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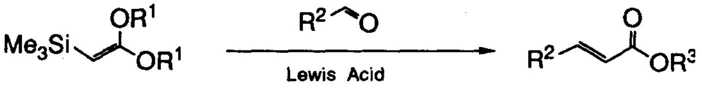
A New Route to α,β-Unsaturated Aldehydes Using the Condensation of Trimethylsilyl β-Trimethylsilyl Enol Ethers with Aldehydes.

Lucette Duhamel*, Jean Gralak and Abdelhamid Bouyanzer.

Unité de Recherche Associée au CNRS, Faculté des Sciences et des Techniques de Rouen et Institut de Recherche en Chimie Organique Fine 76821 Mont Saint Aignan Cedex (France).*fax (+33) 35 14 66 70

Abstract: β-Trimethylsilyl enol ethers **1** (*Z*) obtained from β-bromoenolethers **2** were condensed with aliphatic and aromatic aldehydes in the presence of a catalytic quantity of trimethylsilyl triflate leading to ethylenic aldehydes **3** (*E*) with good yields (79-90%).

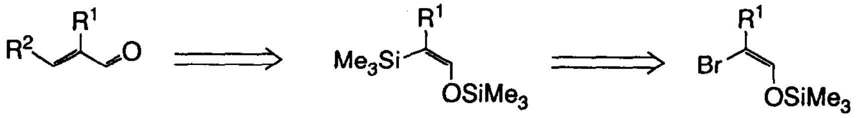
The condensation of aldehydes and β-trimethylsilyl ketene acetals catalysed by Lewis acids leading to α,β-unsaturated acid derivatives is a well documented reaction [1-3].



R^1 = Me, $SiMe_3$; R^2 = alkyl, aryl; R^3 = H, Me.

Surprisingly enough, the same reaction starting from β-trimethylsilyl enol ethers such as **1** is to-day unknown. In fact, only the preparation of some β-trimethylsilyl enol ethers with the basic skeleton of ethylene [4,5] and cyclic or bicyclic alkenes [6] is given in the literature.

In this paper we report a general preparation of β-trimethylsilyl enol ethers **1** starting from β-bromo enol ethers **2** and their condensation with aldehydes leading to α-substituted α,β-unsaturated aldehydes **3** of *E* configuration [7].



3 **1** **2**

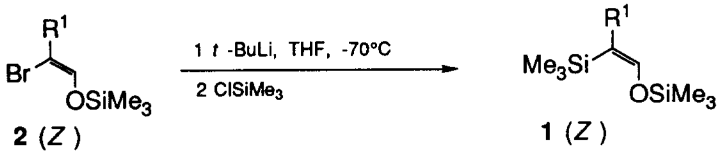
The bromine-lithium exchange from bromo enol ethers **2** [8], followed by the condensation with trimethylchlorosilane led to β-trimethylsilyl enol ethers **1** of *Z* configuration (table 1) [9].

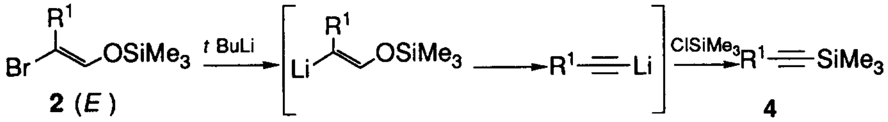
Table 1 : Trimethylsilyl enol ethers 1

R^1	Me	Et	*i*-Pr	*n*-Pent	*t*-Bu
Starting 2 (Z/E)	67/33	80/20	82/18	83/17	100/0
1 yield % (a)	60	57	59	54	50

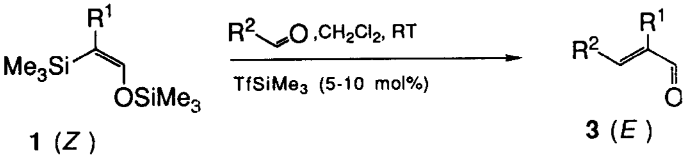
a) After chromatography on florisil.

The modest yield of **1** (50-60%) is mainly due to the fact that the starting bromo enol ethers **2** were mixtures of *Z* and *E* isomers (table 1) : the *Z* isomers only lead to **1** while the *E* isomers, after halogen-lithium exchange are subjected to an elimination-reaction [10,11] leading to acetylenic silanes **4**. For identification, **4** (R^1=*n* -Pent) was prepared from 1-heptyne. Trimethylsilyl enol ethers **1** were easily isolated from the reaction mixture [9].





Since the pioneering work of Wittig, many syntheses of unsaturated aldehydes by formal condensation of two different aldehydes have been reported. Therefore it should be noted that methods to accede to aldehydes **3** [11,12] with mild and non basic conditions, as the method we propose, are not well documented [12f]. Conversion of enol ethers **1** to unsaturated aldehydes **3** was achieved by condensation



with aldehydes in the presence of Lewis acids such as trimethylsilyl triflate, *ter*- butyldimethylsilyl triflate or zinc chloride. Ethylenic aldehydes **3** were isolated in good yields [13].

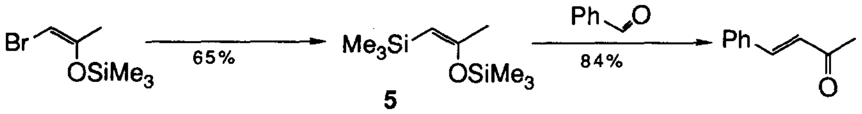
The *E* isomers were obtained except when the R^1 substituent was the crowded isopropyl group. As expected, the condensation occured more rapidly with aliphatic aldehydes than with benzaldehyde (table 2).

Table 2 : Aldehydes 3

R^2	R^1	yield % (a)	Conditions (b) time (cat %)	R^2	R^1	yield % (a)	Conditions (b) time (cat %)
Ph	Me	79	14 (5) (c)	Ph-CH=CH	Me	85	7 (10) (e)
	Et	80	15 (5) (d)		*i*-Pr	86	7 (10)
	i-Pr	85	16 (5)		*n*-Pent	87	7 (10)
p-$CH_3C_6H_4$	Me	92	4 (5)	*n*- Bu	Me	79	3 (6) (f)
	Et	90	4 (5)		Et	88	3.5 (6)
	n-Pent	90	4 (5)		*i*-Pr	90 (g)	4 (6)
p-$NO_2C_6H_4$	Me	80	12 (10)	*n* -Hex	Me	93	3 (6)
	Et	81	13 (10)		Et	90	4 (6)
					i-Pr	92 (g)	5 (6)

a) After chromatography on Florisil; b) See ref. [13]; c) Litt. ref [12f,14,15]; d) Litt. ref [11] ; e) Litt. ref[12c,14]; f) Litt. ref.[16-18]. g) Isolated as a mixture of *Z* and *E* isomers (*Z*/*E* :1/1).

The following model reaction shows that this condensation in mild and non basic conditions can be generalized to silyl enol ethers such as **5** which behave as the synthetic equivalents of ketone enolates.



In the same conditions, the reaction of enol ethers **1** with ketones such as acetone or acetophenone don't occur.

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9. To bromo enol ether **2** (4 mmol) in 10 ml of THF was added *t*-BuLi (1.7M in pentane, 10 mmol, T<-65°C) under argon. After 45 min at -70°C, $ClSiMe_3$ (0.43g, 4 mmol) was added. The mixture was kept at -70°C (50 min) then warmed to 0°C in 10 min, then treated with 5% Na_2CO_3 (2.5 ml). After the usual work-up the crude product was isolated by chromatography (Florisil, eluant : PE, 30-50°C). Enol ether **1** (Z) was obtained after removal of the residual **4** by evaporation at RT/1 mmHg. Compounds **1** are caracterized in IR by an absorption at 1600-1615 cm^{-1} (film) and in ^1H NMR by a vinylic singlet (6.65-6.88 in C_6D_6). The Z configuration of **1** (R^1=*n* -Pent) was attributed by nOe experiment.

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13. To trimethylsilyl enol ether **1** (1.5 ml) in dichloromethane (5 ml) was added at 0°C, under argon, aldehyde R^2CHO (1.4 mmol), then trimethylsilyl triflate (5-10% in mol, see table 2). After 3-16h at RT (TLC, see table 2), the mixture was treated with a 5% Na_2CO_3 aqueous solution. After the work-up, aldehydes **3** were isolated by chromatography on florisil (eluant, PE/Et_2O : 95/5). ^1H, ^{13}C and MS data are in agreement with the proposed structure **3** (*E*) (except for R^1 = *i*-Pr and R^2 = alkyl, see table 2, note g).

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