

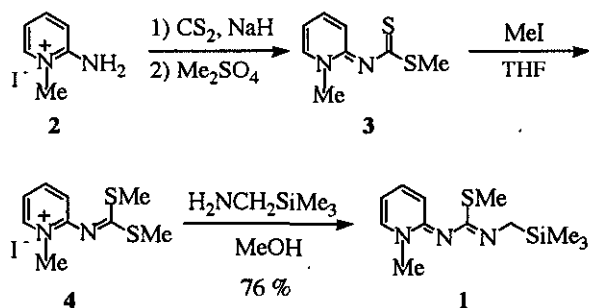
**FLUORIDE ION PROMOTED AZOMETHINE YLID GENERATION FROM 1-METHYL-2-[METHYLTHIO(TRIMETHYLSILYLMETHYLIMINO)METHYLIMINO]-1,2-DIHYDROPYRIDINE, A SYNTHETIC EQUIVALENT OF AMINONITRILE YLID**

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**Abstract** - 1-Methyl-2-[methylthio(trimethylsilylmethylimino)methylimino]-1,2-dihydropyridine (1), prepared from 2-amino-1-methylpyridinium iodide in 3 steps, reacted with carbonyl compounds in the presence of cesium fluoride in acetonitrile to give 2-(1-methyl-1,2-dihydropyridylidene)aminooxazoline derivatives (6) via the 1,3-dipolar cycloaddition. This reaction was the first example of reaction of aminonitrile ylid with the C=O double bond.

1,3-Dipolar cycloaddition reaction is one of the most important and interesting reactions to construct five-membered ring heterocycles from a synthetic point of view.<sup>1</sup> Among these reactions, azomethine ylides are used for the preparation of *N*-containing five-membered heterocycles. The fluoride ion promoted desilylation of *N*-(silylmethyl)imines has been unique and valuable methodology to generate azomethine ylides.<sup>2</sup> We have reported that alkylideneazomethine ylides<sup>3</sup> and iminoazomethine ylides<sup>4</sup> can be generated by 1,3-elimination reactions of *N*-trimethylsilylmethyl-substituted ketene *N,S*-acetals and *N*-silylmethyl-substituted isothiouras promoted by fluoride ion and that [3+2] cycloadditions to a variety of dipolarophiles are achieved, giving *N*-containing 2-alkylidene- and 2-imino-heterocycles. In the extension of the studies on organosilicon compounds in



Scheme 1

synthesis, we have found that 1-methyl-2-[methylthio(trimethylsilylmethylimino)methylimino]-1,2-dihydropyridine (1) reacts with carbonyl compounds under mild conditions to afford the corresponding oxazoline derivatives *via* the [3+2] cycloaddition.

1-Methyl-2-[*N*-bis(methylthio)methylene]aminopyridinium iodide (4),<sup>5</sup> readily prepared by the reaction of 2-amino-1-methylpyridinium iodide (2) and carbon disulfide in the presence of sodium hydride followed by methylation, was treated with aminomethyltrimethylsilane in methanol to afford the title compound (1)<sup>6</sup> as a mixture of two isomers in 76% yield (Scheme 1).

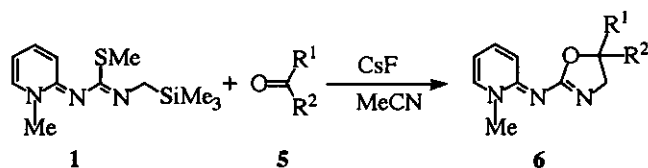
The reaction of 1, thus obtained, with 1 equivalent of benzaldehyde (5a) promoted by cesium fluoride proceeded in acetonitrile at room temperature for a week to afford the corresponding 2-(1-methyl-1,2-dihydropyridylidene)amino-5-phenyloxazoline (6a)<sup>7</sup> in 71% yield. As shown in Table 1, a variety of aromatic aldehydes (5b-5j) reacted with 1 in a similar manner to that described for 5a to give the corresponding 5-substituted 2-(1-methyl-1,2-dihydropyridylidene)aminooxazoline derivatives (6b-6j) in moderate yields. Cinnamaldehyde (5k) and benzil (5l),  $\alpha$ -diketone, were also reacted with 1 to give [3+2] cycloaddition products (6k and 6l). However aliphatic aldehydes, simple ketones, and active alkene such as dimethyl fumarate and *N*-methylmaleimide did not undergo the reaction under the present reaction conditions. Using tetra-*n*-butylammonium fluoride (TBAF) instead of cesium fluoride as fluoride ion source, the reaction of 1 and 5a gave 6a in 67% yield.

A typical experimental procedure is as follows: A solution of benzaldehyde (5a) (0.106 g, 1.0 mmol) and 1 (0.267 g, 1.0 mmol) in acetonitrile (3 ml) was added to a suspension of cesium fluoride (0.304 g, 2.0 mmol) in acetonitrile (1 ml) and the reaction mixture was stirred at room temperature for 1 week under nitrogen atmosphere. After evaporating of the solvent, the residue was poured into water (30 ml) and the aqueous layer was extracted with ethyl acetate (2 x 30 ml). The organic

layer was washed with water (30 ml) and then brine (30 ml). After dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The crude product was chromatographed on an alumina (Merck, Aluminum oxide 90 active, basic) column using dichloromethane as an eluent to give 2-(1-methyl-1,2-dihydropyridylidene)amino-5-phenyloxazoline (6a) (0.180 g, 71 % yield).

This work demonstrates that 1-methyl-2-[methylthio(trimethylsilylmethylimino)methylimino]-1,2-dihydropyridine (1), storable and easy to handle, can be viewed as a synthetic equivalent of aminonitrile ylid.

Table 1. Reaction of Organosilicon (1) and Carbonyl Compounds (5)<sup>a)</sup>



Entry	5		Yield of 6 (%) <sup>b)</sup>	
	R <sup>1</sup>	R <sup>2</sup>		
1	C <sub>6</sub> H <sub>5</sub>	H	(5a)	71 (6a)
2	4-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub>	H	(5b)	73 (6b)
3	4-MeC <sub>6</sub> H <sub>4</sub>	H	(5c)	71 (6c)
4	4-MeOC <sub>6</sub> H <sub>4</sub>	H	(5d)	57 (6d)
5	4-ClC <sub>6</sub> H <sub>4</sub>	H	(5e)	73 (6e)
6	2,6-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	H	(5f)	77 (6f)
7	4-NCC <sub>6</sub> H <sub>4</sub>	H	(5g)	52 (6g)
8	1-Naphthyl	H	(5h)	55 (6h)
9	2-Thienyl	H	(5i)	44 <sup>c)</sup> (6i)
10	3-Pyridyl	H	(5j)	43 (6j)
11	(E)-C <sub>6</sub> H <sub>4</sub> CH=CH	H	(5k)	38 <sup>d)</sup> (6k)
12	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub> CO	(5l)	42 (6l)

a) All reactions were carried out using 1 (1.0 mmol) and 5 (1.0 mmol) in the presence of CsF (2.0 mmol) in MeCN (4 ml) at room temperature for 1 week, unless otherwise noted.

b) Yield after isolation by column chromatography

c) Cesium fluoride (4.0 mmol) was used.

d) Carbonyl compound (5) (2.0 mmol) was used.

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6. **1**: Yield 76 %; ir (neat)  $\nu_{\text{max}}$ : 2950, 1640, 1600, 1550, 855  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  ( $\text{CDCl}_3$ )  $\delta$ : major isomer 0.04 (9H, s,  $\text{SiMe}_3$ ), 2.34 (3H, s,  $\text{SMe}$ ), 2.99 (2H, s,  $\text{NCH}_2\text{Si}$ ), 3.48 (3H, s,  $\text{NMe}$ ), 5.91 (1H, t,  $J = 6.8$  Hz, 5-H on pyridine ring), 6.45 (1H, d,  $J = 8.8$  Hz, 3-H on pyridine ring), 6.90-7.30 (2H, m, 4 and 6-H on pyridine ring); minor isomer 0.13 (9H, s,  $\text{SiMe}_3$ ), 2.30 (3H, s,  $\text{SMe}$ ), 3.15 (2H, s,  $\text{NCH}_2\text{Si}$ ), 3.51 (3H, s,  $\text{NMe}$ ), 5.91 (1H, t,  $J = 6.8$  Hz, 5-H on pyridine ring), 6.45 (1H, d,  $J = 8.8$  Hz, 3-H on pyridine ring), 6.90-7.30 (2H, m, 4 and 6-H on pyridine ring) (major : minor = ca. 1.6 : 1). *Anal.* Calcd for  $\text{C}_{12}\text{H}_{12}\text{N}_3\text{SSi}$ : C, 53.88; H, 7.92; N, 15.71. Found; C, 53.90; H, 7.83; N, 15.69.
7. **6a**: Yield 71 %; mp 109-110  $^\circ\text{C}$  (*n*-hexane-ethyl acetate); ir (neat)  $\nu_{\text{max}}$ : 3075, 2905, 2855, 1635, 1595, 1545, 1505, 1385, 1015  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  ( $\text{CDCl}_3$ )  $\delta$ : 3.70 (3H, s,  $\text{NMe}$ ), 3.87 (1H, dd,  $J = 13.0$  and 7.9 Hz, 4-H on oxazoline ring), 4.36 (1H, dd,  $J = 13.0$  and 9.4 Hz, 4-H on oxazoline ring), 5.46 (1H, dd,  $J = 9.4$  and 7.9 Hz, 5-H on oxazoline ring), 6.26 (1H, td,  $J = 6.6$  and 1.3 Hz, 5'-H on pyridine ring), 7.12-7.47 (7H, m, 3'- and 4'-H on pyridine ring and phenyl-H), 8.19 (1H, dd,  $J = 9.7$  and 1.3 Hz, 6'-H on pyridine ring). *Anal.* Calcd for  $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_2$ : C, 71.12; H, 5.97; N, 16.59. Found; C, 71.18; H, 6.03; N, 16.64.  
Other **6** were fully characterized by  $^1\text{H-nmr}$ , ir, and HR-*ms* or elemental analysis.

Received, 4th February, 1994