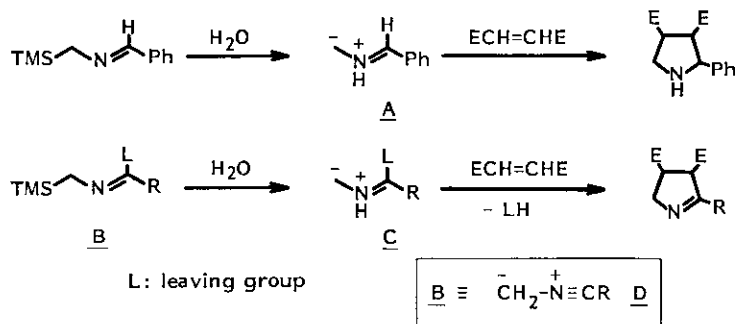


WATER-INDUCED AZOMETHINE YLIDE GENERATION FROM N-(SILYLMETHYL)THIO-
IMIDATES, SYNTHETIC EQUIVALENTS OF NONSTABILIZED NITRILE YLIDES

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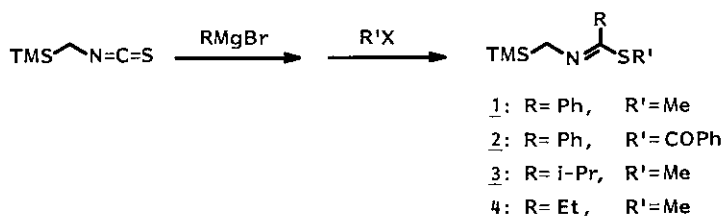
Abstract — N-(Silylmethyl)thioimides undergo a water-induced desilylation generating azomethine ylide 1,3-dipoles which cycloadd to a variety of electron-deficient olefins providing 1- or 2-pyrrolines after the elimination of thiol, indicating that the thioimides are synthetic equivalents of nonstabilized nitrile ylides.

N-(Silylmethyl)imines owe their importance in heterocyclic synthesis much to the applications toward the generation of azomethine ylide 1,3-dipoles under mild conditions. The general route into the ylides consists of the initial quaternarization on the nitrogen and the subsequent desilylation with a fluoride ion¹. A variety of azomethine ylides have been prepared according to this method and found wide applications in organic synthesis². A rather exceptional generating method discovered in our laboratory involves the action of water to N-(silylmethyl)imines in polar solvents such as HMPA or DMF³. Cycloadditions of the ylide A thus formed to olefins provide pyrrolidines as shown below.



The present research is aiming at an extension of our method to an N-(silylmethyl)-imine B bearing a leaving group at the imine carbon. The cycloadditions of ylide C to olefinic dipolarophiles, followed by elimination of the leaving group, would lead to 1-pyrroline derivatives. By this sequence, the imine B will become the

synthetic equivalent of a nonstabilized nitrile ylide D. We have chosen some N-(silylmethyl)thioimides as candidates for B.



Scheme 1.

The thioimides 1-4 were readily available in one-pot reactions of trimethylsilylmethyl isothiocyanate⁴ with Grignard reagents and then with methyl iodide or benzoyl chloride as shown in Scheme 1 (1: 83%; 2: 71%; 3: 71%; 4: 76%). This route might allow the introduction of a variety of substituents at the imine carbon of thioimides⁵.

The reaction of 1 with N-methylmaleimide 5 in the presence of an equivalent amount of water in HMPA at room temperature (method A) gave an excellent yield of the 1-pyrroline 10 (Scheme 2 and Table 1)⁶. Although some initial cycloadduct E was detected in the crude reaction mixture, it suffered from the ready and complete

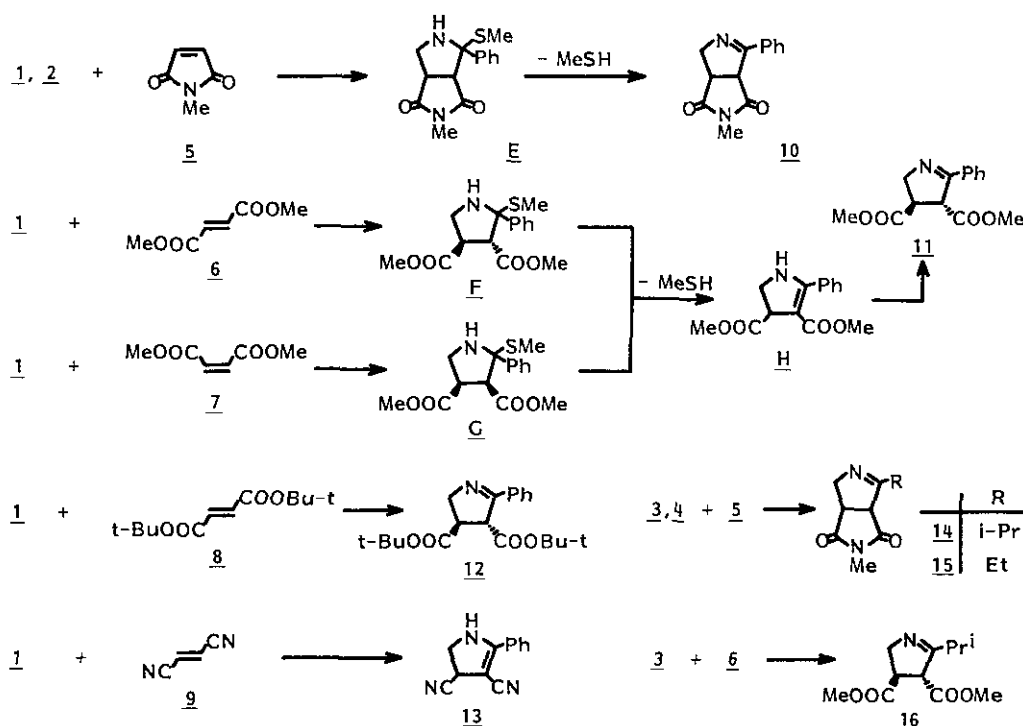
Table 1. Cycloadditions of 1-4 to Symmetrically Substituted Olefins.

N-Silylmethyl thioimide	Olefin	Reaction conditions ^{a)}		Product	Yield/% ^{c)}
		Method ^{b)}	Time/h		
<u>1</u>	<u>5</u>	A	24	<u>10</u>	98
		B	16	<u>10</u>	25
		C	16	<u>10</u>	44
<u>2</u>	<u>5</u>	D	36	<u>10</u>	70
<u>1</u>	<u>6</u>	A	24	<u>11</u>	80
		B	24	<u>11</u>	38
<u>1</u>	<u>7</u>	A	24	<u>11</u>	62
<u>1</u>	<u>8</u>	A	24	<u>12</u>	70
<u>1</u>	<u>9</u>	A	24	<u>13</u>	77
<u>3</u>	<u>5</u>	A	24	<u>14</u>	15
<u>4</u>	<u>5</u>	A	24	<u>15</u>	10
<u>3</u>	<u>6</u>	E	24	<u>16</u>	23

a) Each equivalent amounts of the thioimides and olefins were used. b) A: H₂O (equiv) in HMPA at rt; B: TMSOTf-CsF (each equiv) in HMPA at 60 °C; C: PhCOF (equiv) in MeCN at 60 °C; D: AcOH (equiv) in HMPA at 60 °C; E: AcOH (equiv) in HMPA at rt. c) All isolated yields.

elimination of methanethiol during the chromatographic procedure over silica gel providing 10. The conventional generating method using TMSOTf-CsF (method B) or PhCOF (method C) resulted in poorer yield of 10. The thioimide 2 bearing benzoylthio moiety as a leaving group showed no advantage over the methylthio-substituted thioimide 1.

It is surprising that the same *trans*-1-pyrroline 11 was the only product either in the reaction of 1 with dimethyl fumarate 6 or with dimethyl maleate 7, because the cycloaddition of nonstabilized azomethine ylide to olefins is known to be highly stereospecific³. The initial cycloadducts F and G must have been *trans* and *cis*, respectively. The thiol elimination at the 2-3 bond leads to the same 2-pyrroline H. The sterically hindered enamine of H undergoes a hydrogen migration forming the sterically more favored *trans*-1-pyrroline 11.



Scheme 2.

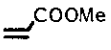
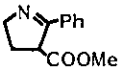

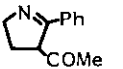
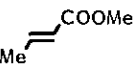
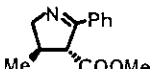
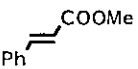
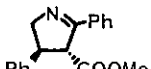
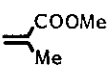
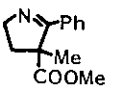
Similar reactions of 1 with di(*t*-butyl) fumarate 8 and fumaronitrile 9 gave the 1-pyrroline 12 and 2-pyrroline 13, respectively (Scheme 2 and Table 1). The cyano moiety at the 3-position of 13 is small in size so that it tolerates the fixation of double bond at the 2-position.

Although the thioimides 3 and 4 carrying an alkyl substituent at the imine carbon underwent similar cycloadditions to 5 and 6, the yields of 14-16 were unfortunately

quite poor. This low yield might be partly due to the lack of ylide-stabilizing ability of the alkyl substituent. In these cases, the major reaction path was the polymerization of olefins employed.

The reactions of 1 with a variety of unsymmetrically substituted olefins 17-21 produced the regioselective 1-pyrrolines 22-26 in good yields (Table 2).

Table 2. Cycloadditions of 1 to Unsymmetrically Substituted Olefins.^{a)}

Olefin	Product	Yield/% ^{b)}
 <u>17</u>	 <u>22</u>	62
 <u>18</u>	 <u>23</u>	75
 <u>19</u>	 <u>24</u>	68
 <u>20</u>	 <u>25</u>	75
 <u>21</u>	 <u>26</u>	71

a) Conditions: H₂O (equiv) in HMPA at rt for 24 h. b) All isolated yields.

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5. Other substituents such as alkyl, aryl and vinyl moieties can be successfully introduced (unpublished results).
6. All new compounds reported herein gave satisfactory spectral and analytical results.

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