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STEREOSELECTIVE SYNTHESIS OF (E)- α , β -UNSATURATED ACIDS FROM C,O,O-TRI(TRIMETHYLSILYL) KETENE ACETAL AND ALDEHYDES.

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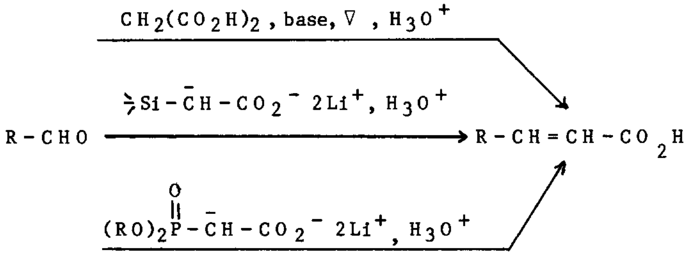
Abstract : Aldehydes are converted into (E)- α , β -unsaturated carboxylic acids by means of C,O,O-tri(trimethylsilyl) ketene acetal and a catalytic amount of $ZnBr_2$.

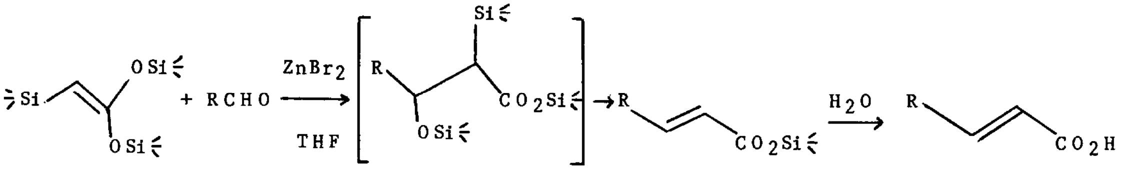
Several ways have been described to transform aldehydes into α , β -unsaturated esters. However, the hydrolysis of the resultant esters to the corresponding α , β -unsaturated acids can sometimes result in low yields[1]. To our knowledge, three general methods could be used for the <u>direct</u> conversion of aldehydes to α, β-unsaturated carboxylic acids : the Knoevenagel reaction with malonic acid[2], the Peterson olefination with trimethylsilylacetic acid dianion[3] and the Wittig-Horner type reactions[4,5] (scheme).



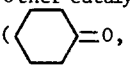
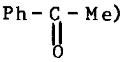
Scheme

However, the Knoevenagel reaction gave low yields with enolisable aldehydes[6], the Peterson olefination suffered from a lack of stereoselectivity and the Wittig-Horner reaction required fairly stringent conditions to isolate the α , β -unsaturated acids. Diethyl trimethylsiloxycarbonylmethane phosphonate, which is prepared from trimethylsilyl bromoacetate by way of the Arbuzov reaction, compensates this disadvantage[7].

We have reported that ketene bis (trimethylsilyl) acetals react with aldehydes to give aldol type products in the presence of an activating agent as catalyst[8-12]. We wish to show herein that C,O,O-tri (trimethylsilyl) ketene acetal <u>1</u> could react at room temperature with aldehydes to directly give the corresponding α , β-unsaturated acids in the Peterson manner. In the hope of realizing this transformation, substrate 1 (20 mmol, 5.52 g) in 10 ml of THF was added to a THF (20 ml) solution of benzaldehyde (22 mmol, 2.4 g) and $ZnBr_2$ (2.2 mmol, 0.5 g) at room temperature under a nitrogen atmosphere. The mixture was allowed to stir at 20°C for 24 h. Acido-basic work-up, to remove any remaining non-acidic organic material, affords (E)-cinnamic acid in almost quantitative yield (table, entry 2).



1 2 3 4

As shown in the table, aliphatic aldehydes react in the same way to produce α,β-unsaturated carboxylic acids in fairly good yields. Other catalysts can be used such as TBAF, $TiCl_4$ or CsF (entries 3, 6, 10). The non-reactivity of ketones (,  $\mathrm{Ph-\underset{\underset{O}{\|}}{C}-Me}$) demonstrates the selectivity and synthetic utility of our method.

In a similar work on the reactivity of O-methyl C,O-bis (trimethylsilyl) ketene acetal towards aldehydes, Mutsuda[13] has shown that the geometrical ratio of the obtained α,β-unsaturated esters reflects the diastereomeric ratio of the intermediate β-hydroxy α-silylesters. In our case, attempts to isolate the intermediate 2 have failed. Before aqueous work-up, we directly obtained compound 3.

To our knowledge, the requisite reagent 1 was prepared for the first time by Emde[14] using trimethylsilyltriflate and trimethylsilylacetic ester. However, a mixture of three silylated products was obtained from which compound 1 must be separated. We have found that C,O,O-tri (trimethylsilyl) ketene acetal 1 can be easily obtained in excellent yield from α-trimethylsilyl trimethylsilylacetic ester[15] 5, LDA and chlorotrimethylsilane.

$$\underset{\underline{5}}{\gtrless\mathrm{Si-CH_2-CO_2Si}\lessgtr} \xrightarrow[\mathrm{ClSi}\lessgtr,\ -78^\circ\rightarrow 20^\circ]{\mathrm{LDA,\ THF,\ -78^\circ}} \underline{1}\ (\mathrm{Yield} = 91\ \%)^{16}$$

We note that the lithio derivative of 5 reacts readily with benzaldehyde to give, after acidic hydrolysis, cinnamic acid without any stereoselectivity (E : Z = 1 / 1 ; yield = 86 %) as does trimethylsilylacetic acid dianion[3].

TABLE

Yields of (E)-α,β-unsaturated acids <u>4</u> in the reaction of reagent <u>1</u> with aldehydes.

Entry	R	Reaction conditions	Yield[a] (%) of <u>4</u>
1	Ph	no catalyst, THF, reflux, 24 h	0
2	Ph	$ZnBr_2$[b], THF, rt, 24 h	95
3	Ph	TBAF[b], THF, rt, 4 h	97
4	Me	$ZnBr_2$[b], THF, rt, 14 h	83
5	Et	$ZnBr_2$[b], THF, rt, 14 h	75
6	Et	$TiCl_4$[c], CH_2Cl_2, -70°, 3 h	60
7	n-Pr	$ZnBr_2$[b], THF, rt, 24 h	68
8	i-Pr	$ZnBr_2$[b], THF, reflux, 6 h	58
9	i-Pr	$ZnBr_2$[c], THF, rt, 48 h	52
10	i-Pr	CsF[b], THF, rt, 14 h	66

[a] The structure of these acids was confirmed by ^1H-N.M.R. comparison with authentic samples.

[b] 10 %.

[c] 1 equivalent.

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16 - A typical experiment is as follows : LDA was prepared under nitrogen atmosphere as described in reference[17] from phenanthrene (4.6 g, 25 mmol), diisopropylamine (21.2 g, 0.21 mol), hammered lithium (1.4 g, 0.2 mol) in ether (40 ml)-THF (40 ml). To this solution, α-trimethylsilyl trimethylsilylacetic ester (36.7 g, 0.18 mol) in 20 ml of THF was added at -78° in 15 mn and the solution was stirred at the same temperature for 1 h. Then chlorotrimethylsilane (21.7 g, 0.2 mol) was added in 5 mn at -78°. The reaction mixture was then allowed to reach room temperature overnight. The precipitate was filtered off on celite, the solvent evaporated and the product distilled in vacuo (b.p. 86°/10 mm Hg ; Lit.[13] 82-84°/10 mm Hg).

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