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Publication details, including instructions for authors and subscription information:

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**To cite this Article** Heimgartner, Heinz , Fu, Changchun , Blagoev, Milen and Linden, Anthony(2005) 'Regio- and Stereoselective Formation of 1,3-Oxathiolanes by Reactions of Thiocarbonyl Compounds with Oxiranes', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 180: 5, 1309 — 1313

**To link to this Article:** DOI: 10.1080/10426500590912240

**URL:** <http://dx.doi.org/10.1080/10426500590912240>

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## Regio- and Stereoselective Formation of 1,3-Oxathiolanes by Reactions of Thiocarbonyl Compounds with Oxiranes

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*Lewis acid-catalyzed reactions of oxiranes with a variety of C=S compounds yield 1,3-oxathiolanes. The ring enlargement of monosubstituted oxiranes occurs regioselectively via cleavage of the O,C(3) bond of alkyl substituted oxiranes and the O,C(2) bond of phenyl oxirane. Furthermore, the reaction proceeds with inversion of the configuration at the center of the nucleophilic attack by the S-atom. The formation of thiocarbonyl cations as intermediates is supported by Wagner–Meerwein-type rearrangements. Enolized thioketones react with oxiranes to give enesulfanyl alcohols, which undergo an acid-catalyzed cyclization to yield 1,3-oxathiolanes.*

**Keywords** 1,3-Oxathiolanes; oxiranes; ring enlargement; stereoselectivity

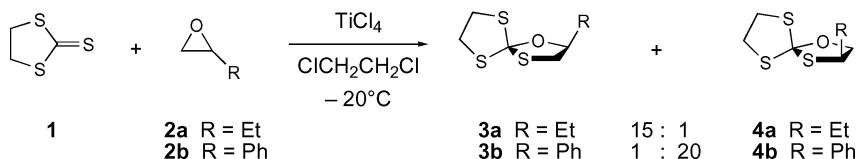
### INTRODUCTION

In general, 1,3-oxathiolanes are prepared by the reaction of carbonyl compounds with 2-sulfanylalkan-1-ols. Alternatively, 1,3-dipolar cycloadditions of carbonyl ylides with C=S and thiocarbonyl ylides with C=O compounds, respectively, lead to the same heterocyclic system (compare to references cited by Tromm and Heimgartner<sup>1</sup>). Some years ago, we discovered that the Lewis acid-catalyzed reaction of oxiranes with 4,4-disubstituted 1,3-thiazole-5(4*H*)-thiones and trithiocarbonates, respectively, offers another convenient access to 1,3-oxathiolanes.<sup>1,2</sup> For example, 1,3-dithiolane-2-thione (**1**) and 2-ethyloxirane (**2a**) in 1,2-dichloroethane and TiCl<sub>4</sub> at –20°C gave the spirocyclic 1,3-oxathiolanes **3a** and **4a** (R = Et) in a ratio of 15:1

Received July 9, 2004; accepted October 5, 2004.

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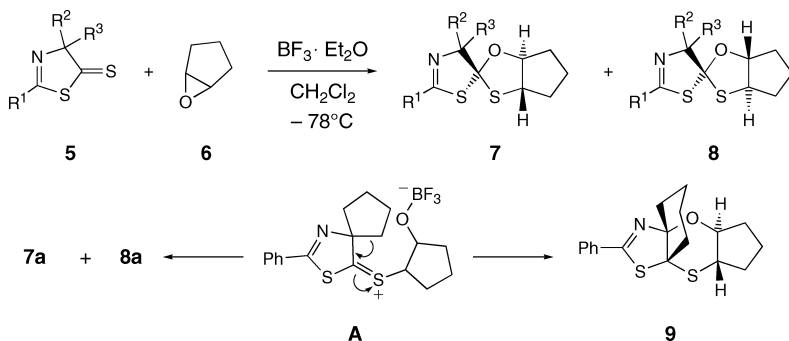
(Scheme 1). On the other hand, the ratio **3b/4b** ( $R = \text{Ph}$ ) was determined to be 1:20.<sup>2</sup>



**SCHEME 1**

## RESULTS

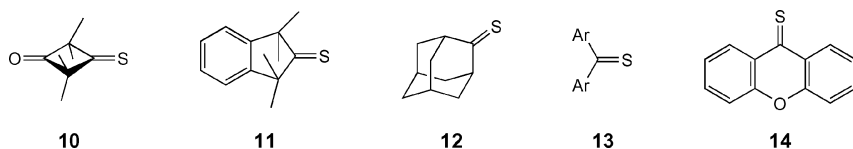
Treatment of a mixture of 1,3-thiazole-5(4*H*)-thione **5** and 1,2-epoxycyclopentane (**6**) in dichloroethane at  $-78^\circ\text{C}$  with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  gives the two diastereoisomeric 1,3-oxathiolanes **7** and **8** in 74–84% yield (ratio approximately 8:1)<sup>3</sup> (Scheme 2). Another efficient catalyst is  $\text{SnCl}_4$ . Both isomers show a *trans*-fusion of the cyclopentane and 1,3-oxathiolane ring. Analogous results are obtained with 1,2-epoxycyclohexane<sup>3</sup> and *cis*- and *trans*-2,3-dimethyloxirane.<sup>4</sup> Obviously, the opening of the oxirane ring occurs by nucleophilic attack of the S-atom under inversion of the configuration ( $\text{S}_\text{N}2$ -type), leading to an intermediate thiocarbonylium cation of type **A**. An indication of the cationic intermediate is the Wagner–Meerwein rearrangement, which leads to the minor product **9**.



**SCHEME 2**

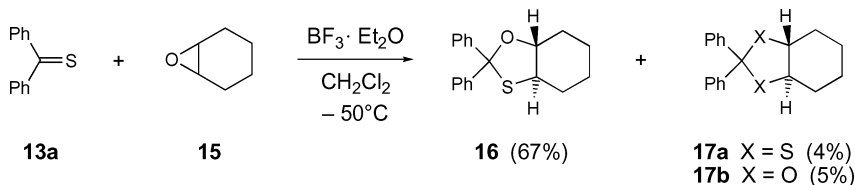
Recently, it has been shown that the reaction of 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione (**5a**) and (*R*)-2-phenyloxirane ((*R*)-**2b**) in dichloromethane can also be catalyzed by  $\text{SiO}_2$ .<sup>5</sup> The corresponding spirocyclic 1,3-oxathiolanes are formed with high diastereoselectivity

and inversion of the configuration of the oxirane. Similar results are obtained with nonenolizable thioketones such as **10–14**<sup>4–7</sup> (Scheme 3).



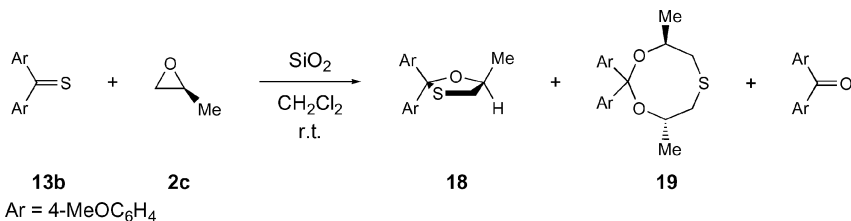
SCHEME 3

In some cases, 1,3-dithiolanes and 1,3-dioxolanes are formed in addition to 1,3-oxathiolanes.<sup>4,6,7</sup> For example, the  $\text{BF}_3$ -catalyzed reaction of thiobenzophenone (**13a**) and 1,2-epoxycyclohexane (**15**) in dichloromethane at  $-50^\circ\text{C}$  yields **16**, **17a**, and **17b**.<sup>6</sup> It has been shown that **17a** and **17b** are secondary products, which are formed by decomposition of **16** to give benzophenone and 1,2-epithiocyclohexane and subsequent reaction with oxirane **15** and thiobenzophenone **13a**, respectively (Scheme 4).



SCHEME 4

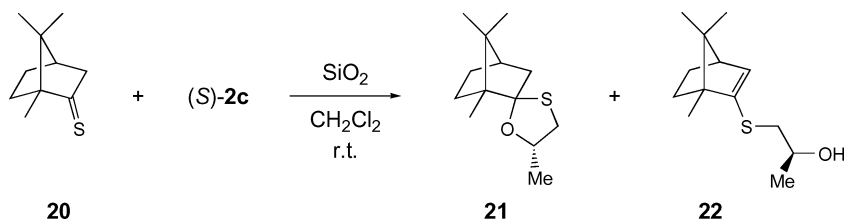
Another minor product, observed in the reaction of 4,4'-dimethoxythiobenzophenone (**13b**) with 2-methyloxirane (**2c**) is the 1,3,6-dioxathiocane **19**<sup>7,8</sup> (Scheme 5). It is noteworthy that only the homochiral *trans* isomer is formed even though racemic **2c** is used. The same product is obtained when a mixture of the major product **18** and **2c** is treated with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  at  $-90^\circ\text{C}$ . Using (*S*)-**2c** in the reaction with



SCHEME 5

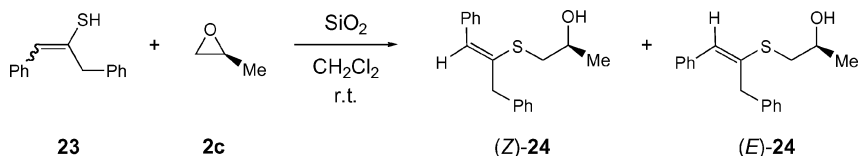
**13b**, (*S*)-**18** and (*S,S*)-**19** are formed with **98** and >99% enantiomeric excess (ee), respectively. On the other hand, no 1:2 adduct (*R,S*)-**19** could be detected in attempted reactions of (*R*)-**18** with (*S*)-**2c**.

In the case of enolizable thiocamphor (**20**), the SiO<sub>2</sub>-catalyzed reaction with (*S*)-**2c** leads to a mixture of the 1,3-oxathiolane **21** and the enesulfanyl alcohol **22**<sup>9</sup> (Scheme 6). The latter can be cyclized under acidic conditions to give a mixture of **21** and a diastereoisomer. The 1,3-oxathiolane **21** is acid-sensitive and undergoes a rearrangement to the second diastereoisomer. This isomerization shows clearly that the formation of the 1,3-oxathiolanes is reversible.



**SCHEME 6**

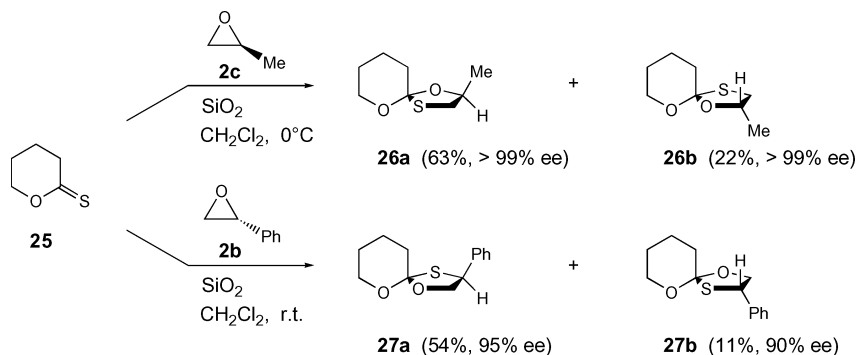
With 1,3-diphenylprop-1-ene-2-thiol (**23**), the enolized form of dibenzylthio ketone, 2-methyl- and 2-phenyloxirane react under SiO<sub>2</sub> catalysis to give *E/Z* isomers of the corresponding enesulfanyl alcohols with high ee values<sup>8</sup> (Scheme 7). Upon treatment with HCl gas, a cyclization to yield 1,3-oxathiolanes takes place.



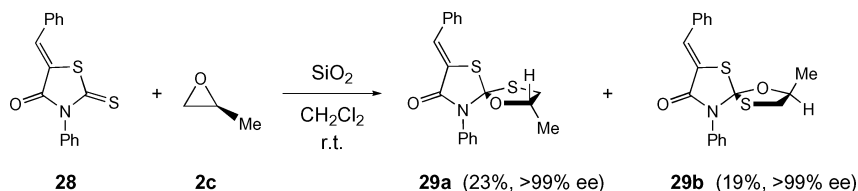
**SCHEME 7**

Similar to thioketones, thiolactones react with **2b** and **2c**. For example, the SiO<sub>2</sub>-catalyzed reaction of **25** leads to spirocyclic O,O,S-orthoesters **26** and **27**, respectively, with high stereoselectivity<sup>10</sup> (Scheme 8).

Furthermore, chemo-, regio-, and stereoselective 1,3-oxathiolane formations are observed with (*Z*)-5-benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one **28**<sup>11</sup> (Scheme 9). With (*S*)-2-methyloxirane [(*S*)-**2c**], after 50% conversion of **28**, the 1,3-oxathiolanes **29a** and **29b** are obtained in 23 and 19% yield, respectively.



SCHEME 8



SCHEME 9

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