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

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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 reaction[1] and other modified reactions[2] 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]

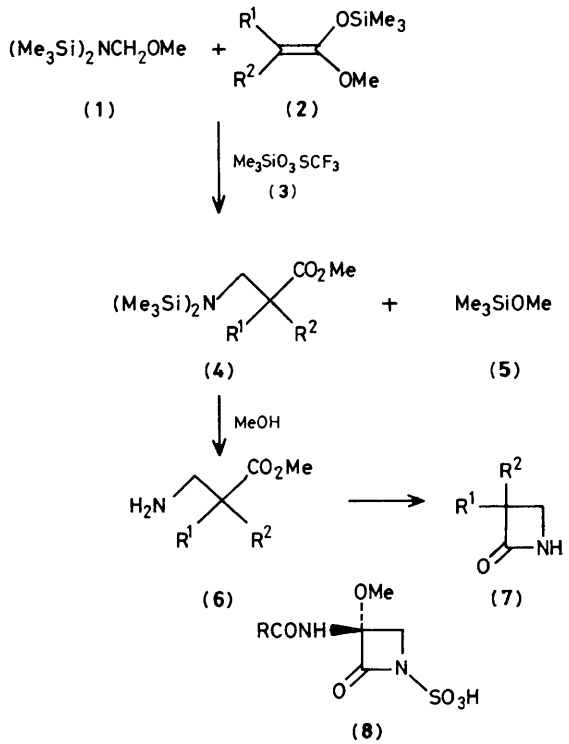
The reagent (**1**) itself was quite stable in neutral and basic media but susceptible to acids and Lewis acids. Compound (**3**) induced catalytically the decomposition of (**1**) with the release of methoxytrimethylsilane (**5**) (detected by n.m.r. spectroscopy). A probable path of this decomposition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

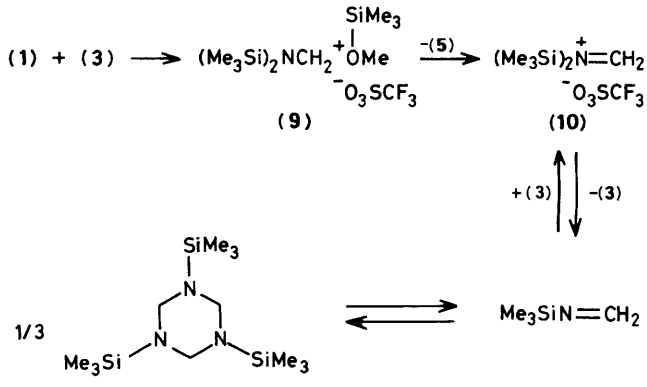
A trial to carry out the reaction of (**2a**) with the decomposed solution also gave the product (**4a**) in somewhat lower yield. Therefore, the reactive species attacking ketene silyl acetal (**2**) is considered to be the iminium salt (**10**) which is probably very electrophilic, although an oxonium 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	$Me_2SiNSiMe$	H	93

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





Scheme 1

similar trifluoromethanesulphonate-catalysed *N,N*-dialkylaminomethylation.[2a]

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