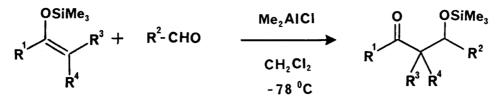
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## ALDOL CONDENSATIONS CATALYZED BY ORGANOALUMINUM REAGENTS

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A new synthetic procedure for the practical synthesis of  $\beta$ -trimethylsiloxyketones from silyl enol ethers and aldehydes has been described which heavily depends on organoaluminum reagent as an effective catalyst.

The aldol condensation is a highly useful synthetic operation in organic synthesis. A number of reagents and processes are currently available<sup>1)</sup> fox effecting such a synthetically important transformation. The majority of the previous work has involved the preformed enolate associated with lithium and boron.<sup>1,2)</sup> Not much work has been done on the aldol condensations involving aluminum enolate.<sup>3)</sup> We describe herein a new method for the synthesis of  $\beta$ trimethylsiloxycarbonyl compounds<sup>2)</sup> using organoaluminum catalyst which appear to offer special advantages in procedural simplicity and mildness of reaction conditions. The new process is illustrated below:



To a solution of the trimethylsilyl enol ether and the aldehyde (1.0-1.5 equiv.) in dichloromethane was added a hexane solution of dimethylaluminum chloride (0.05-1.0 equiv.) at -78 <sup>O</sup>C and the mixture was stirred for 45 min at the same low temperature. After TLC analysis of the reaction mixture revealed the consumption of the most of the starting enol ether, the solution was treated with sodium fluoride (4 equiv. to aluminum reagent) and water (3 equiv. to aluminum reagent) and the resulting suspension was stirred vigorously for 1 h. The mixture was filtered and the filtrate was concentrated in vacuo to give an oil which was subjected to column chromatography on silica gel to afford the pure trimethyl-siloxyketone. Some of our results are summarized in Table 1.

Characteristic features of the present reaction follow: (1) Other organoaluminum reagent including Me<sub>3</sub>Al, EtAlCl<sub>2</sub>, Et<sub>2</sub>AlCl, and MeAlCl<sub>2</sub> are also effective for the reaction with the slightly lower yields. (2) Unfortunately, the diastereoselectivity of the reaction was low (see legend of Table 1). (3) Excess aluminum reagent gave us the  $\beta$ -hydroxyketone as the major product (see entry 8).

Entry	Enol ether	Aldehyde (equiv.)	Method <sup>b)</sup>	Yield/% <sup>c)</sup>
1	OTMS	Benzaldehyde (1.0)	B (0.05x2; 0.1;	0.2) 88 <sup>d)</sup>
2		Benzaldehyde (1.0)	A (1.0)	50
3		Cyclohexanecarbaldehyde (1.8)	A (0.4)	59
4		Hexanal (1.5)	A (0.4)	47
5		Benzaldehyde (1.5)	B (0.03x2)	85 <sup>e)</sup>
6	OTMS	Cyclohexanecarbaldehyde (1.5)	A (0.5)	34
7		Hexanal (1.6)	A (0.5)	55
8		Hexanal (1.5)	A (1.0)	26 <sup>f)</sup>
9		Benzaldehyde (1.0)	B (0.05x2)	85
10	OTMS Ph	Cyclohexanecarbaldehyde (1.9)	A (0.5)	62
11		Hexanal (1.5)	A (0.5)	73
12	OTMS O <sup>i</sup> Pr	Benzaldehyde (1.0)	B (0.05x2)	85
13		Cyclohexanecarbaldehyde (1.0)	B (0.05x2; 0.1;	0.2) 52
14		Hexanal (1.5)	B (0.05x2; 0.1;	0.2) 61

Table 1. Aldol reaction of silyl enol ethers and aldehydes<sup>a)</sup>

a) All the reactions were performed as 1-3 mmol scale. b) Method A: see text. Method B: The solution of an ether and an aldehyde in methylene chloride was cooled at  $-78^{\circ}$ C and the aluminum reagent was added every 30 min until most of the starting material was consumed. After the addition, the mixture was stirred for an additional 30 min before workup (see text). c) Isolated yields. d) Erythro/Threo = 37:63 by nmr assay. e) Erythro/Threo = 38:62 using the enol ether of  $\underline{E}/\underline{Z}$  = 92:8. Erythro/Threo = 32:68 with the enol ether of  $\underline{E}/\underline{Z}$  = 34:66. f) The major product was the deprotected aldol (53% yield).

References

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