Episulfidation of Strained Cycloalkenes in the Thermolysis of 5-Aryloxy-1,2,3,4-thiatriazoles

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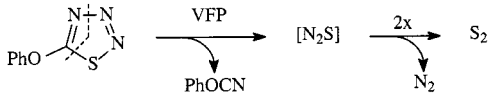
The thermolysis of 5-aryloxythiatriazoles **1** in the presence of norbornene (**2a**) and *trans*-cyclooctene (*trans*-**2b**) affords the corresponding thiiranes **3a** and *trans*-**3b** in moderate yields. First-order kinetics are observed, suggesting that a sulfur intermediate, presumably dinitrogen sulfide, is generated in the fragmentation process of **1**, which then serves as the active sulfur atom donor.

Introduction

The thermal denitrogenation of oxy-substituted 1,2,3,4-thiatriazoles has been reported to yield aryl cyanates and elemental sulfur at room temperature (ca. 25 °C).[1] Additionally, Pilgram found that phosphanes promote the denitrogenation of 5-phenyloxy-1,2,3,4-thiatriazole (**1a**) by nucleophilic attack at the sulfur site, thereby affording phenyl cyanate and phosphane sulfide.[2] The mechanism of thermal denitrogenation of this heterocycle was elucidated only recently by Wentrup and co-workers, who characterized the labile dinitrogen sulfide by vacuum flash pyrolysis (VFP) of 5-phenyloxy-1,2,3,4-thiatriazole (**1a**) under matrix-isolation conditions (Scheme 1).[3]



Scheme 1. The thermal denitrogenation of 5-phenyloxy-1,2,3,4-thiatriazole (**1a**) to give phenyl cyanate and disulfur by vacuum flash pyrolysis (VFP)

The fact that elemental sulfur is extruded in the thermolysis of thiatriazoles presents an opportunity to explore the episulfidation[4] of strained olefins, as we have demonstrated for the sulfur-transfer agents thiophene endoperoxides,[5a,5b] oxathiiranes,[5c–5e] and a sultene.[5f] Indeed, we demonstrate herein that the thermolysis of 5-aryloxy-1,2,3,4-thiatriazoles **1** in the presence of the cycloalkenes norbornene (**2a**) and *trans*-cyclooctene (*trans*-**2b**) affords the respective thiiranes **3** in moderate yields.

Results and Discussion

The thiatriazoles **1** were prepared from the corresponding phenols according to a literature procedure (Scheme 2).[1]

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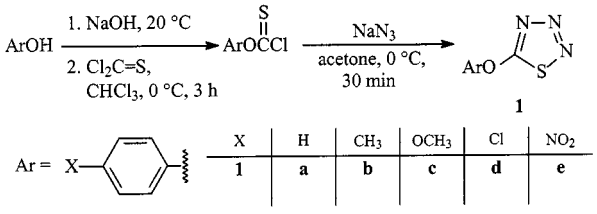
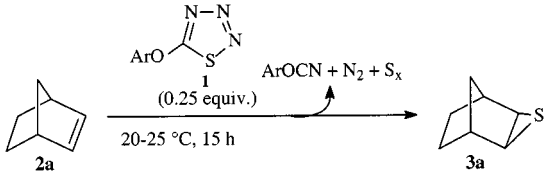


Scheme 2. Synthesis of the thiatriazoles **1**

The thermal reaction between 5-phenyloxy-1,2,3,4-thiatriazole (**1a**) and norbornene (**2a**) as a sulfur acceptor led to the thiirane **3a**. The best yield of **3a** (45%) was obtained by using 0.25 equiv. of **1a** in CH_3CN at 25 °C (Table 1).

Table 1. Episulfidation of norbornene (**2a**) in the thermolysis of the thiatriazoles **1**



Thiatriazole[a]	Equiv.	Solvent	Yield of **3a** [%][b][c]
1a	0.25	$CDCl_3$	30
1a	1.0	$CDCl_3$	17
1a	2.0	$CDCl_3$	17
1a	0.25	CD_3CN	45
1a	0.5	CD_3CN	42
1a	1.0	CD_3CN	25
1b	0.25	CD_3CN	7
1c	0.25	CD_3CN	7
1d	0.25	CD_3CN	9
1e	0.25	CD_3CN	19

[a] 0.372 M, equivalents relative to **2a**. – [b] % conversion of **1** ≥ 95%; mass balance of **1** ≥ 90%. – [c] Determined by analysis of characteristic ^1H NMR signals of the crude product mixture using 1,1,2,2-tetrachloroethane as an internal standard (error ± 5%).

Efforts to improve the efficiency of sulfur transfer by the use of other *para*-substituted thiatriazoles **1** were unsuccessful, leading only to lower yields (≤ 20%) of the thiirane **3a**.

A relative-rate experiment revealed that the *para*-nitro derivative **1e** decomposed ca. twice as rapidly as the unsubsti-

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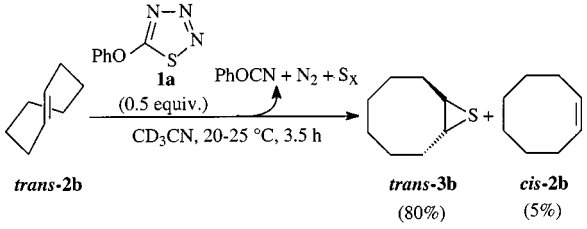
tuted thiatriazole **1a**, as determined by HPLC analysis of the conversion of a mixture of these derivatives (see Exp. Sect.). Evidently, enhancement of the decomposition rate of the thiatriazole **1** is detrimental to sulfur transfer to the olefinic substrate. In line with this supposition, thermolyses of the thiatriazole **1a** and of the *para*-nitro derivative **1e** (faster decomposition) in the presence of norbornene (**2a**) afforded the episulfide **3a** in yields of 45% and 19%, respectively, under identical reaction conditions (Table 1). Furthermore, lower yields ($\leq$ 10%) of norbornene episulfide (**3a**) were also found when the thermolysis of the thiatriazole **1a** was carried out at 60 °C, at which **1a** decomposes very rapidly. Elemental sulfur was excluded as a possible sulfur donor by the following control experiment. Norbornene (**2a**) was added to the thermolysate of the thiatriazole **1a**, which contained the extruded elemental sulfur, and the mixture was analyzed by ^{1}H NMR. Even after 15 h at 25 °C, no thiirane **3a** could be detected. *trans*-Cyclooctene (*trans*-**2b**), which has proved to be the most efficient olefin as a sulfur atom acceptor,[5] was converted in good yields (80%) to its episulfide *trans*-**3b** along with small amounts (5%) of *cis*-cyclooctene (*cis*-**2b**) (Scheme 3).

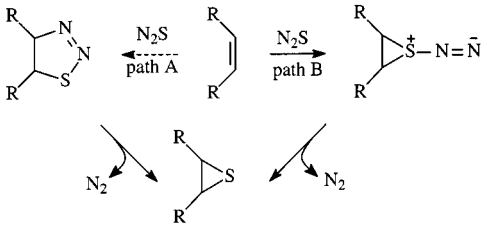


Scheme 3. Episulfidation of *trans*-cyclooctene (*trans*-**2b**) by thiatriazoles **1a** (complete consumption)

The rate constant for this reaction was determined to be $k = 3.17\ (\pm\ 0.10) \times 10^{-4}\ s^{-1}$, regardless of the amount of olefin used (see Exp. Sect.), which establishes first-order kinetics for the sulfur transfer. This kinetic behaviour rules out any possibility of thiirane **3** being generated by direct sulfur-atom transfer between cycloalkene **2** and thiatriazole **1**.

These results suggest that a labile sulfur intermediate is generated upon thermolysis of the thiatriazole, which is responsible for the sulfur transfer. Wentrup and co-workers showed that vacuum flash pyrolysis (Scheme 1) of 5-phenyloxy-1,2,3,4-thiatriazole (**1a**) releases dinitrogen sulfide and disulfur as the exclusive reaction intermediates,[3] which may serve as sulfur donors. The reaction of disulfur with norbornene (**2a**) has been extensively investigated,[6] but in none of these studies have even traces of the thiirane **3a** been reported. Besides, the control experiment showed that the extruded sulfur did not episulfidize norbornene (**2a**). This leaves dinitrogen sulfide as the sole candidate for the species responsible for sulfur atom transfer.

In view of the dipolarophilic reactivity of the strained norbornene (**2a**) and *trans*-cyclooctene (*trans*-**2b**)[7] and their propensity for thiirane formation, we propose a concerted cycloaddition with the dinitrogen sulfide dipole[3b] through either a traditional 1,3-dipolar mechanism (pathway A) or a monocentered route (pathway B), with subsequent denitrogenation (Scheme 4).



Scheme 4. Proposed mechanistic pathways for the sulfur transfer by dinitrogen sulfide

A 1,2,3-thiadiazoline (pathway A) has previously been reported in the 1,3-dipolar cycloaddition of diazomethane to adamantanethione and, indeed, this system affords thiiranes upon thermal denitrogenation, albeit only at elevated temperatures ($\geq$ 80 °C).[8] In the present case, efforts to detect a 1,2,3-thiadiazoline intermediate by low-temperature ^{1}H-NMR spectroscopy proved unsuccessful, although accumulation of such a species would have been expected. Therefore, instead of the 1,3-dipolar cycloaddition (pathway A), we favor the monocentered mechanism for the sulfur transfer (pathway B in Scheme 4).

Conclusion

The present episulfidation by using 5-phenyloxy-1,2,3,4-thiatriazole (**1a**) as a sulfur atom donor leads to the norbornene (**3a**) and *trans*-cyclooctene (*trans*-**3b**) episulfides under mild conditions, albeit only in moderate yields. The fragmentation of 5-aryloxy-1,2,3,4-thiatriazoles **1** generates the transient dinitrogen sulfide, which presumably functions as a sulfur-atom transfer agent in the presence of the strained olefins.

Experimental Section

General Remarks: All solvents were dried and distilled prior to use. For flash chromatography, Woelm silica gel (0.032−0.063 mm) was used. For TLC detection at −20 °C, the plates were precooled with liquid nitrogen and the chamber containing the eluent was cooled in a freezer. − ^{1}H NMR (200 MHz or 600 MHz): Bruker AC 200 or Bruker AC 600. − ^{13}C NMR (50 MHz): Bruker AC 200. − Chemical shifts are expressed in δ values relative to tetramethylsilane. Low-temperature ^{1}H and ^{13}C NMR spectra of the thiatriazoles **1** were recorded at −28 °C. For quantitative measurements, the characteristic ^{1}H NMR signals of the crude reaction mixture were determined relative to 1,1,2,2-tetrachloroethane as an internal standard. − Melting points (uncorrected values): Büchi B-545 apparatus. − Chlorothiocarbonic acid *O*-phenyl and *O*-(4-chlorophenyl) esters were purchased from Lancaster, thiophosgene from Fluka. All other *O*-aryl chlorothiocarbonates were synthesized from the corresponding phenols and thiophosgene according to literature procedures.[9]

General Procedure for the Preparation of Thiatriazoles 1: To a well-stirred solution of sodium azide (715 mg, 11.0 mmol) in water (4.0 mL) and acetone (9.0 mL) at −5 to 0 °C (ice/salt bath), a solu-

tion of the *O*-aryl chlorothiocarbonate (10.0 mmol) in acetone (3.0 mL) was added over a period of 5 min. After stirring for a further 30 min at this temperature, iced water (25 mL) was added to the suspension, and the thiatriazoles **1** (except **1e**) were extracted with diethyl ether (3 × 30 mL) that had been precooled to −20 °C. The combined extracts were dried with anhydrous calcium chloride and the ether was removed by means of a rotary evaporator (−5 to 0 °C/250 Torr). The oily residue was taken up in methanol (30 mL) and crystallization was induced by cooling in a dry-ice bath at −70 °C. The deposited crystals were collected on a liquid-nitrogen-precooled sintered glass funnel, redissolved in methanol (30 mL) at room temperature (ca. 25 °C), and recrystallized at −70 °C. The thiatriazoles **1** were dried at −20 to −15 °C (ice/salt bath) at 0.01 Torr. It was found that they could be stored without decomposition for at least 4 months at −20 °C.

5-Phenyloxy-1,2,3,4-thiatriazole (1a):[1b] Yield 1.52 g (79%) (ref.[1b] 85%); m.p. 33−34 °C (ref.[1b] 33−34 °C). − ^{1}H NMR (CD_3CN, 200 MHz): δ = 6.70−6.90 (m, 3 H, 2-, 4-, 6-H), 7.10−7.30 (m, 2 H, 3-, 5-H). − ^{13}C NMR (CD_3CN, 50 MHz): δ = 119.6 (d, C-2, C-6), 128.1 (d, C-4), 130.9 (d, C-3, C-5), 157.2 (C-1), 190.3 (s, SCN).

5-(4-Methylphenyloxy)-1,2,3,4-thiatriazole (1b):[1b] Yield 1.93 g (100%) (ref.[1b] 96%); m.p. 21−22 °C (ref.[1b] 20.5−21 °C). − ^{1}H NMR (CD_3CN, 200 MHz): δ = 2.35 (s, 3 H, CH_3), 7.25−7.35 (m, 4 H). − ^{13}C NMR (CD_3CN, 50 MHz): δ = 20.8 (CH_3), 120.1 (d, C-2), 132.0 (d, C-3), 139.1 (s, C-4), 156.1 (s, C-1), 191.2 (s, SCN).

5-(4-Methoxyphenyloxy)-1,2,3,4-thiatriazole (1c):[1b] Yield 1.99 g (95%) (ref.[1b] 97%); m.p. 39−40 °C (ref.[1b] 38−39 °C). − ^{1}H NMR (CD_3CN, 200 MHz): δ = 3.80 (s, 3 H, OCH_3), 7.02−7.06 (m, 2 H, 2-, 6-H), 7.31−7.38 (m, 2 H, 3-, 5-H). − ^{13}C NMR (CD_3CN, 50 MHz): δ = 54.8 (t, OCH_3), 115.2 (d, C-2, C-6), 120.7 (d, C-3, C-5), 151.4 (s, C-4), 158.7 (s, C-1), 191.0 (s, SCN).

5-(4-Chlorophenyloxy)-1,2,3,4-thiatriazole (1d):[1b] Yield 1.92 g (90%) (ref.[1b] 100%); m.p. 40−41 °C (ref.[1b] 38−39 °C). − ^{1}H NMR (CD_3CN, 200 MHz): δ = 7.39−7.57 (m, 4 H). − ^{13}C NMR (CD_3CN, 50 MHz): δ = 122.5 (d, C-2), 131.4 (d, C-3), 133.4 (s, C-4), 155.8 (s, C-1), 189.9 (s, SCN).

5-(4-Nitrophenyloxy)-1,2,3,4-thiatriazole (1e):[1b] This thiatriazole was immediately collected by filtration, washed with iced water (2 × 5 mL), and recrystallized. Yield 2.02 g (90%) (ref.[1b] 95%); m.p. 69−70 °C (ref.[1b] 68−69 °C). − ^{1}H NMR (CD_3CN, 200 MHz): δ = 7.61−7.66 (m, 2-, 6-H), 8.37−8.42 (m, 3-, 5-H). − ^{13}C NMR (CD_3CN, 50 MHz): δ = 121.1 (d, C-2, C-6), 130.9 (d, C-3, C-5), 146.1 (s, C-4), 159.3 (s, C-1), 187.4 (s, SCN).

General Procedures for the Thermolysis of 1,2,3,4-Thiatriazoles 1 in the Presence of Alkenes 2. − NMR-Scale Product Studies: In an NMR tube, the relevant thiatriazole **1** (200 μmol), the olefin **2** (800 μmol), and 1,1,2,2-tetrachloroethane (5.00 μL, 47.6 μmol) as an internal ^{1}H NMR standard were taken up in 0.6 mL of the appropriate deuterated solvent ($CDCl_3$, CD_3CN, [D_6]benzene, [D_6]acetone, [D_8]THF, [D_6]DMSO, or CD_3OD). The tube was sealed and left for 15 h at room temperature (ca. 25 °C). After the reaction was complete, as checked by TLC at −20 °C (silica gel; CH_2Cl_2/petroleum ether, 2:1, as eluent), the ^{1}H NMR spectrum of the crude reaction mixture was recorded. The results are collected in Table 1 (see Results Section).

Preparative Product Studies: A 5-mL round-bottomed flask was charged with 5-phenyloxy-1,2,3,4-thiatriazole (**1a**) (1.01 g, 5.63 mmol) and norbornene (**2a**) (2.12 g, 22.5 mmol) or *trans*-cyclooctene (*trans*-**2b**) (2.92 g, 22.5 mmol) in dry acetonitrile (3.0 mL). The flask was capped with a rubber septum and was fitted with a gas outlet to vent the N_2 formed. The reaction mixture was stirred for 15 h at room temperature (ca. 25 °C); after evaporation of the solvent (40 °C, 150 Torr), the residue was purified by flash chromatography on silica gel (petroleum ether as eluent) to afford the desired thiirane **3** as a colorless waxy solid.

3-Thiatricyclo[3.2.1.0^{2,4}]octane (3a):[5b] Yield 142 mg (20%); m.p. 31−32 °C (ref.[5b] 31−32 °C). − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.65 (d, *J* = 10 Hz, 1 H), 1.24 (m, 2 H), 1.45−1.70 (m, 3 H), 2.46 (s, 2 H), 2.74 (s, 2 H, CHS). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 27.5 (2 t), 37.5 (d), 37.6 (d).

***trans*-9-Thiabicyclo[6.1.0]nonane (*trans*-3b):**[5b] Yield 641 mg (80%); m.p. 57−58 °C (ref.[5b] 57−58 °C). − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.95−1.20 (m, 4 H), 1.60 (m, 2 H), 1.85−2.10 (m, 4 H), 2.45 (m, 2 H), 2.68 (m, 2 H, CHS). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 26.3 (t), 29.3 (t), 29.5 (t), 41.2 (t).

Control Experiment: A solution of thiatriazole **1a** (41.1 mg, 0.229 mmol) in CD_3CN (0.6 mL) was allowed to stand for 15 h at room temperature (ca. 25 °C). After the thermolysis was complete, as checked by low-temperature TLC at −20 °C (silica gel; CH_2Cl_2/petroleum ether, 2:1, as eluent), norbornene (**2a**) (21.0 mg, 0.223 mmol) was added to the thermolysate. After leaving the mixture to stand for an additional 15 h at ca. 25 °C, no signals due to the norbornene episulfide **3a** could be detected in the ^{1}H NMR spectrum (error limit < 5%).

Decomposition of Thiatriazoles 1a and 1e: A solution of thiatriazole **1a** (60.5 mg, 338 μmol) and thiatriazole **1e** (47.0 mg, 209 μmol) in CD_3CN (0.6 mL) was prepared at room temperature (ca. 25 °C). Immediately, a 25.0 μL aliquot was removed, diluted with dichloromethane (10.0 mL; precooled to 0 °C), and a sample was subjected to HPLC analysis to determine the percentages of consumption of the thiatriazoles **1a** (55%) and **1e** (90%); the latter were calculated from the peak areas of the thiatriazoles **1** by calibration against authentic samples.

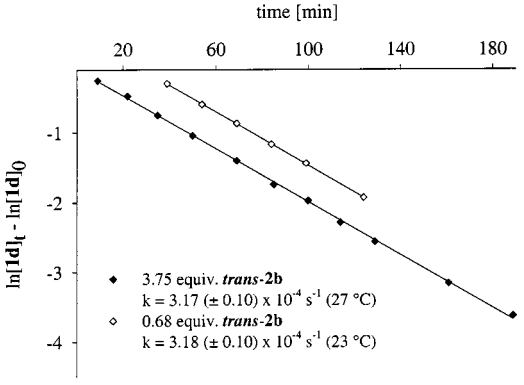


Figure 1. Thermolysis of thiatriazole **1d** in the presence of *trans*-cyclooctene (*trans*-**2b**)

Kinetic Studies: An NMR tube was charged with 5-(4-chlorophenyloxy)-1,2,3,4-thiatriazole (**1d**) (18.2 mg, 85.2 μmol), *trans*-cyclooctene (*trans*-**2b**) (40.0 μL, 308 μmol) [or 11.7 μL, 90.0 μmol], and 1,1,2,2-tetrachloroethane (5.00 μL, 47.6 μmol) in $CDCl_3$ (0.6 mL). The tube was sealed with a rubber stopper and Parafilm®, and a 600-MHz ^{1}H NMR spectrum was recorded every 10 min at 27 °C. After each measurement, the tube was vented to release the nitrogen gas formed in the reaction. The conversion of the starting material was determined by analysis of its ^{1}H-NMR signals. The aro-

matic signals of the thiatriazole **1d** in the crude product mixture were monitored in relation to the singlet of 1,1,2,2-tetrachloroethane as an internal standard. A relaxation delay of 23 s was applied for the acquisition. The time-dependent conversion of thiatriazole **1d** (Figure 1) was found to obey a first-order rate law and was independent of the initial amount of *trans*-cyclooctene (*trans*-**2b**) used.

Acknowledgments

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