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A DEFINITE EVIDENCE ON THE AMBIVALENT AZOMETHINE YLIDE INTERMEDIATE IN TRIFLUOROACETIC ACID- AND FLUORIDE ANION-PROMOTED 1,3-CYCLOADDITIONS INVOLVING THE SILICON-CARBON BOND CLEAVAGE

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Trifluoroacetic acid- and fluoride anion-promoted 1,3-cycloadditions of N-benzyl-N-(methoxymethyl)trimethylsilylmethylamine to dipolarophiles were found to proceed via the ambivalent azomethine ylide intermediates.

KEYWORDS ——— azomethine ylide; 1,3-cycloaddition; ambivalence; N-benzyl-N-(methoxymethyl)trimethylsilylmethylamine; dipolarophile

The chemistry of non-stabilized azomethine ylides derived from trimethylsilylmethylamine derivatives has been much developed recently by us$^{1)}$ and the other groups$^{2)}$ from the interest in the organosilicon chemistry and also for new synthesis of heterocyclic compounds. Although many works including the regio- and stereoselectivities of the 1,3-cycloadditions have been reported, the fundamental properties of the intermediary non-stabilized azomethine ylides produced by cleavage of the silicon-carbon bond have not been clearly disclosed.

We wish to describe here the chemical evidence indicating that such 1,3-cycloadditions proceed via the ambivalent azomethine ylide intermediates. For this purpose, we carried out the trifluoroacetic acid- and fluoride anion-pormoted 1,3-cycloadditions using deuterated N-benzyl-N-(methoxymethyl)trimethylsilylmethylamine (**1**)$^{3)}$ which was expected to produce the simplest azomethine ylide without any electric and steric effects of substituents at the dipole termini as shown in Chart 1.

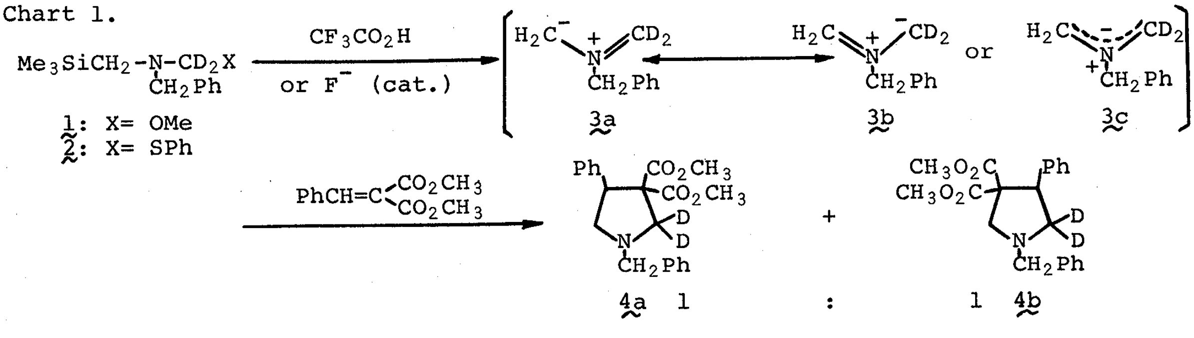


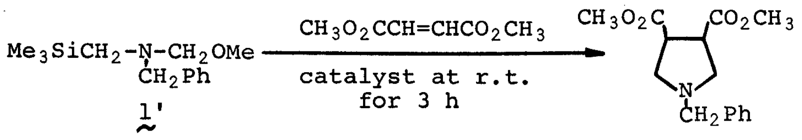
Chart 1

The starting material **1**$^{4)}$ was prepared from N-(benzyl)trimethylsilylmethylamine, methanol, and deuterated formaldehyde by a usual Mannich reaction. Treatment of **1** with dimethyl benzylidenemalonate as an unsymmetrical dipolarophile in the presence of a catalytic amount of trifluoroacetic acid in CH_2Cl_2 at r.t. afforded a 1 : 1 mixture of pyrrolidines **4a** and **4b** in 65% yield. Ratio of the regioisomers was estimated on the basis of ^{1}H-NMR spectrum of the crude product.$^{5)}$ This result indicates that the negative charge formed by desilylation is delocalized between two carbons adjacent to the nitrogen atom. Therefore, it is suitable that the intermediary azomethine ylide is illustrated as **3c** at least in this reaction.

Next experiment was carried out by using tetrabutylammonium fluoride (TBAF), instead of trifluoroacetic acid as a catalyst, in dimethylformamide (DMF) at r.t., where the ratio of **4a** was expected to increase because the anion resulted by fluoride anion-induced desilylation should attack to the dipolarophiles at the initial step and be followed by cyclization. Contrary to our expectation the mixture of the two regioisomers was obtained in the same ratio, which suggested that even in the case of fluoride anion catalyst the reaction proceed via the same intermediate (**3c**).

Following experimental facts are also in agreement with this view. In the 1,3-cycloadditions of **1'** (non-deuterated) to dimethyl maleate and dimethyl fumarate the stereochemistry at the 3- and 4-positions of the products was concluded to retain that of the dipolarophiles as indicated in Table I.

Table I



Entry	Dipolarophile	Catalyst/solvent	Configuration at the 3- & 4-positions	Yield (%)
1	Dimethyl maleate	CF_3CO_2H/CH_2Cl_2	cis	94
2	Dimethyl fumarate	CF_3CO_2H/CH_2Cl_2	trans	97
3	Dimethyl maleate	TBAF/DMF	cis/trans= 1/1$^{a)}$	30
4	Dimethyl fumarate	TBAF/DMF	trans	35

a) In this case, the epimerization from cis to trans was observed under the conditions.

Furthermore, since these results may be caused by ease of elimination of methoxy group, which was revealed by conversion of **1'** to bis(N-benzyltrimethylsilylmethylamino)methane under acidic conditions or on heating, we examined the 1,3-cycloaddition of deuterated N-benzyl-N-(phenylthiomethyl)trimethylsilylmethylamine (**2**)$^{4)}$ under the similar conditions. The reaction furnished the same result as that of **1**.

In conclusion, these experimental facts provided a definite evidence that 1,3-cycloaddition of trimethylsilylmethylamine derivatives proceeds via non-stabilized azomethine ylide produced by simultaneous desilylation and demethoxylation or dephenylthiolation, and such ylide has fundamentally the ambivalent structure.

Therefore, the regioselectivities in the 1,3-cycloadditions involving silicon-carbon bond cleavage should be discussed only on the basis of the substituent effects on 1,3-dipole termini, which will be described in detail elswhere.

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3) The 1,3-cycloaddition of N-(alkoxymethyl)trimethylsilylmethylamines to olefins in the presence of trimethylsilyl triflate or iodotrimethylsilane and cesium fluoride was reported by Hosomi and co-workers (ref. 2b), and we also revealed that trifluoroacetic acid was a convenient catalyst for this reaction (ref. 1b). However, any definite evidence for azomethine ylide intermediate has not been presented.

4) These compounds **1** and **2** were prepared as follows. N-(benzyl)trimethylsilylmethylamine (10 mmol) was added dropwise on ice-cooling to a solution of deuterated formaldehyde (12 mmol) in deuterium oxide and methanol or thiophenol (12 mmol). After stirring at the temperature for 3 h, potassium carbonate was added to the mixture. The oily layer was separated and the residue was washed with ether and the combined solution was dried over anhydrous magnesium sulfate. The product obtained by evaporation of the ether solution was almost pure without further purification. **1**, oil, yield 89%, ^{1}H-NMR δ ($CDCl_3$): 0.07(9H, s, $Si(CH_3)_3$), 2.18(2H, s, $SiCH_2N$), 3.20(3H, s, OCH_3), 3.71(2H, s, NCH_2Ph), 7.71(5H, s, C_6H_5). **2**, oil, yield 93%, ^{1}H-NMR δ ($CDCl_3$): 0.04(9H, s, $Si(CH_3)_3$), 2.22(2H, s, $SiCH_2N$), 3.65(2H, s, NCH_2Ph), 7.17(10H, s, C_6H_5, SC_6H_5). These compounds gave the satisfactory results of the other spectral data.

5) The NMR spectra of the product **4'** obtained from non-deuterated starting material **1'** and dimethyl benzylidenemalonate are shown below. ^{1}H-NMR δ ($CDCl_3$): 2.75-3.20(3H, m, CH_2NCH_A), 3.05(3H, s, OCH_3), 3.54(1H, d, J= 10.0Hz, NCH_B), 3.66(2H, s, NCH_2Ph), 3.72(3H, s, OCH_3), 4.34(1H, t, J= 7.1Hz, CHPh), 7.10-7.23(10H, m, $2\times C_6H_5$). ^{13}C-NMR δ ($CDCl_3$): 49.57(d), 51.74(q), 52.82(q), 59.59(t), 59.97(t), 60.68(t), 65.55(s), 127.05(d), 127.91(d), 128.30(d), 128.56(d), 129.00(d), 129.38(d), 138.70(s), 139.89(s), 169.47(s), 171.80(s). In this ^{1}H-NMR spectrum, the methine proton absorbs as a triplet at 4.34 ppm. However, in the case of the mixture of **4a** and **4b**, the signal appeared as a triplet with slightly broad and higher center peak due to overlap of a triplet (**4a**) and a singlet (**4b**), the ratio of which was calculated at 1 : 1 from the integlation value. In the ^{13}C-NMR spectrum of a mixture of **4a** and **4b**, the intensities of two signals due to the carbons adjacent to the nitrogen (59.59 and 60.68 ppm in the spectrum of **4'**) was observed to decrease in the same ratio. This indicates that undeuterated methylene carbon of **4a** exists with that of **4b** in the same ratios.

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