25$), methyltrichlorosilane ($[CH_3SiCl_3]/[CH_3COOH]=0.17$) and tetrachlorosilane ($[SiCl_4]/[CH_3COOH]=0.13$) in the reaction of acetic acid and methanol, methyl acetate was obtained in 98, 97, and 96% yields respectively.

Experimental

The gas-chromatographic analyses were made by a Yanagimoto GCG-5DH apparatus on a 3-m column containing 30% dioctyl phthalate on Celite 545 or a 2.5-m column containing 25% silicon DC-200 on Celite 545, using helium as the carrier gas. The NMR spectrum was obtained on a JEOL JNM-100 apparatus, with tetramethylsilane as the internal standard.

All of the reagents and solvents were used after distillation. The products were identified and estimated by GLPC. Commercial materials were used as the standerds except for *s*-butyl pivalate. The *s*-butyl pivalate used as a standard was prepared by the reaction of pivalic acid and *s*-butyl alcohol using $(CH_3)_3SiCl$: bp 150 °C, NMR (CCl_4); δ 0.92 (d, 6, $CH(C\underline{H}_3)_2$), 1.15 (s, 9, $C(CH_3)_3$), 1.88 (m, 1, CH), 3.72 (d, 2, OCH_2).

Reaction of Acetic Acid with Methoxytrimethylsilane. CH_3COOH (1.2 mmol), $(CH_3)_3SiOCH_3$ (1.2 mmol), dry HCl (0.6 mmol), and 2-methyltetrahydrofuran (0.33 cm^3) were transferred from individual bulbs to a glass tube under a vacuum. The tube, after being sealed, was allowed to stand overnight at room temperature. The products were analysed by GLPC. Methoxytrimethylsilane was prepared from trimethylchlorosilane and methanol, using pyridine as the hydrogen chloride acceptor.

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6) V. Bazant, V. Chvalovsky, and J. Rathousky, "Organosilicon Compounds," Academic Press, New York and London (1965), Vol. 1, p. 56; the reaction of silanols with an excess of methanol is of importance for determining the Si–OH bands. The equilibrium is rapidly established under acid catalysis and shifts toward the right by the removal of the water released. In our reaction, the equilibrium of Eq. 3 is shifted in the same direction by the removal of alkoxytrimethylsilane by means of Eq. 2.