J|A|C|S
A R T I C L E S

Unusual Sulfur Chemistry in the Thermal Reaction of Sultene and Thiophene Endoperoxide Sulfur Donors with Cyclic Alkynes: Reversible Formation of a Persistent Thiirenium Ion and Trapping of a Thiirene by [4 + 2] Cycloaddition

Waldemar Adam,*,† Sara G. Bosio,† Bettina Fröhling,† Dirk Leusser,‡ and
Dietmar Stalke‡

Contribution from the Institut für Organische Chemie and Institut für Anorganische Chemie der Universität,
Am Hubland, D-97074 Würzburg, Germany

Received February 14, 2002

Abstract: The highly reactive cyclooctyne **2b** serves as sulfur acceptor for both sulfur donors, namely the sultene **1A** and thiophene endoperoxide **1B** to afford sulfur-transfer products. With the acid-activated sultene **1A**, the persistent thiirenium ion **3Ab** is formed, which has allowed the direct observation of the initial sulfur-transfer adduct. On treatment with base, the thiirenium ion **3Ab** reverts quantitatively to the cyclooctyne and sultene, whereas in neutral media it rearranges to the diene **6Ab**. The rearrangement to the diene **6Ab**, as well as the formation of spirocyclic adduct **6Ac** in the reaction with dithiocyclononyne **2c**, is proposed to proceed through a carbene mechanism. In the reaction of the cyclooctyne **2b** with thiophene endoperoxide **1B**, a thiirene is formed through sulfur transfer by an intermediary oxathiirane derived from the thiophene endoperoxide; as final product, the episulfide (*R**,*R**,*R**)-**3Bb** is produced diastereoselectively by immediate [4 + 2] cycloaddition of the thiirene with the heterodiene **4B**.

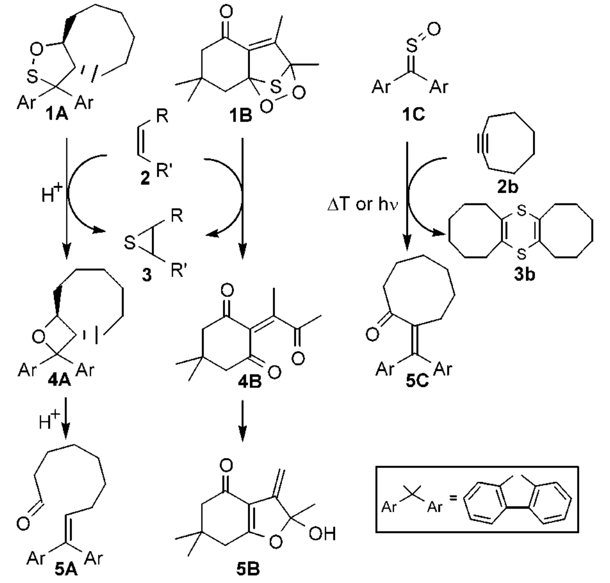
Introduction

Recent work from our group showed that a persistent cyclic sulfenate, the sultene **1A** and the in situ generated thiophene endoperoxide **1B** effect sulfur-atom transfer to strained cyclic olefins in very good yields, especially cyclooctene *trans*-**2a** (Scheme 1).[1] Such sulfur transfer to a triplebond would correspondingly lead to a thiirene, a highly reactive substance in view of its expected antiaromatic character. Indeed, our work on the sulfur transfer from fluorenethione *S*-oxide (**1C**) to cyclooctyne **2b** showed that the thiirene does not persist and dimerizes to the 1,4-dithiin **3b**.[2] It was, therefore, of mechanistic interest to investigate the sulfur-transfer chemistry of strained cyclic alkynes, namely cyclooctyne **2b** and 1,5-dithiacyclonon-7-yne (**2c**), with the sulfur donors sultene **1A** and endoperoxide **1B**. Our present results disclose some unusual and hardly predictable transformations in the sulfurization of strained acetylenes.

Results

Sulfur Transfer from the Sultene 1A to Cyclooctyne 2b. With catalytic amounts of Brønsted and Lewis acids, the sultene **1A** did not react at all with cyclooctyne **2b** even at elevated temperature (up to 80 °C). However, when this cycloalkyne was treated with 1 equiv of TFA, the sultene **1A** was quantitatively converted to the unprecedented thiirenium ion **3Ab** in only 1 min at ca. 20 °C (Scheme 2, path *a*). The assigned structure is supported by the two ^{13}C NMR signals at δ 112.9 and 113.2 ppm for the ring carbons of the thiirenium functionality. These resonances are in good agreement with those reported[3] for the

Scheme 1



---

[*] To whom correspondence should be addressed. E-mail: adam@chemie.uni-wuerzburg.de. FAX: Int +49-931-8884756.

[†] Institut für Organische Chemie.

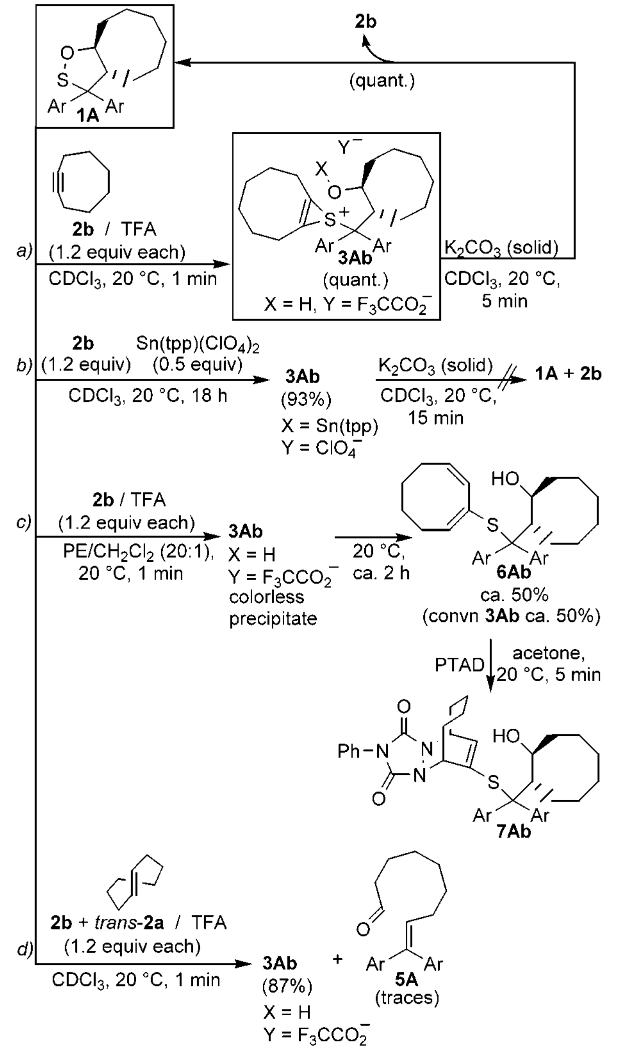
[‡] Institut für Anorganische Chemie.

(1) (a) Adam, W.; Weinkötz, S. *J. Am. Chem. Soc.* **1998**, *120*, 4861−4862. (b) Adam, W.; Weinkötz, S. *Chem. Commun.* **1996**, 177−178. (c) Adam, W.; Fröhling, B.; Peters, K.; Weinkötz, S. *J. Am. Chem. Soc.* **1998**, *120*, 8914−8919.

(2) Adam, W.; Fröhling, B.; Weinkötz, S. *J. Org. Chem.* **1998**, *63*, 9154−9155.

10.1021/ja025934x CCC: $22.00

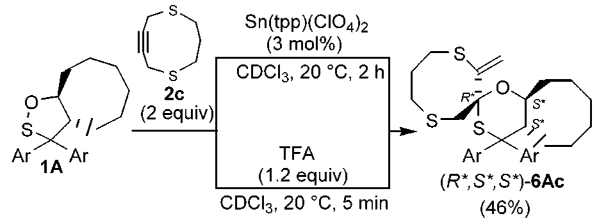
Scheme 2



di-*tert*-butyl-substituted thiirenium ions (δ 114.98 and 115.86 ppm). Additionally, the mass spectrum of the crude reaction mixture contains a *m*/*z* peak at 431 amu for the elemental composition of the thiirenium cation.

The persistence of the thiirenium ion **3Ab** depends on the amount of TFA added: With exactly 1 equiv or a slight excess (1.2 equiv) of acid, **3Ab** survived only up to 1 h; subsequently the diene **6Ab** (cf. Scheme 2, path *c*) slowly appeared. When a large excess (3 to 5 equiv) of acid was used, **3Ab** remained unchanged for about 24 h and then slowly decomposed to a complex mixture. With other strong Brønsted acids such as picric acid, perchloric acid, and tetrafluoroboric acid, the thiirenium ion **3Ab** was also formed, but with aqueous acids (70% $HClO_4$ and 50% HBF_4), vigorous shaking of the heterogeneous system was necessary to ensure full conversion of **1A** into **3Ab**. In the case of the aqueous acid HCl (37%), the thiirenium ion **3Ab** persisted only ca. 7 min in $CDCl_3$ solution to decompose subsequently to a mixture of unidentified products. With concentrated (98%) H_2SO_4, additionally a second, unidentified product appeared right from the beginning, as monitored by ^1H NMR spectroscopy; similar results were obtained in d_3-acetonitrile and d_4-methanol as solvent.

Scheme 3



Since the Lewis acid $Sn(tpp)(ClO_4)_2$ (Scheme 2, path *b*) has two free coordination sites, only 0.5 equiv was necessary to generate the thiirenium ion **3Ab**, although the latter was formed more slowly. After 10 min at ca. 20 °C, only 75% of **3Ab** was obtained.

On silica gel chromatography of the persistent thiirenium ion **3Ab**, ca. 25% of the sultene **1A** was recovered. When solid potassium carbonate was added to the solution of **3Ab** to neutralize excess acid, NMR analysis disclosed quantitative reversal to the starting materials **1A** and **2b** (Scheme 2, path *a*). When TFA was added again, the thiirenium ion **3Ab** was regenerated quantitatively, and this reversible process may be repeated several times. In the case of the Lewis acid Sn(tpp)(ClO_4)$_2$ (path *b*), no regeneration of the starting materials **1A** and **2b** from the thiirenium ion was observed on addition of solid K_2CO_3.

On addition of TFA to a mixture of the sultene **1A** and cyclooctyne **2b** in petroleum ether (PE) and methylene chloride (20:1), immediately a colorless solid precipitated (Scheme 2, path *c*). On attempted isolation of this colorless powder, fast deterioration was observed even under the rigorous exclusion of air and moisture. The NMR spectrum of this powder shows that it consists of ca. 50% each of the thiirenium ion **3Ab** and the diene **6Ab**. The structure of this diene was elucidated by various spectroscopic methods (^1H and ^{13}C NMR, INADEQUATE, H,H- and C,H-COSY, MS) and by the fact that with *N*-phenyl-1,2,4-triazoline-3,5-dione (PTAD) it afforded the [4 + 2] cycloadduct **7Ab** (Scheme 2, path *c*).

A competition experiment between cyclooctyne **2b** and *trans*-cyclooctene (*trans*-**2a**) (Scheme 2, path *d*) manifested almost exclusive formation of the thiirenium ion **3Ab**. No sulfur transfer to the usually highly reactive *trans*-**2a** was observed, since only traces of the desulfurized product of **1A**, the aldehyde **5A**, were detected.

Sulfur Transfer from the Sultene 1A to 1,5-Dithiacyclonon-7-yne (2c). Treatment of the readily accessible[4] dithiacyclononyne **2c** and sultene **1A** (Scheme 3) with 3 mol % of the Lewis acid $Sn(tpp)(ClO_4)_2$ gave the adduct **6Ac** as main product in 46% yield. Its spirocyclic structure was elucidated by NMR and mass spectroscopy; the (*R**,*S**,*S**) diastereomer was formed predominantly (dr = 91:9). With stoichiometric amounts of TFA, full conversion of the sultene **1A** occurred within 5 min at ca. 20 °C; however, the spirocyclic **6Ac** did not persist under these strongly acidic conditions and decomposed into a complex product mixture on prolonged standing (60 h). A control experiment confirmed that the authentic adduct **6Ac** deteriorated on exposure to TFA into a complex mixture.

Sulfur Transfer from the Thiophene Endoperoxide 1B to Cyclooctyne 2b. For these sulfur-transfer experiments, the

---

(3) Fachini, M.; Lucchini, V.; Modena, G.; Pasi, M.; Pasquato, L. *J. Am. Chem. Soc.* **1999**, *121*, 3944−3950.

(4) Kerton, F. M.; Mohmand, G. F.; Tersteegen, A.; Thiel, M.; Went, M. J. *J. Organomet. Chem.* **1996**, *519*, 177−184.

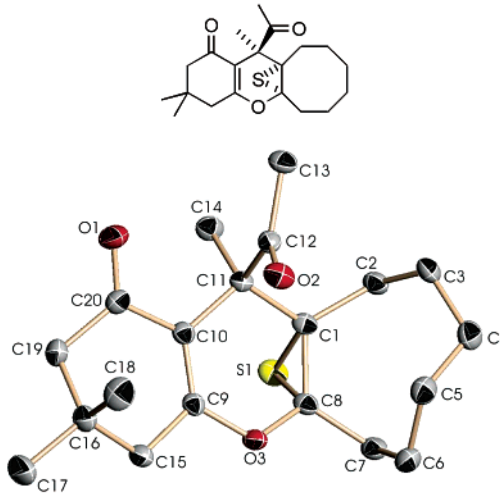
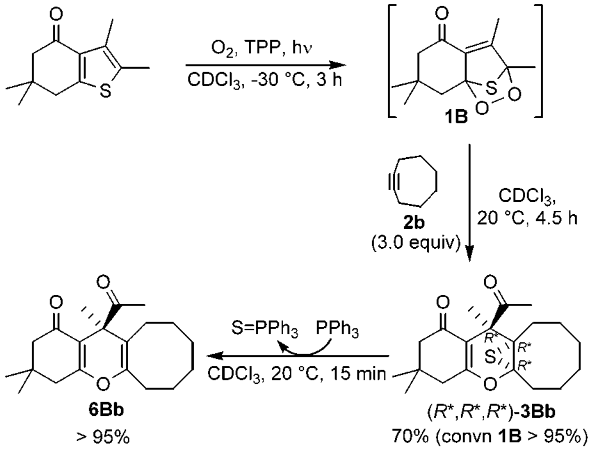


Figure 1. X-ray structure of episulfide **3Bb**.

Scheme 4



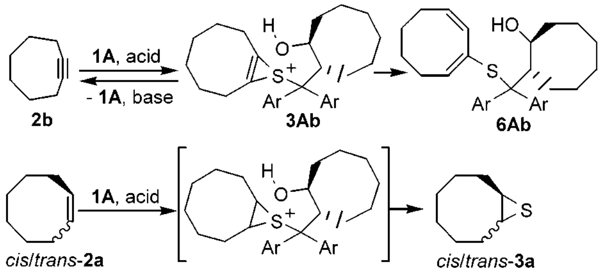
endoperoxide **1B** was generated by photooxygenation of the corresponding thiophene at −30 °C.[1c] Addition of the cyclooctyne **2b** to the photooxygenated mixture and warm-up to room temperature (ca. 20 °C) revealed by ^{1}H NMR spectroscopy that after 3 h all of the thiophene endoperoxide **1B** was consumed and the episulfide **3Bb** was obtained in 70% yield (Scheme 4). Its structure was assigned by various NMR-spectral methods (H,H-COSY, C,H-COSY, INADEQUATE), mass spectrometry, and X-ray analysis (Figure 1). Addition of cyclooctyne **2b** to the thermolysate of the thiophene endoperoxide **1B** did not lead to the episulfide **3Bb**. On treatment with triphenylphosphine at room temperature (Scheme 4), expectedly this episulfide was quickly (15 min) and quantitatively desulfurized to the pyran **6Bb**. Also, heating of this episulfide in CDCl$_3$ at 70 °C for 17 h caused 70% sulfur extrusion. When the thermolysis was carried out in the presence of *trans*-cyclooctene (*trans*-**2a**), no sulfur transfer was observed to afford the episulfide *trans*-**3a**.

The thiophene endoperoxide **1B** did not effect sulfuration of the dithiacyclononyne **2c**. On thermolysis, only the desulfurized products **4B** and **5B** of the endoperoxide **1B** were detected, along with elemental sulfur and unreacted alkyne **2c**.

Discussion

The formation of the thiirenium ion **3Ab** in the reaction of the sultene **1A** with cyclooctyne **2b** and stoichiometric amounts of acid (Scheme 5) is analogous to that of the thiiranium ion, proposed as the logical intermediate in the reaction of sultene **1A** with *cis*- or *trans*-cyclooctene, except that the thiirenium ion **3Ab** has been directly observed. The following experimental facts establish unequivocally the existence of the thiirenium ion **3Ab**: First, the reaction is reversible upon base treatment (K$_2$CO$_3$) when a Brønsted acid (TFA) is used for generating **3Ab**; second, the diene **6Ab** is formed in slightly acidic or neutral media. Expectedly, the reversal of the reaction, that is, the quantitative recovery of the starting materials **1A** and **2b**, is not possible on base treatment when the Lewis acid Sn(tpp)(ClO$_4$)$_2$ is employed. This implies that the oxygen atom of thiirenium ion **3Ab** is protonated or ligated to the metal, which makes **3Ab** persist for many hours under acidic conditions.

Scheme 5



The reversible generation of the persistent thiirenium ion **3Ab** is truly remarkable, since the few thiirenium ions that are known to date are irreversibly formed.[3,5] In fact, most of the reported thiirenium ions bear sterically demanding alkyl substituents (^{i}-Pr, ^{t}Bu) and have nonnucleophilic counterions such as SbF$_6^-$ or BF$_4^-$ to persist sufficiently for spectral observation.[3,6] Only the di-*tert*-butyl-*S*-methyl thiirenium ion was persistent enough at room temperature for X-ray analysis.[5c] The most common transformations of such thiirenium ions are ring-opening reactions, but Modena and Pasquato have also reported an unusual ring expansion of a ^{t}Bu-substituted thiirenium ion to its four-membered thietium ion.[3] Such ring opening of the thiirenium ion **3Ab** by the trifluoroacetic anion does not take place because the nucleophile has to approach the vinyl carbon by backside attack (a S$_N$2-Vin mechanism[5f]) which is encumbered by steric hindrance of the eight-membered ring. Rearrangement to a thietium ion is also not feasible, since an unstabilized primary carbocation would be formed.

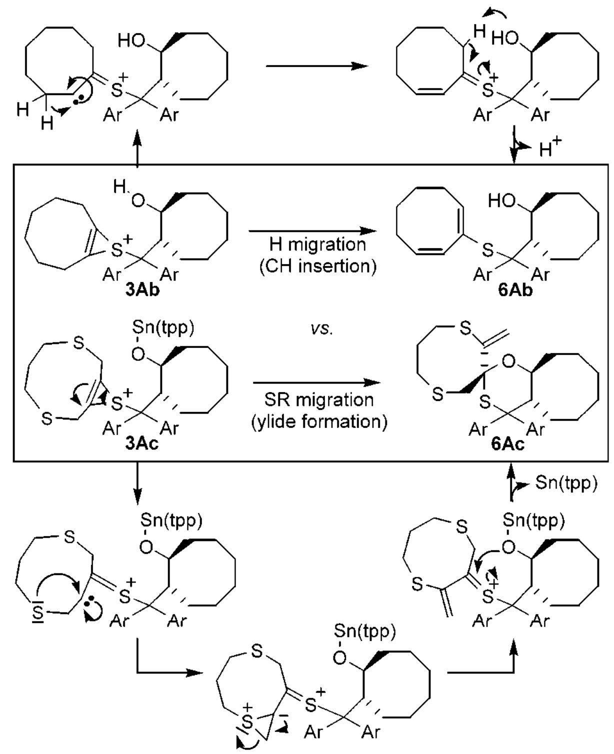
The mechanism for the formation of the thiirenium ion **3Ab** is analogous to the sulfur transfer from the sultene **1A** to the *cis*/*trans*-**2a** cyclooctenes, in which the saturated thiiranium ion intervenes as a short-lived intermediate to afford the *cis*/*trans*-**3a** thiiranes as the final products (Scheme 5).[1] The reaction entails nucleophilic attack by the strained triple or double bond of the olefin or alkyne on the acid-activated sultene **1A**. Usually, a double bond is more reactive in its nucleophilicity than a triple bond; however, a competition experiment revealed that the reaction of sultene **1A** with *trans*-cyclooctene (*trans*-**2a**) is

---

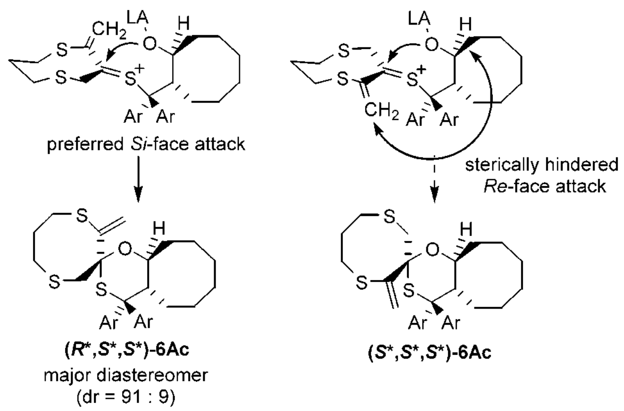
(5) (a) Lucchini, V.; Modena, G.; Valle, G.; Capozzi, G. *J. Org. Chem.* **1981**, *46*, 4720−4724. (b) Capozzi, G.; DaCol, L.; Lucchini, V.; Modena, G.; Valle, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 68−73. (c) Capozzi, G.; Lucchini, V.; Modena, G.; Scrimin, P. *Tetrahedron Lett.* **1977**, 911−912. (d) Benati, L.; Montevecchi, P. C.; Spagnolo, P. *Gazz. Chim. Ital.* **1991**, *121*, 387−391. (e) Destro, R.; Lucchini, V.; Modena, G.; Pasquato, L. *J. Org. Chem.* **2000**, *65*, 3367−3370. (f) Modena, G.; Pasquato, L.; Lucchini, V. *Phosphorus, Silicon Sulfur* **1994**, *95−96*, 265−282. (g) Lucchini, V.; Modena, G.; Pasquato, L. *Gazz. Chim. Ital.* **1997**, *127*, 177−188.

(6) Destro, R.; Pilati, T.; Simonetta, M. *J. Chem. Soc., Chem. Commun.* **1977**, 576.

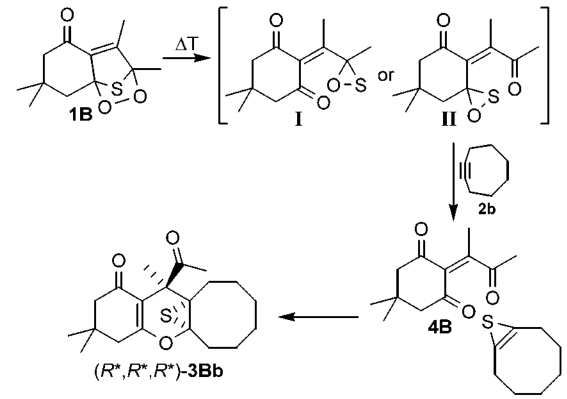
Scheme 6



Scheme 7



Scheme 8



definitely much slower than with cyclooctyne **2b**. Thus, no episulfide *trans*-**3a** was observed; instead, the thiirenium ion **3Ab** was formed nearly quantitatively. It should be emphasized that *trans*-cyclooctene has thus far been the most reactive sulfur-atom acceptor.[1] Presumably, the higher reactivity of the cyclooctyne derives from the more extensively deformed triple bond on account of the greater ring strain. Another significant difference in the reactivity between *trans*-cyclooctene and cyclooctyne is the fact that the resulting thiiranium ion releases the episulfide as final product, whereas the persistent thiirenium ion **3Ab** eventually rearranges to the diene **6Ab**. Evidently, sulfur transfer in the case of the thiirenium ion **3Ab** through the formation of the aldehyde **5A** is less favored than the rearrangement to the diene **6Ab** because the first process would require CC-bond cleavage. Moreover, an antiaromatic thiirene would have to be set free, which is energetically unfavorable.

The mechanism of diene **6Ab** formation may be understood, when a closer look is taken at the similar reaction of sultene **1A** with the heterocyclic dithiacyclononyne **2c** and Sn(tpp)-$(ClO_4)_2$ as Lewis acid (Scheme 3). In this case, neither thiirene liberation nor diene formation occurs, but instead the spirocyclic product **6Ac** is generated. The formation of this unexpected adduct may be rationalized in terms of ring opening of the thiirenium ion **3Ac** to an α-thiono carbene, in analogy to the ring opening of oxirenes[7] (Scheme 6). Subsequently, the neighboring thioether functionality of the nine-membered ring attacks the carbene to result in the ylide, which by ring opening leads to the exocyclic methylene group. Such intramolecular rearrangements of *β*-thioalkyl carbenes through ylide-like intermediates have been documented.[8] Finally, the spirocyclic adduct **6Ac** is obtained by nucleophilic attack of the juxtaposed oxygen atom on the thiono carbon atom with simultaneous release of the Lewis acid. The spirocyclic adduct **6Ac** is obtained preferentially (dr 91:9) as the (R*,S*,S*) diastereomer. This pronounced diastereoselectivity may be reconciled in terms of the steric interactions between the exocyclic methylene group and the cyclooctane ring during the nucleophilic attack by the oxygen functionality in the precursor of **6Ac** (Scheme 7); thus, the *si*-face attack that leads to the (R*,S*,S*) diastereomer is preferred. For better visualization of the steric interactions, the position of the attacking nucleophile has been maintained in the same place and the thiocarbonyl moiety has been rotated to expose either the *si*-face or the *re*-face.

Analogous to reactions with the sulfur-substituted cyclononyne **2c**, for the reaction of the sultene **1A** with the carbocyclic cyclooctyne **2b**, the first step is also proposed to entail carbene formation (Scheme 6). Subsequent hydrogen shift to the carbene center leads to the endocyclic double bond and deprotonation to the diene **6Ab**.

In the reaction of thiophene endoperoxide **1B** with cyclooctyne **2b**, still another reactivity was observed; namely, the sulfur transfer to the unexpected episulfide **3Bb** occurred (Scheme 4). To explain this transformation, we recall that in our previous work on the thermal sulfur transfer from thiophene endoperoxide **1B** to strained cyclic alkenes,[1c] as well as in earlier work by Matturro,[9] oxathiiranes or carbonyl *O*-sulfides or both have been

---

(7) Lewars, E. G. *Chem. Rev.* **1983**, *83*, 519−534.

(8) (a) Robson, J. H.; Shechter, H. *J. Am. Chem. Soc.* **1967**, *89*, 7112−7114. (b) Bissolino, P.; Alpegiani, M.; Borghi, D.; Perrone, E.; Franceschi, G. *Heterocycles* **1993**, *36*, 1529−1539. (c) Tamura, Y.; Ikeda, H.; Chisato, M.; Bayomi, S. M. M.; Ikeda, M. *Chem. Pharm. Bull.* **1980**, *28*, 3430−3433.

(9) (a) Matturro, M. G.; Reynolds, R. P.; Kastrup, R. V.; Pictroski, C. F. *J. Am. Chem. Soc.* **1986**, *108*, 2775−276. (b) Matturro, M. G.; Reynolds, R. P. *Tetrahedron Lett.* **1987**, *28*, 4981−4984.

postulated as transients. In the present case with cyclooctyne **2b**, carbonyl *O*-sulfides may be excluded as sulfur-transferring intermediates because such dipolar structures would hardly lead to the observed product, the episulfide (*R**,*R**,*R**)-**3Bb** (cf. Scheme 4). Instead, it is more likely that the oxathiiranes **I** and **II** (Scheme 8) serve as sulfur-transfer agents to the cyclooctyne **2b**.

Since the oxathiirane **I** is cross-conjugated and oxathiirane **II** extendedly conjugated, we stipulate that the latter is preferentially formed and serves as sulfur-transferring intermediate to the triple bond. A very reactive thiirene is set free, as previously demonstrated in the reaction of fluorenethione *S*-oxide (**1C**) with cyclooctyne,[2] in which the released thiirene dimerized to the dithiin **3b**. In view of proximity, the thiirene cycloadds immediately to the simultaneously generated trienone **4B** and affords the observed (*R**,*R**,*R**)-episulfide **3Bb**.

Conclusions

The present work demonstrates that the sulfur donors sultene **1A** and thiophene endoperoxide **1B** exhibit a totally different reactivity with strained cycloalkynes compared to that with cycloalkenes. For both substrates, three-membered-ring cycloadducts are formed, namely the thiirenium ions from the cycloalkynes and thiiranium ions from the cycloalkenes. Whereas the thiiranium ion releases the thiirane as sulfur-transfer product, under appropriate conditions, the thiirenium ion either reverts to the starting materials or rearranges to more complex sulfur-functionalized products. The antiaromatic thiirene is only reluctantly released as sulfur-transfer product in view of its higher energy, but if it is set free, it either dimerizes or is trapped. This distinctive chemical reactivity between cycloalkynes and cycloalkenes toward the sulfur donors **1A** and **1B** has provided valuable mechanistic insight into the sulfur-transfer process through the direct observation of a persistent and reversible thiirenium ion.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for generous financial support. This work is dedicated to Professor P. Welzel (Leipzig) on the occasion of his 65th birthday in appreciation of his important scientific contributions.

Supporting Information Available: Experimental procedures and full characterization for products **6Ab**, **7Ab**, **6Ac**, **3Bb** with the pertinent NMR spectral data and X-ray crystallographic data for **3Bb** (PDF). This material is available free of charge in the Internet at http://pubs.acs.org.

JA025934X