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Thermal Reactions of Regioisomeric 1,2,4-Trithiolane S-Oxides

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The products of the gas-phase pyrolysis of two regioisomeric 1,2,4-trithiolane S-oxides were collected in an argon matrix at 10 K and studied by means of spectroscopic as well as computational methods. Whereas the main products of the pyrolysis of the "symmetrical" S-oxide were identified as

Introduction

Recent studies on "sulfur-centered" 1,3-dipoles focused on applying matrix isolation techniques to examine the thiocarbonyl ylides **1a** and **1b**^[1a] generated in the gas phase by thermal elimination ([2+3]-cycloreversion) of nitrogen from the corresponding 2,5-dihydro-1,3,4-thiadiazoles 2a and 2b (Scheme 1).^[1b]

1,2,4-Trithiolanes 3 are common in nature^[2] and there is a variety of preparative methods for their synthesis.^[2a,2g,2h,3] In an earlier study we demonstrated that the gas phase pyrolysis of the parent 1,2,4-trithiolane (3a) yields the thioformaldehvde S-sulfide (thiosulfine, 4a), which is another representative of a "sulfur-centered" 1,3-dipole.^[4] The forma-

thioformaldehyde S-oxide and thioformaldehyde S-sulfide, the "non-symmetrical" S-oxide gave predominantly dithioformic acid, which exists as a mixture of s-cis and s-trans conformers. We present a rationalization of the reaction pathways including density functional theory computations.

tion of 4a was accompanied by small amounts of dithiirane (5a) that was detected at 10 K in the matrix-isolated pyrolyzate. Subsequent irradiation of this mixture led to nearly complete conversion of 4a into the isomeric 5a (Scheme 1).^[4]

A similar result of a thermal [2+3]-cycloreversion was obtained in the case of 3,3,5,5-tetramethyl-1,2,4-trithiolane (3b) but in this case, in addition to the thioacetone S-sulfide (4b) and 3,3-dimethyldithiirane (5b) formed as minor products, the isopropenyl disulfane (6), present as a mixture of two conformers, was found as the major component of the frozen pyrolyzate. The latter is believed to form from the thiosulfine 4b via a 1,4-H shift (Scheme 2).^[5]



Scheme 1.

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Spirocycloaliphatic 1,2,4-trithiolane 3c was reported to undergo gas phase thermolysis yielding a mixture of thiosulfine 4c, the spirocyclic dithiirane 5c, and dithiolactone 7.^[5] The five-membered product 7 apparently forms via the ring enlargement of 5c, which occurred under both thermal and photolytic conditions.

The mono-oxidation reactions of 1,2,4-trithiolanes 3a,b,d are well documented and it is known that irrespective of the oxidizing agent [sodium periodate, m-chloroperbenzoic acid (mCPBA) or peracetic acid], mixtures of comparable



Scheme 2.

amounts of regioisomeric monoxides **8a,b,d** and **9a,b,d** ensue (Scheme 3).^[2c,6] Wratten and Faulkner^[2c] showed that 1,2,4-trithiolane 4-S-oxide (**8a**) and the isomeric 1-S-oxide **9a** can be isolated from red algae *Chondria Californica*.^[2c] After isolation from the biological material, both compounds were separated by preparative thin layer chromatography. Biological tests proved that both S-oxides **8a** and **9a** display a remarkable antimicrobial activity.^[2c] It is worth mentioning that propanethial S-oxide (*n*-propyl sulfine), known as the "lachrymatory factor" isolated from *allium* species has been postulated to form via an enzymatic conversion of S-propen-1-yl-cystein S-oxide.^[7]



Scheme 3.

In contrast to 1,2,4-trithiolanes of type **3**, the reactions of the respective monoxides **8** and **9** are less well known. Only recently, the reactions of **8a,d** and **9a,d** (R, R = H, H or cyclohexylidene) with Pt^0 -phosphane complexes have been reported.^[6b,8] In the case of 1,2,4-trithiolanes and their *S*-oxides, the complexation reactions occur via dissociation of the heterocyclic ring and result in the release of the corresponding sulfine.

In a very recent paper, in an attempt to photolyze thioformaldehyde S-oxide (the parent sulfine, **10**) to oxathiirane (in Ar matrix at 10 K), we reported the unexpected formation of a very rare product of "methylidyne(hydroxy)sulfanyl type" **11**, possessing a CS triple bond.^[9] We describe in this paper the high-vacuum flash pyrolysis (HVFP) products of 4-S-oxide **8a** and 1-S-oxide **9a**, derived from 1,2,4-trithiolane (**3a**) isolated at low temperature (10 K). Density functional theory (DFT) computations are used to rationalize our findings.

Results and Discussion

We utilized the monoxides **8a** and **9a**, obtained as pure samples after treatment of the parent 1,2,4-trithiolane (**3a**) with *m*CPBA and chromatographic separation, for the pyrolysis experiments using an empty quartz tube heated up to 700 °C. A stream of gaseous products was condensed on a cold spectroscopic window (CsI or BaF₂) together with a large excess of argon. The matrix-isolated pyrolysis products were examined by IR and UV/Vis spectroscopy.

The first series of pyrolysis experiments was carried out with the "symmetrical" 4-*S*-oxide **8a**. The IR spectrum of the pyrolyzate collected at 10 K revealed the presence of very strong absorption bands at 766.7 and 1165.6 cm⁻¹, which were attributed to the wagging vibrations of the CH₂ group and the S=O strechings in thioformaldehyde *S*-oxide (**10**), respectively (Scheme 4).





These strong bands are accompanied by less intense absorptions at 1153.1 and 1357.2 cm⁻¹ (Figure 1) and fit well with the literature data reported for $10^{[9,10]}$ The second main product present in the mixture was identified as thioformaldehyde *S*-sulfide (**4a**). Its presence was clearly confirmed in the IR spectrum by absorptions found at 622.8, 756.8, 910.2, and 970.9 cm⁻¹. All of these bands were already found and described in our earlier paper reporting on the [2+3] thermal cycloreversion of the parent 1,2,4-trithiolane (**3a**) (Scheme 2).^[4] Thioformaldehyde (**12**) was also

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Figure 1. IR spectrum of matrix-isolated (argon, 10 K) high-vacuum flash pyrolysis products of 1,2,4-trithiolane 4-S-oxide (8a) generated at 650 °C.



Figure 2. UV/Vis spectrum of matrix-isolated (argon, 10 K) high-vacuum flash pyrolysis products of 1,2,4-trithiolane 4-S-oxide (8a) generated at 650 °C.

present in the mixture (IR bands located at 987.4 cm⁻¹ and 1055.2 cm⁻¹). The computed intensities of the CH₂-wagging vibrations of products **10**, **4a**, and **12** [B3LYP/6-311+G(3df,3dp)]^[11] were used to estimate of the ratio of all three compounds. This procedure led to the conclusion that the **10/4a/12** ratio is approximately 2:1:1. Moreover, small amounts of S₂ also formed as evident from the presence of its characteristic UV-absorptions between 280 and 310 nm.^[12] In addition, the UV spectrum of a mixture of all compounds shows two intense bands at 356 nm (attributed to thiosulfine **4a**^[4]) and at 242 nm (attributed to sulfine **10**^[9]) (Figure 2).

The simultaneous formation of two main products, the sulfine 10 and thiosulfine 4a, results from the thermal [2+3]-cycloreversion of the five-membered ring of 8a. According to the presented reaction mechanism of the ring

dissociation, the formation of equal amounts of **10** and **4a** are expected. The presented pathway fits well with the prediction resulting from our computational studies, which give an activation energy of 31 kcalmol^{-1} (Figure 3).

Apparently, some amount of thiosulfine **4a** undergoes decomposition in the gas phase and therefore thioformaldehyde **12** as well as disulfur S₂ were also detected in the matrix. However, it must be stressed that elimination of S₁, either from **4a** or from **5a**, is an endothermic process with $\Delta E \approx 80 \text{ kcal mol}^{-1}$ [B3LYP/6-311+G(3df,3dp)]. Therefore, the pathway leading to S₂ is not clear.

In addition to our results, an earlier paper describes a similar gas phase pyrolysis study of **8a**, and the products formed at 817 °C were characterized by means of photoelectron spectroscopy.^[13] In this case the formation of **10** and **12** was shown but the formation of **4a** had not been





Figure 3. Reaction profile (kcalmol⁻¹) for the [2+3] cycloreversion of 1,2,4-trithiolane 4-*S*-oxide (**8a**) at the B3LYP/6-311+G(3df,3pd) level including zero-point vibrational energy corrections.

mentioned. The same authors studied the pyrolysis of the parent 1,2,4-trithiolane (**3a**) and reported only the appearance of thioformaldehyde (**12**); thiosulfine **4a** was not mentioned as a possible product of this reaction.

In our hands, careful analysis of the IR spectrum of the pyrolysis products obtained from **8a** provides clear evidence for the presence of trace amounts of dithiirane (**5a**; a weak IR band at 581.4 cm⁻¹), formed side by side with isomeric thiosulfine **4a**. As already reported,^[4] dithiirane **5a** forms from **4a** via a 1,3-dipolar electrocyclization reaction. The ratio of **4a** and **5a**, formed in the gas phase, was shown to depend on the temperature and the lower the temperature, the less of the cyclic product forms. In comparison with earlier reports^[4,5,9] the pyrolysis temperature applied in the

present study was relatively low. Therefore, the open form of the thiosulfine **4a** is strongly favored in comparison to the cyclic product **5a**.

The isomeric, "non-symmetrical" 1,2,4-trithiolane 1-Soxide (9a) was pyrolyzed under similar conditions and the products formed in the gas phase were isolated in an argon matrix and studied by means of their IR and UV spectra. The IR spectrum of the pyrolysis products taken at 10 K showed intense bands attributed to 10 and another group of bands, which revealed the presence of a mixture of s-cis $(1290.3, 1058.0, 933.5, 826.5, 682.8 \text{ cm}^{-1})$ and *s*-trans (1265.1, 1082.1, 925.4, 806.5, 725.9 cm⁻¹) dithioformic acid (13c and 13t) as the major components of this mixture (Scheme 5).^[14] These absorptions fit well with those found in the photolysis products of 4a.^[4] Along with 10 and 13, a small amount of 12 was also found in the mixture. Based on a comparison of the intensities of the corresponding bands, the 10/12 ratio was estimated to be ca. 10:1 (Figure 4).



Scheme 5.

The corresponding UV spectrum differed from that recorded for the pyrolysis products of **8a**. The characteristic strong UV band of **4a** was completely missing. Instead, the bands located at $\lambda_{max} = 284$ nm and 288 nm (partly resolved vibrational fine structure) as well as $\lambda_{max} = 242$ nm proved the formation of **13** and **10** (Figure 5).



Figure 4. The IR spectrum of matrix-isolated (argon, 10 K) high-vacuum flash pyrolysis products of 1,2,4-trithiolane 1-S-oxide (9a) generated at 700 °C.



Figure 5. The UV/Vis spectrum of matrix-isolated (argon, 10 K) high-vacuum flash pyrolysis products of 1,2,4-trithiolane 1-S-oxide (9a) generated at 650 °C. * Traces of *m*-chlorobenzoic acid.

The formation of a mixture of 13c and 13t as the major pyrolysis products of 9a suggests that the fragmentation of the five-membered ring follows a completely different mechanism in comparison with "symmetrical" 8a(Scheme 6).



Scheme 6.

In order to elucidate the most likely reaction mechanism, we performed a computational study at the B3LYP/

6-311+G(3df,3dp) level of theory (for details see Experimental). The computed energy profile of the lowest energy pathway is depicted in Figure 6. As the key intermediate we postulate the sulfenic acid derivative **14**, formed via 1,4-H shift and simultaneous ring opening.

This process requires an activation energy of $32.2 \text{ kcal mol}^{-1}$, which is in good agreement with the value computed previously for the [2+3]-cycloreversion of **8a** (Figure 3). The second step, which requires a lower activation energy (19.0 kcal mol⁻¹) results from the fragmentation of the intermediate **14** into the observed products **10** and **13**. It is worth emphasizing that the proposed mechanism is similar to that formulated in the reported transformation of disulfane *S*-oxide into a mixture of thioformal-dehyde and a sulfenic acid derivative.^[15]



Figure 6. Reaction profile (kcalmol⁻¹) for the thermal decomposition of 1,2,4-trithiolane-1-S-oxide (9a) at the B3LYP/6-311+G(3df,3pd) level of theory including zero-point vibrational energy corrections.

Conclusions

The present study shows that the pyrolysis of the regioisomeric 1,2,4-trithiolane S-oxides 8a and 9a, irrespective of the structure of the isomer, results in the formation of thioformaldehyde S-oxide (10) as one of two major products of the fragmentation process. In the case of "symmetrical" S-oxide 8a, a [2+3]-cycloreversion leads to thioformaldehyde S-sulfide (5a) as the second major component of the collected pyrolyzate.

On the other hand, the fragmentation of the "non-symmetrical" *S*-oxide **9a**, does not involve a 1,3-dipolar intermediate. Instead, a more complex fragmentation mechanism, including migration of an H-atom, smoothly leads to the formation of a *s*-*cis* and *s*-*trans* mixture of dithioformic acid (**13**). Moreover, our studies show that vacuum pyrolysis of symmetrical 4-*S*-oxide derived from a 1,2,4-trithiolane can be a useful method for the preparation of the corresponding thiocarbonyl *S*-oxide (sulfine) that otherwise is difficult to prepare or cannot be prepared by using known procedures.^[16] Sulfines are gaining growing importance in modern organic synthesis.^[16b]

Experimental Section

1,2,4-Trithiolane 4-oxide (8a) and 1,2,4-trithiolane 1-oxide (9a) were prepared by oxidation of the parent 1,2,4-trithiolane $(3a)^{[2a]}$ using known protocols.^[6a]

Matrix Isolation Experiments: Compounds 2a and 3a were subjected to HVFP at 650 °C and 700 °C, respectively (empty quartz tube, inner diameter: 8 mm, length of heating zone: 50 mm). The products thus formed were trapped immediately thereafter on a cold (10 K) CsI (or BaF₂) window together with a large excess of Ar or N₂. These matrices were examined with FT-IR and UV/Vis spectroscopy.

Computational Methods: All geometries were fully optimized and characterized as minima or transition structures by means of analytical harmonic vibrational frequencies computations at the B3LYP/6-311+G(3df,3pd) level of theory.^[17] Unscaled zero-point vibrational energy corrections were included in all relative energy comparisons (kcalmol⁻¹, relative to **9a**). The Gaussian Program Suite was used for all computations.^[11]

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