

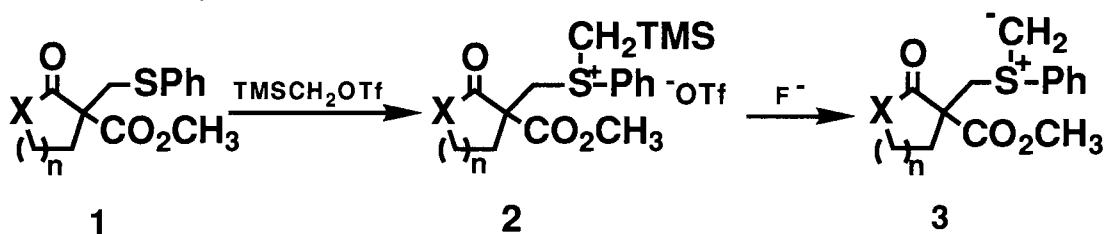
A New Fragmentation Reaction of γ -Oxosulfonium Methylides

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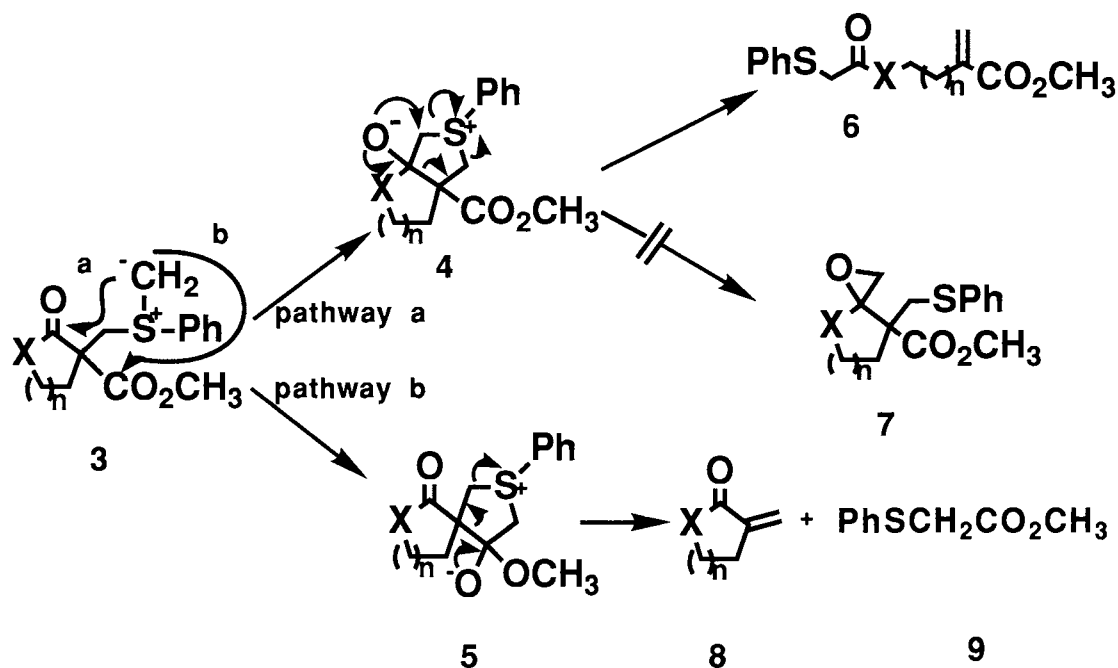
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Reactions of sulfonium methylides attached to a 5- or 6-membered cycloalkanone undergo the ring-fission as a major reaction course to give α -methylene- ω -(phenylthio)carboxylates, whereas sulfonium methylides attached to a larger ring give α -methylene-cycloalkanones predominantly. Reactions of the acyclic compounds are also examined.

Reactions of sulfonium ylides with ketones or aldehydes have been widely exploited for the construction of various epoxides,¹⁾ including annulation accompanied by concomitant formation of an epoxide ring.²⁾ These ylides have been generally generated by the abstraction of a proton α to the sulfonium group with base. Recently the fluoride-induced desilylation of (trimethylsilyl)methylsulfonium salts has provided an easy access to the regiospecific generation of sulfonium methylides from sulfonium salts.³⁾ We now report a novel reaction of sulfonium ylides generated from (trimethylsilyl)methylsulfonium salts of a variety of α -(phenylthio)methyl- β -ketoesters.



In the reaction of the sulfonium ylide **3** it would be expected that **3** undergoes fragmentation through at least two pathways involving attack by the ylide carbanion at either the carbonyl carbon (pathway **a**) or the ester carbon (pathway **b**) as illustrated in Scheme 1. In fact, treatment of the (trimethylsilyl)methylsulfonium salt **2** ($\text{X}=\text{CH}_2$, $n=2$) with tetrabutylammonium fluoride gave the ring-fissioned α,β -unsaturated ester **6** ($\text{X}=\text{CH}_2$, $n=2$) via pathway **a** together with small amounts of α -methylene-cyclohexanone **8** ($\text{X}=\text{CH}_2$, $n=2$) and methyl (phenylthio)acetate **9** both of which were obviously derived via pathway **b**. The results obtained in the reaction of various sulfonium ylides are shown in Table 1.

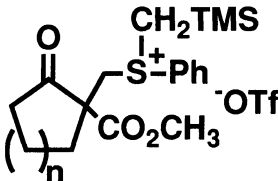
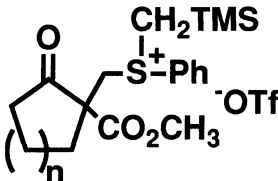
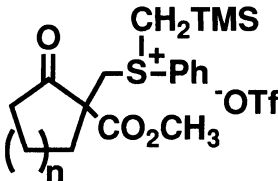
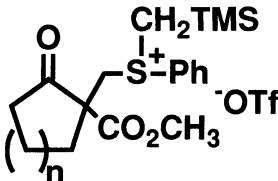
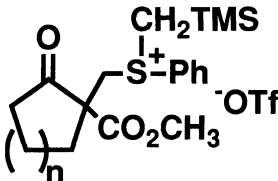
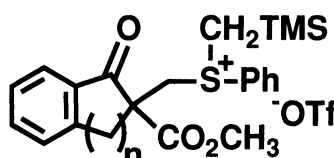
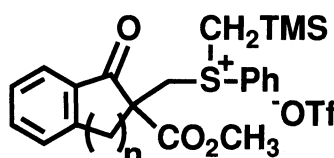
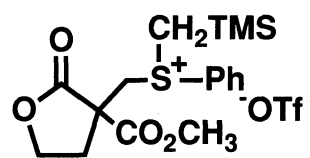
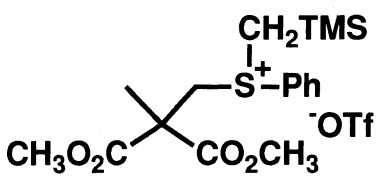
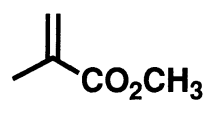
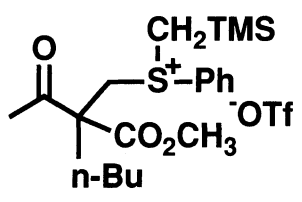
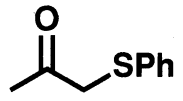
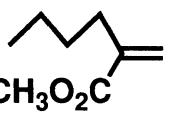


Scheme 1.

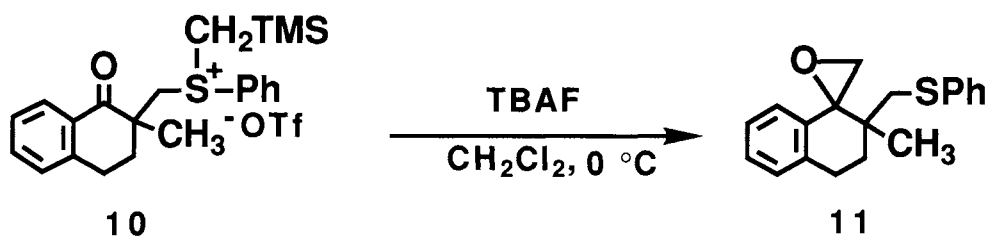
In the reaction of the ylides bearing a cycloalkanone it depends upon the ring size of the cycloalkanone whether the reaction proceeds via pathway **a** or **b**. The cyclopentanone sulfonium methylide afforded the ring-fissioned product **6** ($\text{X}=\text{CH}_2$, $n=1$, entry 1) predominantly as in the case of the cyclohexanone sulfonium methylide (entry 2), while the reaction of the ylides having a larger ring cycloalkanone such as cycloheptanone, cyclooctanone or cyclododecanone resulted in the predominant fragmentation via pathway **b** (entries 3-5), affording the α -methylene-cycloalkanones⁴⁾ **8** ($\text{X}=\text{CH}_2$, $n=3, 4$, or 8) and methyl (phenylthio)acetate **9** in high yields. The reaction of the ylides bearing an indanone or tetralone moiety proceeded predominantly via pathway **a** as being similar to that of the corresponding cyclopentanone and cyclohexanone ylides (entries 6 and 7). In the reaction of the γ -butyrolactone ylide (entry 8) attack by the ylide occurred predominantly at the ester carbon through pathway **b**. The ketone carbonyl was more susceptible than the ester carbonyl as shown in the reaction of the acyclic ylide (entry 10).

It should be noted that formation of the epoxide **7** could not be observed in the present reaction, because reactions of sulfonium ylides bearing a carbonyl group have been reported to give epoxides.^{1,2)} Electron-withdrawing properties of the ester (pathway **a**) and carbonyl (pathway **b**) groups may cause the preferred cleavage of the bridged bond in the intermediate **4** and **5**, respectively. Indeed, 2-methyltetralone sulfonium salt **10** gave the epoxide **11** in 93% yield, wherein no ring-fissioned products via either pathway **a** or **b** were not formed. The present process provides a new ring cleavage reaction through sulfonium ylides, giving the α -methylene- ω -(phenylthio)carboxylate **6** which can be transformed to carbocycles.⁵⁾

Table 1. Fragmentation of sulfonium methylides

| Entry | Sulfonium salt 2 | Products, yield / % ^{a)} | | | |
|-------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|----|------------------|
| | | 6 | 8 | 9 | |
| 1 |  | n = 1 | 65 | — | 5 |
| 2 |  | n = 2 | 58 | 4 | 22 |
| 3 |  | n = 3 | 23 | 13 | 75 ^{b)} |
| 4 |  | n = 4 | 3 | 75 | 90 |
| 5 |  | n = 8 | 12 | 69 | 70 |
| ----- | | | | | |
| 6 |  | n = 1 | 66 | 5 | 14 |
| 7 |  | n = 2 | 57 | 33 | 31 |
| ----- | | | | | |
| 8 |  | n = 1 | 17 | — | 63 |
| ----- | | | | | |
| 9 |  |  | 80 | — | 84 |
| ----- | | | | | |
| 10 |  |   | 61 50 | — | 5 |

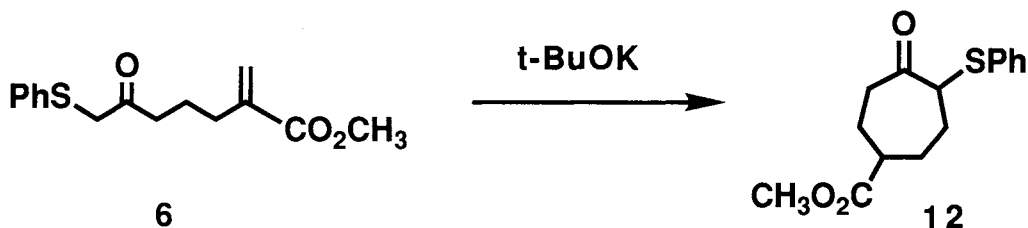
a) Isolated yield. b) When the sulfonium salt was treated with CsF (1.3 equiv.) in CH₂Cl₂ under reflux for 22 h, the yields of **6**, **8**, and **9** were 30, 35, and 48%, respectively.



A typical procedure is as follows: A mixture of sulfide **1** and (trimethylsilyl)-methyl trifluoromethanesulfonate (1.2 equiv.) in CH_2Cl_2 was stirred at room temperature for 1 day. After removal of the solvent under reduced pressure the salt was washed with a mixture of hexane and ethyl acetate (9 : 1). The salt **2** was then treated with a THF solution of tetrabutylammonium fluoride (1.5 equiv.) at 0°C for 3 h in the presence of powdered molecular sieves 4A.⁶⁾ Then the reaction was quenched with water. The mixture was extracted with ether. The combined extracts were washed with brine, dried with MgSO_4 , filtrated and concentrated under reduced pressure. Purification of this crude product by silica gel chromatography (10% ethyl acetate in hexane) gave products.

References

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- 2) J. K. Crandall, H. S. Magaha, R. K. Widener, and G. A. Tharp, *Tetrahedron Lett.*, **21**, 4807 (1980); M. E. Garst and A. T. Johnson, *ibid.*, **21**, 4812 (1980).
- 3) E. Vedejs and F. G. West, *Chem. Rev.*, **88**, 941 (1986); E. Vedejs and G. R. Martinez, *J. Am. Chem. Soc.*, **101**, 6452 (1979).
- 4) In some reactions exo-methylene compounds **8** could not be obtained or otherwise isolated in lower yields compared with those of the (phenylthio)acetate **9** probably because of the instability of **8** under the reaction conditions.
- 5) The α -methylene- ω -(phenylthio)carboxylate **6** ($\text{X}=\text{CH}_2$, $n=1$) obtained from the cyclopentanone sulfonium methyllide was cyclized to the α -(phenylthio)-cycloheptanone **12** in 82% yield by treatment with potassium *t*-butoxide at 0°C .



- 6) R. M. Hanson and K. B. Sharpless, *J. Org. Chem.*, **51**, 1922 (1986).

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