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New Synthesis of Thiiranes by Fluoride Ion-Promoted Reaction of S-Methyl-S'-trimethylsilylmethyl N-(*p*-Toluenesulfonyl)dithioiminocarbonate and 2-(Trimethylsilylmethylthio)thiazoline with Aldehydes[1]

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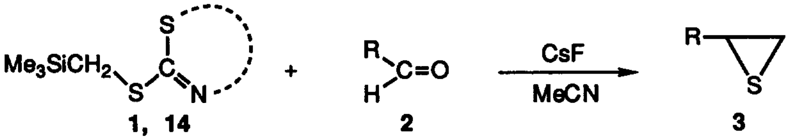
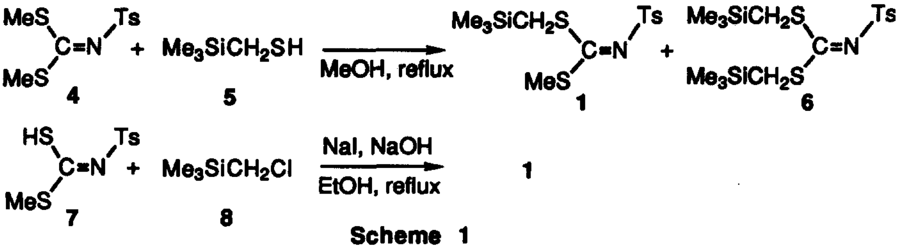
Key Words: thiirane; S-methyl-S'-(trimethylsilylmethyl) N-*p*-toluenesulfonyldithioiminocarbonate; 2-(trimethylsilylmethylthio)thiazoline; iminothiocarbonyl ylide; 1,3-dipolar reagent

Abstract: *The title compounds, readily prepared by the reaction of the corresponding S-methyl N-(p-toluenesulfonyl)dithioiminocarbonate and 2-mercaptothiazoline with (chloromethyl)trimethylsilane in the presence of a base, were used as new reagents for the introduction of a thioformaldehyde unit to a carbonyl carbon. The reaction of these compounds with aldehydes in the presence of cesium fluoride afforded thiiranes via the 1,3-dipolar cycloaddition of iminothiocarbonyl ylide to C=O double bond.*

Thiocarbonyl ylides are important 1,3-dipolar reagents for the construction of five-membered ring sulfur-containing heterocycles such as thiophene derivatives, 1,3-oxathiolanes, and 1,3-thiazolidines.[2] Recently we reported that α-thio carbanion species can be readily generated by the fluoride ion-promoted desilylation of trimethylsilylmethyl sulfides under mild conditions;[3] contrary to rather drastic conditions in the deprotonation of alkyl sulfides which requires a strong lithium base.[4] This method has been conveniently applied to the generation of various 1,3-dipolar reagents such as tailor-made azomethine ylides and related species, and further to their [3+2]cycloadditions giving pyrrolidine, oxazolidine, and thiazolidine derivatives.[2b-d,5] We wish to report here preparations of S-methyl-S'-trimethylsilylmethyl N-(*p*-toluenesulfonyl)dithioiminocarbonate (**1**) and 2-(trimethylsilylmethylthio)thiazoline (**14**) as synthetic equivalents of iminothiocarbonyl ylides, new 1,3-dipolar reagents, and a novel synthesis of thiiranes *via* their 1,3-dipolar [3+2]cycloaddition to aldehydes.



In a similar manner to alkylidene- and imino-azomethine ylides derived by the fluoride ion-promoted reaction of N-(trimethylsilylmethyl)substituted ketene N,S-acetals and their aza analogs,[5b-d] the generation of iminothiocarbonyl ylides and the reaction with dipolarophiles will be certainly of interest from a viewpoint of synthesis of sulfur-containing heterocycles. We planned to prepare S-methyl-S'-trimethylsilylmethyl N-(*p*-toluenesulfonyl)dithioiminocarbonate (**1**) by addition-elimination reaction of (mercaptomethyl)trimethylsilane (**5**) to S,S'-dimethyl N-(*p*-toluenesulfonyl)dithioiminocarbonate (**4**).[6] Although this reaction in methanol gave a easily separable mixture of **1**[7] and S,S'-bis(trimethylsilylmethyl) N-(*p*-toluenesulfonyl)dithioiminocarbonate (**6**)[8] in 42 and 20% yields, respectively, the desired **1** was obtained alternatively and more conveniently by treatment of S-methyl N-(*p*-toluenesulfonyl)dithioiminocarbonate (**7**)[9] with (chloromethyl)trimethylsilane (**8**) in the presence of sodium iodide and sodium hydroxide in ethanol at reflux temperature for 20 h in 71% yield (Scheme 1).



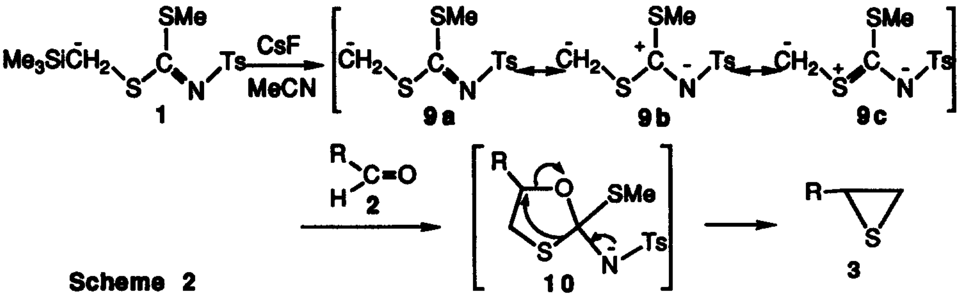
Scheme 1

The reaction of **1**, thus obtained, with an equivalent of 4-methoxybenzaldehyde (**2d**) promoted by cesium fluoride[10] proceeded in acetonitrile at room temperature for 43 h to afford the corresponding 2-(4-methoxyphenyl)thiirane (**3d**) in 19% yield, instead of an expected 2-imino-1,3-oxathiolane. The yield of **3d** increased up to 85% by use of three equivalents of **2d** toward **1**. This reaction was also carried out without solvent at room temperature, though the yield was 52%. As summarized in Table 1,[11] **1** reacted smoothly with various aldehydes (**2a-i**) to give the corresponding 2-substituted thiiranes (**3a-i**). The plausible reaction pathway to give **3** is reasonably shown in Scheme 2.[12] Treatment of **1** with fluoride ion generates a novel 1,3-dipolar species (**9**)[5,12] in the initial stage which adds to an aldehyde to lead the formation of an anionic 1,3-oxathiolane intermediate (**10**). Ring contraction of **10** gives a thiirane (**3**), instead of the formation of an 2-imino-1,3-oxathiolane, *via* elimination of a methylthio group.

Table 1. Synthesis of Thiiranes (3a-i) from 1 and Aldehydes (2a-i)[a]

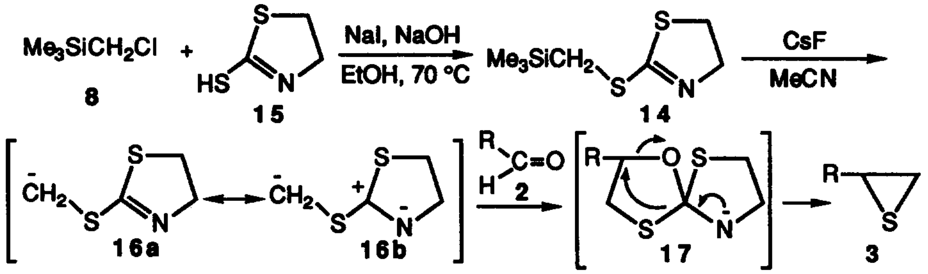
No.	R	Yield /%[b]
3a	C_6H_5	66
b	$4\text{-}MeC_6H_4$	77
c	$2\text{-}MeC_6H_4$	64
d	$4\text{-}MeOC_6H_4$	85
e	$3\text{-}MeOC_6H_4$	65
f	$2\text{-}MeOC_6H_4$	83
g	$2,6\text{-}Cl_2C_6H_3$	29
h	$4\text{-}C_6H_5C_6H_4$	68
i	1-Naphthyl	48

[a] All reactions were carried out in a system of 1 (0.5 mmol), 2 (1.5 mmol) and CsF (0.5 mmol) in MeCN at rt. [b] Yield after isolation by silica gel column chromatography.



Scheme 2

Similarly 2-(trimethylsilylmethylthio)thiazoline (14),[13] prepared by the reaction of 8 with 2-mercaptothiazoline (15) in the presence of sodium hydroxide and sodium iodide in ethanol, reacted with aldehydes (2d and 2h) to give the corresponding thiiranes (3d and 3h) in 58 and 75% yields, respectively (Scheme 3).



Scheme 3

A typical experimental procedure is as follows: A solution of 4-methoxybenzaldehyde (2d) (1.5 mmol, 0.204 g), 1 (0.5 mmol, 0.179 g) and cesium fluoride (0.60 mmol, 0.091 g) in dry acetonitrile (10 ml) was stirred at room temperature for 43 h under an argon atmosphere. After water and ether were added with stirring, the organic layer was separated and dried over sodium sulfate, and the solvent was evaporated. After purification of a crude product by silica gel column chromatography, a thiirane (3d) (0.0615 g, 0.375 mmol) was obtained in 85% yield.

In conclusion, S-methyl-S'-trimethylsilylmethyl N-(*p*-toluenesulfonyl)dithioiminocarbonate (1) and 2-(trimethylsilylmethylthio)thiazoline (14), which are readily prepared, storable and easy to handle, have been found to be not only precursors to new 1,3-dipolar reagents, otherwise inaccessible iminothiocarbonyl ylides, under mild conditions but also new reagents for the synthesis of thiiranes (3) by the introduction of a thioformaldehyde unit to a carbonyl carbon.

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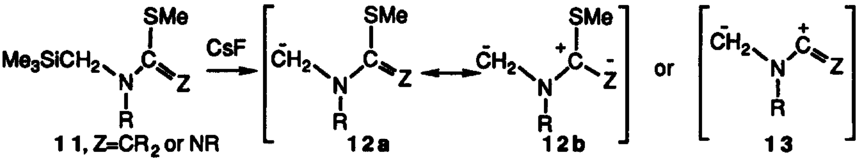

1 1, Z=CR$_2$ or NR **1 2a** **1 2b** **1 3**

6. Y. Kuwayama and S. Kataoka, *Yakugaku Zasshi*, **85**, 391 (1965).
7. **1**: colorless leaflets, mp 87 °C. MS(m/z): 347(M$^+$, 0.5), 332(M$^+$-15, 5), 228(14), 155(95), 91(90), 73(100, SiMe$_3$); ^{1}H-NMR(CDCl$_3$) δ 0.13(9H, s, SiMe$_3$), 2.31(2H, s, CH$_2$), 2.42(3H, s, *p*-Me), 2.49(3H, s, SMe), 7.28(2H, d, *J*=8.4 Hz, aromatic-H), 7.87(2H, d, *J*=8.4 Hz, aromatic-H). Fluoride ion-promoted protodesilylation of **6** in wet acetonitrile gave the corresponding **1** in quantitative yield.
8. **6**: colorless needles, mp 103 °C. ^{1}H-NMR (90MHz, CDCl$_3$) δ 0.13(18H, s, SiMe$_3$), 2.29 (4H, s, CH$_2$), 2.42(3H, s, *p*-Me), 7.28(2H, d, *J*=8.4Hz, aromatic H), 7.87(2H, d, *J*=8.4Hz, aromatic H).
9. Compound (**7**) was readily prepared by the reaction of *p*-toluenesulfonamide with carbon disulfide in the presence of sodium hydroxide at 0 °C in dimethyl sulfoxide followed by methylation with dimethyl sulfate in 91% yield. cf: R. Gompper and W. Hagele, *Chem. Ber.*, **99**, 2885 (1966).
10. Tetrabutylammonium fluoride (TBAF) can be used as a source of fluoride ion, though the yield was not so good. In the reaction of **1** with **2d**, **3d** was obtained in only 19% yield.
11. Satisfactory spectral (IR, ^{1}H-NMR, and MS) data were obtained for all new compounds in this work.
12. The reaction of **1** with dimethyl fumarate and maleate in the presence of cesium fluoride in acetonitrile gave 1,3-dipolar cycloadducts, dimethyl *trans*- and *cis*-2-(N-*p*-toluenesulfonylimino)tetrahydrothiophene-3,4-dicarboxylate, in 37% and 22% yields, respectively. This outcome strongly suggests that the formation of thiiranes from **1** takes place *via* the 1,3-dipolar [3+2]cycloaddition similarly to reactions of alkylidene- and imino-azomethine ylides with carbonyl compounds.[5b-d] These results with activated alkenes will be published in a forthcoming paper.
13. **14**: bp 145 °C(19 mmHg). MS(m/z): 205(M$^+$, 12), 190(M$^+$-15, 100), 158(7), 133(4), 131(6), 116(19) 73(51, SiMe$_3$); ^{1}H-NMR(90MHz, CDCl$_3$) δ 0.00(9H, s, SiMe$_3$), 2.27(2H, s, Si-CH$_2$-S), 3.26(2H, t, *J*=7.9Hz, CH$_2$-S), 4.07(2H, t, *J*=7.9Hz, CH$_2$-N).

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