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THE TITANIUM TETRACHLORIDE-PROMOTED REACTION OF KETENE ALKYL TRIALKYLSILYL ACETALS WITH ACETALS OR AN ORTHOFORMATE

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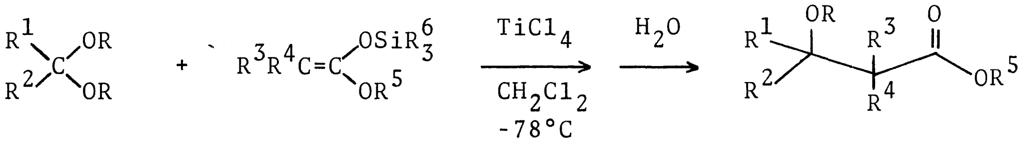
In the presence of $TiCl_4$, ketene alkyl trialkylsilyl acetals reacted with acetals or an orthoformate at -78°C to afford the corresponding β-alkoxyesters or β,β-dialkoxyester in good yields, respectively.

In the previous paper,[1] it was shown that β-hydroxyesters and β-trialkylsiloxyesters were obtained in high yields by the $TiCl_4$-promoted reaction of ketene alkyl trialkylsilyl acetals with various carbonyl compounds. It was reported from our laboratory that acetals which are generally used as a carbonyl protecting group, reacted smoothly with various nucleophiles such as silyl enol ethers,[2] enol acetates[3] and diketene[4] in the presence of $TiCl_4$ to give the corresponding β-alkoxycarbonyl compounds. In this communication, we wish to report the single-step preparation of β-alkoxyesters and β,β-dialkoxyesters by the $TiCl_4$-promoted reactions of ketene alkyl trialkylsilyl acetals with acetals or an orthoformate, respectively.

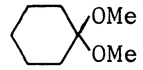
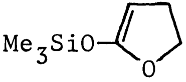
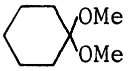


The following experimental procedure is illustrative: To a dichloromethane solution (5 ml) of 3-phenylpropionaldehyde dimethyl acetal (181 mg, 1.0 mmol) was added a dichloromethane solution (1.5 ml) of $TiCl_4$ (209 mg, 1.1 mmol) at -78°C under an argon atmosphere. After stirring for 15 min, a dichloromethane solution of methylketene methyl trimethylsilyl acetal (176 mg, 1.1 mmol) was added dropwise to the solution over a period of 5 min, and the mixture was stirred for 20 min. The mixture was quenched with 5% aq K_2CO_3 solution, filtered and extracted with ethyl acetate. After concentration of the organic layer under reduced pressure, thin layer chromatography (silica gel) afforded methyl 3-methoxy-2-methyl-5-phenylpentanoate in 90% yield (215 mg).

In a similar fashion, several β-alkoxyesters were obtianed in good yields and the results are summarized in the Table.

On the other hand, when 2-trimethylsiloxy-4,5-dihydrofuran was employed as ketene alkyl trialkylsilyl acetal in the above reaction, the desired product was obtained in a low yield. However, the yield of the desired product increased when

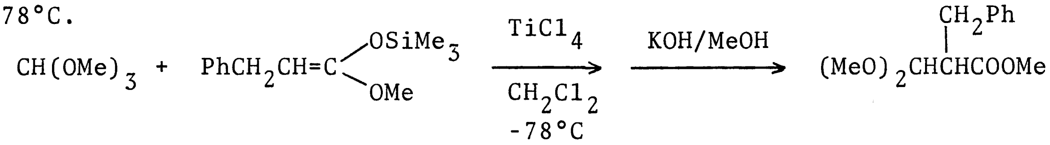
Table. The Preparation of β-Alkoxyesters

Ketene Alkyl Trialkylsilyl Acetal (1.1 mmol)	Acetal (1.0 mmol)	Reaction Time (min)	Yield (%)*	
			in CH_2Cl_2	in Et_2O
$Me_3SiO(MeO)C=CCHCH_2Ph$	$PhCH(OMe)_2$	20	quant.	
		20	92	
	$CH_2(OMe)_2$	10	47	
$Me_3SiO(MeO)C=CHCH_3$	$PhCH_2CH_2CH(OMe)_2$	20	90	
	$PhCH_2C(OMe)_2CH_3$	10	92	
$Me_3SiO(MeO)C=C(CH_3)_2$	$PhCH_2CH_2CH(OMe)_2$	40	90	
	$PhCH_2C(OMe)_2CH_3$	5	94	
$^tBuMe_2SiO(EtO)C=CH_2$	$PhCH(OMe)_2$	20	65	
		20	trace	47
	$PhCH_2CH_2CH(OMe)_2$	15		75

* All compounds exhibited ir and nmr spectral data in accordance with assigned structures. Yields were based on the acetals.

the same reaction was carried out in diethyl ether instead of dichloromethane.

Further, it was found that ketene alkyl trialkylsilyl acetals reacted smoothly with an orthoformate under the above mentioned conditions. For instance, methyl 2-benzyl-3,3-dimethoxypropionate was obtained in 77% yield by the $TiCl_4$-promoted reaction of benzylketene methyl trimethylsilyl acetal with trimethyl orthoformate at -78°C.



$$CH(OMe)_3 + PhCH_2CH=C\begin{matrix}OSiMe_3\\OMe\end{matrix} \xrightarrow[CH_2Cl_2,\ -78^\circ C]{TiCl_4} \xrightarrow{KOH/MeOH} (MeO)_2CH\overset{CH_2Ph}{C}HCOOMe$$

Concerning the preparation of β-alkoxyesters, 1,4-addition of alcohols to α,β-unsaturated esters has been well known,$^{5)}$ and Curé et al.$^{6)}$ reported that β-alkoxyesters were obtained by the Reformatsky reaction with acetals in the presence of acetyl chloride. Usually, these reactions are carried out under rather drastic conditions to afford β-alkoxyesters in moderate yields.

It should be noted that the present $TiCl_4$-promoted reaction, which proceeds very rapidly even at -78°C, provides a convenient and useful method for the preparation of β-alkoxyesters.

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