CHEMISTRY LETTERS, pp. 15-16, 1974. Published by the Chemical Society of Japan

NEW SYNTHESES OF β-ALKOXY KETONES AND β-KETO ACETALS

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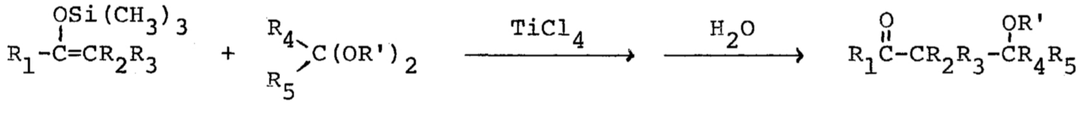
It was found that trimethylsilyl enol ethers derived from aldehydes and ketones react smoothly with acetals or methyl orthoformate at -78°C in the presence of $TiCl_4$ to give β-alkoxy ketones or β-keto acetals, respectively, in good yields.

Recently, it was found¹⁾ in our laboratory that trimethylsilyl enol ethers²⁾ derived from aldehydes and ketones react with aldehydes and ketones very rapidly in the presence of $TiCl_4$ to afford the aldol type addition products, β-hydroxy ketones, in good yield. In the present investigation, it was established that the trimethylsilyl enol ethers react with various acetals or methyl orthoformate in the presence of $TiCl_4$ to give the corresponding β-alkoxy ketones or β-keto acetals, respectively, at low temperature in good yields.

The typical procedure is described for the reaction of trimethylsilyl enol ether of phenylacetone with benzaldehyde diethyl acetal: To a CH_2Cl_2 (5 ml) solution of $TiCl_4$ (2.6 mmol) was added a CH_2Cl_2 solution of benzaldehyde diethyl acetal (2.5 mmol) at -78°C under argon atmosphere. Then a CH_2Cl_2 solution of trimethylsilyl enol ether of phenylacetone (2.5 mmol) was added immediately, and the reaction mixture was stirred for 3 hr at -78°C. After hydrolysis, the organic layer was extracted with ether. The extract was condensed under reduced pressure and residue was separated by silica gel column chromatography. The reaction product, 3,4-diphenyl-4-ethoxybutan-2-one, was isolated in 95% yield, and a trace amount of unreacted phenylacetone was recovered.

In a similar manner, the reactions of silyl enol ethers derived from various aldehydes or ketones with various acetals were tried and results are listed in the table.

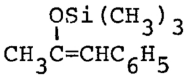
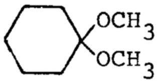
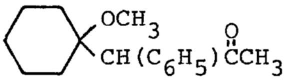
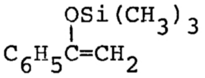
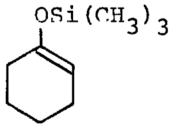
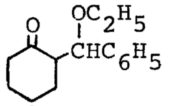
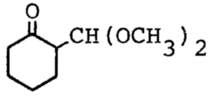
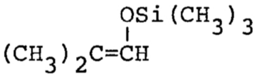
It was also found that methyl orthoformate reacts with silyl enol ethers to give β-keto acetals in good yields by the same procedure as mentioned above. β-Keto aldehyde, hydrolyzed product, and alkoxy diketone, formed by the successive reaction of the β-keto acetal with silyl enol ethers, were not isolated.



$$R_1\text{-}\overset{\overset{\text{OSi(CH}_3)_3}{|}}{\text{C}}\text{=CR}_2\text{R}_3 + \begin{matrix}R_4\\R_5\end{matrix}\!\!>\!\text{C(OR')}_2 \xrightarrow{\quad TiCl_4\quad} \xrightarrow{\quad H_2O\quad} R_1\overset{\overset{\text{O}}{\|}}{\text{C}}\text{-CR}_2\text{R}_3\text{-}\overset{\overset{\text{OR'}}{|}}{\text{C}}\text{R}_4\text{R}_5$$

In general, it is known that a small amount of the dehydrated product is always accompanied with the formation of aldols.³⁾ However, it was established by the pre-

Table. The reactions of silyl enol ethers with acetals or methyl orthoformate

Silyl enol ether	Acetal or methyl orthoformate	Reaction time (hr)	Product*1 (isolated yield, %)
 $CH_3\overset{OSi(CH_3)_3}{C}=CHC_6H_5$	$C_6H_5CH(OC_2H_5)_2$	3	$C_6H_5CH(OC_2H_5)CH(C_6H_5)COCH_3$ (95)*2
	$(CH_3)_2C(OCH_3)_2$	3	$(CH_3)_2C(OCH_3)CH(C_6H_5)COCH_3$ (66)*3 $C_6H_5CH_2COCH_3$ (23)
		3	 (91)
	$HC(OCH_3)_3$	3	$(CH_3O)_2CHCH(C_6H_5)COCH_3$ (64)
 $C_6H_5\overset{OSi(CH_3)_3}{C}=CH_2$	$C_6H_5CH_2CH_2CH(OCH_3)_2$	3.5	$C_6H_5CH_2CH_2CH(OCH_3)CH_2COC_6H_5$ (73) $C_6H_5COCH_3$ (12)
	$NCCH_2CH_2CH(OCH_3)_2$	3	$NCCH_2CH_2CH(OCH_3)CH_2COC_6H_5$ (60) $C_6H_5COCH_3$ (23)
	$(CH_3)_2C(OCH_3)_2$	3	$(CH_3)_2C(OCH_3)CH_2COC_6H_5$ (62)*4
	$C_6H_5CH(OC_2H_5)_2$	2	 (95)*2
	$HC(OCH_3)_3$	3	 (71)
 $(CH_3)_2C=\overset{OSi(CH_3)_3}{CH}$	$C_6H_5CH_2CH_2CH(OCH_3)_2$	3	$C_6H_5CH_2CH_2CH(OCH_3)C(CH_3)_2CHO$ (quant)

*1 The products have ir and nmr spectra and elemental analysis in accord with the assigned structures.
*2 The products were mixtures of threo- and erythro- isomers.
*3 When the reaction was carried out at room temperature, several by-products were detected by tlc along with the condensation product.
*4 The reaction was carried out at -40 ~ -50°C.

sent reaction that only β-alkoxy ketones or β-keto acetals are produced in good yields by the reactions of trimethylsilyl enol ethers derived from aldehydes and ketones with acetals or methyl orthoformate, because the elimination of alcohol from the products does not take place under the reaction conditions.

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(Received October 20, 1973)