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A CONVENIENT METHOD FOR THE PREPARATION OF δ-ALKOXY-α,β-UNSATURATED ALDEHYDES BY REACTION OF ACETALS WITH 1-TRIMETHYLSILOXY-1,3-BUTADIENE

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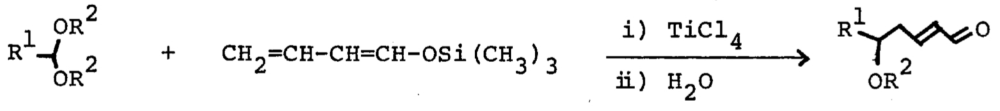
It was found that, in the presence of $TiCl_4$,1-trimethylsiloxy-1,3-butadiene(II)$^{1)}$ reacts with acetals(I) to give δ-alkoxy-α,β-unsaturated aldehydes in good yields. This reaction provides a novel method for the introduction of $-CH_2-CH=CH-CHO$ unit to an electrophile as acetal activated by $TiCl_4$.

In the course of our continuing studies on the development of the useful synthetic method by use of $TiCl_4$, it was recently found in our laboratory that various acetals activated by $TiCl_4$ reacted with silyl enol ethers to afford the corresponding β-alkoxy ketones in good yields.$^{2)}$ This result prompted us to examine the reaction of dienoxysilane(II), produced from crotonaldehyde and trimethylchlorosilane, with acetals(I) in the presence of $TiCl_4$ as shown in the following equation.



(I) (II) (III)

It was found that dienoxysilane(II) reacted with acetals(I) at the carbon atom C-4 of (II)$^{3-5)}$ to give the corresponding δ-alkoxy-α,β-unsaturated aldehydes(III) without accompanying a detectable amount of β-alkoxy aldehyde.

In CH_2Cl_2 or toluene which hardly forms coordinated complex with $TiCl_4$, the dienoxysilane(II) was very sensitive toward $TiCl_4$ leading to the exclusive formation of polymeric products. On the other hand, in THF the reaction of dienoxysilane(II) with α,β-unsaturated acetals proceeded smoothly to form δ-alkoxy-α,β-unsaturated aldehydes at -78°C in good yields (Method A).

The same reaction did not take place when saturated acetals were used in place of α,β-unsaturated acetals in the above experiment. This problem was overcome by treating saturated acetals with the dienoxysilane(II) in CH_2Cl_2 at -40°C in the coexistence of $Ti[OCH(CH_3)_2]_4$ and $TiCl_4$ resulting in the formation of the desired products in good yields (Method B and C).

These results indicate that the combined use of Ti[OCH$(CH_3)_2]_4$ and $TiCl_4$ is indispensable for the purpose of synthesizing δ-alkoxy-α,β-unsaturated aldehydes. Under the condition, undesirable side reactions such as polymerization are suppressed and desired α,β-unsaturated aldehydes are produced exclusively.

Typical procedure for Method A: To a mixture of $TiCl_4$(3.0 mmol) and cinnamaldehyde dimethyl acetal (455 mg, 2.5 mmol) in dry THF (10 ml) was added a solution of the dienoxysilane(II) (426 mg, 3.0 mmol) at -78°C under argon atmosphere. The reaction mixture was stirred for an additional 4 hr and quenched with aqueous K_2CO_3 solution. After the usual work-up, 7-phenyl-5-methoxy-2,6-heptadienal (475 mg) was isolated in 88 % yield by column chromatography on silica gel (Table I).

Table I. Reaction of Acetals with Dienoxysilane(II) (method A)

Acetal(I)		Reaction Time	Aldehyde (III)
R^1	R^2	(hr)	Yield (%)
$C_6H_5CH{=}CH$	CH_3	4	88
$C_6H_5CH{=}CH$	C_2H_5	4	82
$C_6H_5CH{=}CH$	$-CH_2-$	4	60
$CH_3CH{=}CH$	CH_3	2	86

Typical procedure for Method B: To a CH_2Cl_2 solution (10 ml) of 3-phenylpropionaldehyde dimethyl acetal (1 mmol) were added equimolar amounts of Ti[OCH$(CH_3)_2]_4$ (1.2 mmol) and $TiCl_4$ (1.2 mmol) and a CH_2Cl_2 solution of the dienoxysilane(II) in this order. The reaction mixture was kept at -40°C for 30 min and quenched with aqueous K_2CO_3 solution. After the usual work-up, 7-phenyl-5-isopropoxy-2-heptenal was isolated in 77 % yield by thin layer chromatography(t.l.c.) on silica gel (Table II) .

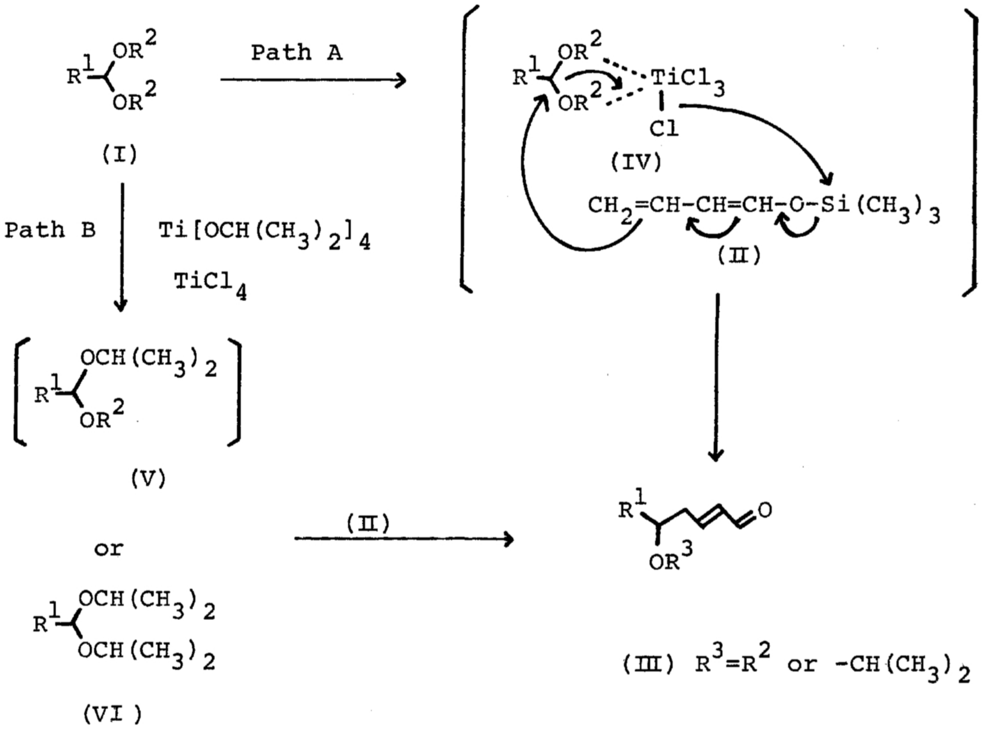
Typical procedure for Method C: To a stirred CH_2Cl_2 solution (10 ml) of equimolar amounts of $TiCl_4$ and Ti[OCH$(CH_3)_2]_4$ were added 3-phenylpropionaldehyde dimethyl acetal and the dienoxysilane(II) at -40°C under argon atmosphere. 7-Phenyl-5-methoxy-2-heptenal was obtained in 51 % yield by t.l.c. on silica gel (Table II).

The result listed in Table II shows that the order of the addition of the reagents influences the δ-alkoxy group(CH_3O-, C_2H_5O-, $(CH_3)_2CHO$-) contained in the aldehyde(III) produced. That is, according to method A and C, the alkoxy group of product(III) is the same as that involved in the starting acetal and, according to method B, the isopropoxy group is introduced in place of the alkoxy group of the acetal(I).

Table II. Reaction of Acetals with Dienoxysilane(II) (Method B and C)

Acetal(I)			(III) Isolated Yield (%)	
R^1	R^2	Method	R^2=$CH(CH_3)_2$ (exchanged)	R^2
$C_6H_5CH_2CH_2$	CH_3	B	77	trace
		C	trace	51
$C_6H_5CH_2CH_2$	C_2H_5	B	79	trace
		C	trace	50
n-C_6H_{12}	CH_3	B	75	2
		C	trace	54
C_6H_5	CH_3	B	70	4
		C	trace	82
$C_6H_5CH{=}CH$	CH_3	B	79	5
		C	trace	80
$CH_3CH{=}CH$	CH_3	B	29	4
		C	7	80

The replacement of alkoxy group appeared to occur at the first stage of the reaction as depicted in the following scheme. Indeed, it was confirmed by the separate experiment that starting acetal(I) was converted into the corresponding diisopropyl acetal(VI) at a low temperature by treatment with a mixture of $TiCl_4$ and $Ti[OCH(CH_3)_2]_4$.



On the basis of the above results, in method A and C, the reaction is assumed to proceed through a similar pathway proposed in the reaction of α,β-unsaturated acetals and Grignard reagents.⁶⁾ That is, the acetal activated with $TiCl_4$ reacts with the dienoxysilane(II) to afford the aldehyde(III) as sketched in the path A.

Similarly, the formation of the aldehyde(III) by method B could be explained by assuming an initial formation of monoisopropyl acetal (V) or diisopropyl acetal(VI) from the complex(IV) and $Ti[OCH(CH_3)_2]_4$ (path B).

In summary, it is noted that the present reaction of dienoxysilane(II) with acetals(I) takes place selectively at the carbon atom C-4 of (II) to afford the δ-alkoxy-α,β-unsaturated aldehydes in good yields.

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