

N,N-Bis(trimethylsilyl)methoxymethylamine as a Convenient Synthetic Equivalent for $+CH_2NH_2$: Primary Aminomethylation of Esters

Kohji Okano, Toshiaki Morimoto, and Minoru Sekiya*

Shizuoka College of Pharmacy, Oshika, Shizuoka 422, Japan

The introduction of a primary aminomethyl unit at the α position of esters can be achieved in high yield by the silyl trifluoromethanesulphonate-catalysed reaction of ketene silyl acetals (2) with *N,N*-bis(trimethylsilyl)methoxymethylamine (1).

The aminomethylation of electron-rich carbon atoms is an important subject in synthetic organic chemistry. The Mannich reaction¹ and other modified reactions² are known for the *N,N*-dialkylaminomethylation of carbonyl compounds at the α -position. The *N*-monoalkylaminomethylation of carboxylic esters has also been reported recently from our laboratory by the silyl trifluoromethanesulphonate-catalysed reaction of ketene silyl acetals with 1,3,5-trialkylhexahydro-1,3,5-triazines.³ However, very few methods have been reported for the introduction of the primary aminomethyl group H_2NCH_2- at carbon,⁴ in spite of its broad usefulness in organic synthesis.

In the preceding paper, we disclosed that *N,N*-bis(trimethylsilyl)methoxymethylamine (1), behaves as an efficient, primary aminomethylating agent for organometallics.⁵ We herein report a convenient synthesis of β -aminocarboxylic esters from esters *via* aminomethylation of ketene silyl acetals (2) with the reagent (1). Introduction of the *N,N*-bis(trimethylsilyl)aminomethyl group into carboxylic esters at the α -position was performed by the trimethylsilyl trifluoromethanesulphonate (3)-catalysed reaction of ketene silyl acetals (2) with (1) and successive desilylation gave the corresponding primary aminomethylated products. The reaction of ketene silyl acetals (2) (1 equiv.) and the reagent (1) (1 equiv.) proceeded smoothly at room temperature in dichloromethane in the presence of a catalytic amount of (3) (0.01 equiv.) to afford *N,N*-bis(trimethylsilyl)- β -aminocarboxylic

esters (4) in high yield with the release of methoxytrimethylsilane (5). The results are summarized in Table 1.

The corresponding β -aminocarboxylic esters (6) were obtained in high yield simply by means of heating of (4) in a protic medium. For example, desilylation of (4a) was carried out by refluxing in methanol for 24 h to give 2,2-dimethyl- β -alanine methyl ester (6a) in 80% yield. The β -amino esters (6) are convertible into *N*-unsubstituted monocyclic β -lactams (7) by treatment with bases;⁶ especially, (4f) can be a precursor of monobactams (8).⁷

The reagent (1) itself was quite stable in neutral and basic media but susceptible to acids and Lewis acids. Compound (3) induced catalytically the decomposition of (1) with the release of methoxytrimethylsilane (5) (detected by n.m.r. spectroscopy). A probable path of this decomposition is shown in Scheme 1.

A trial to carry out the reaction of (2a) with the decomposed solution also gave the product (4a) in somewhat lower yield. Therefore, the reactive species attacking ketene silyl acetal (2) is considered to be the iminium salt (10) which is probably very electrophilic, although an oxonium salt like (9) was postulated as an attacking species in an earlier paper dealing with a

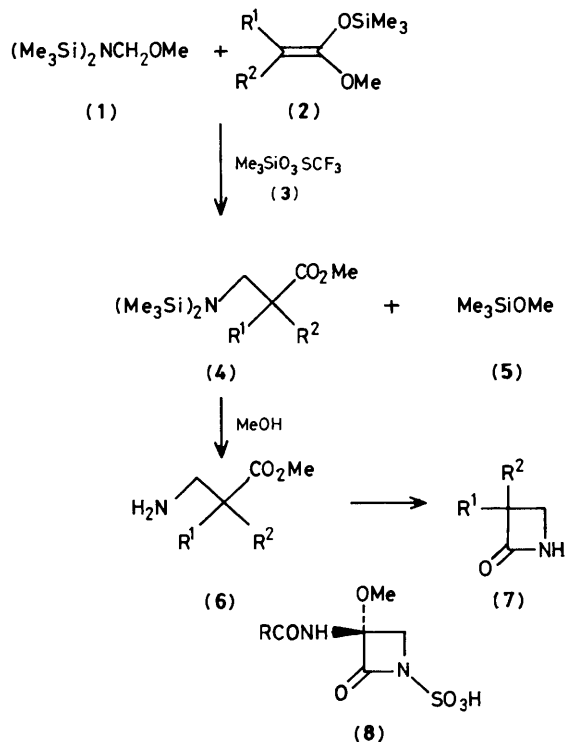
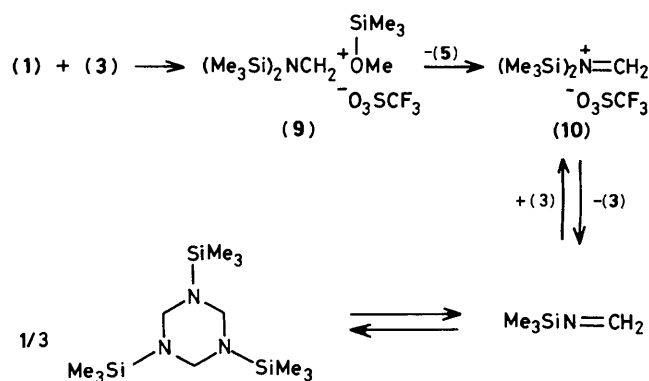


Table 1. Reaction of ketene silyl acetals (2a—f) with the reagent (1).

(2)	R ¹	R ²	Yield of (4a—f) a/%
a	Me	Me	84
b	Me	H	85
c	Ph	H	95
d		-[CH ₂] ₄ -	78
e		-[CH ₂] ₅ -	85
f	Me ₂ SiNSiMe	H	93

* Yield of pure, isolated product; all new compounds gave satisfactory microanalytical and spectroscopic data.



similar trifluoromethanesulphonate-catalysed *N,N*-dialkyl-aminomethylation.^{2a}

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