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CONDENSATION OF O-SILYL KETENE ACETALS WITH ACID CHLORIDES. A SYNTHESIS OF β-KETO ESTERS.

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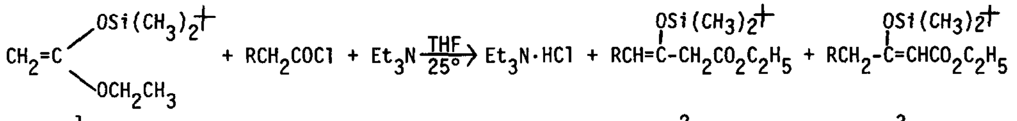
Tetrahydrofuran solutions of the silyl ketene acetal[1] **1** react with acid chlorides in the presence of triethylamine to furnish silylated derivatives (**2**,**3**) of β-keto esters. Hydrolysis



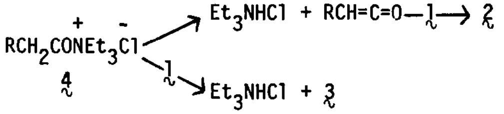
1 **2** **3**

of **2** or **3** with dilute acid occurs under mild conditions and gives the corresponding β-keto ester in essentially quantitative yield.

$$\mathbf{2} + \mathbf{3} \xrightarrow[25°,\ 1\ hr]{HCl,\ H_2O} RCH_2COCH_2CO_2C_2H_5 + \ +Si(CH_3)_2OH$$

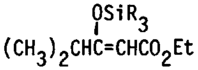
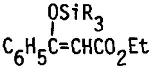
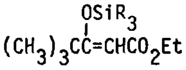
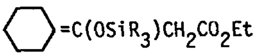
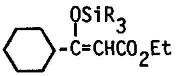
Reaction of **1** with acetyl or butyryl chloride in the absence of triethylamine is sluggish and hydrolysis produces only modest yields (10-25%) of the corresponding β-keto esters[3]. Addition of triethylamine to a mixture of **1** and butyryl chloride in tetrahydrofuran produces an immediate precipitate of material assumed to be the acylammonium salt. This material is slowly replaced by a new precipitate of triethylamine hydrochloride and after 2 hours an 85% yield of **2** (R=ethyl) is present in solution (glpc analysis). Under similar conditions, reaction in ethyl ether or pentane is much slower and increasing amounts of the isomeric silyl derivative **3** (R=ethyl) are formed. Both **2** and **3** are stable to the reaction conditions and their ratio does not change with time following complete reaction.

We rationalize these results by assuming **2** results from the formation of a ketene and its subsequent trapping by **1**. Product **3** is formed by direct attack of **1** on the acylammonium salt, **4**.



Results obtained for the reaction of **1** and triethylamine with a variety of acid chlorides are shown in the table. It can be seen that acid chlorides lacking alpha hydrogens, such as benzoyl or pivaloyl chloride, give satisfactory yields of silylated β-keto esters. It is noteworthy that unsaturated acid chlorides, such as crotonoyl chloride, can be accomodated, providing a synthesis of unsaturated β-keto esters.

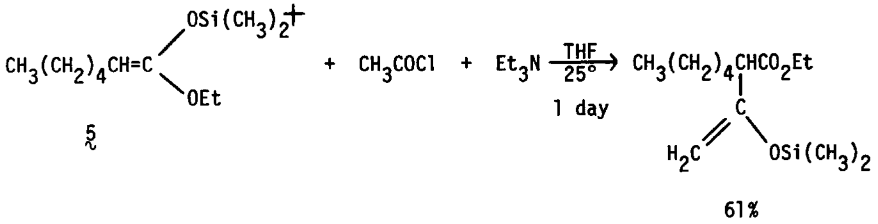
TABLE. *Reaction of **1** with Acid Chlorides in the Presence of Triethylamine*

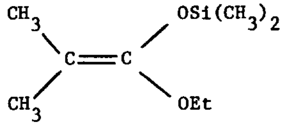
Acid Chloride	Product (yield, glpc)[a]
Acetyl chloride	$CH_2{=}C(OSiR_3)CH_2CO_2Et$ (86%)
Butyryl chloride	$CH_3CH_2CH{=}C(OSiR_3)CH_2CO_2ET$ (85%)
Isobutyryl chloride	$(CH_3)_2C{=}C(OSiR_3)CH_2CO_2Et$ (35%) +  $(CH_3)_2CH\overset{OSiR_3}{C}{=}CHCO_2Et$ (35%)
Crotonoyl chloride	$CH_2{=}CHCH{=}C(OSiR_3)CH_2CO_2Et$ (98%)
Benzoyl chloride	 $C_6H_5\overset{OSiR_3}{C}{=}CHCO_2Et$ (62%)
Pivaloyl chloride	 $(CH_3)_3C\overset{OSiR_3}{C}{=}CHCO_2Et$ (40%)
Cyclohexanecarboxoyl chloride	 (31%)[b] +  (58%)

(a) All products were isolated by vacuum distillation. Structures were established by proton nmr and by hydrolysis to the corresponding β-keto esters.

(b) Determined by nmr analysis of product mixture.

O-silyl ketene acetals with a single alpha substituent also undergo the reaction, as shown by results obtained with 5. However, under similar conditions, the ketene acetal with two alpha substituents, 6, was inert.





6

All of the silylated derivatives shown in the table can be distilled under reduced pressure and stored for long periods without apparent decomposition. Consequently, the present procedure not only provides a simple route to β-keto esters via hydrolysis, but the silyl derivatives offer significant advantages for storing these reactive and useful reagents. Finally, the ability to prepare non-conjugated derivatives of type 7, suggests a number of synthetic possibilities which we are presently investigating.

The following procedure for the preparation of ethyl 3-tert-butyldimethylsiloxy-3,5-hexadienoate from crotonoyl chloride is representative. A dry 100 ml round-bottomed flask is flushed with nitrogen and immersed in an ice-water bath. Crotonoyl chloride (2.9 ml, 30 mmoles) dissolved in 30 ml of dry tetrahydrofuran is placed in the flask followed by 1 (7.1 ml, 30 mmoles) and triethylamine (4.2 ml, 30 mmoles). The ice-bath is then removed and the contents of the flask are stirred for 24 hours at room temperature. The reaction mixture is then extracted with 10 ml of water, the organic layer dried and subjected to vacuum distillation to obtain 7.3 g, 90%, of colorless liquid, bp 80° (0.2 mm), $N^{25}D$ 1.4677.

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