DOI: 10.1002/ejoc.200800023

Generation and Rearrangement of Some Spirocycloaliphatic Thiosulfines and Dithiiranes

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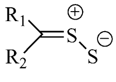
Keywords: Density functional calculations / Flash pyrolysis / Matrix isolation / Sulfur heterocycles

The flash-vacuum pyrolysis of selected dispirodicycloaliphatic 1,2,4-trithiolanes was studied by using matrix isolation techniques. The formation of thiosulfines and dithiiranes along with the corresponding thioketones was detected spectroscopically and confirmed by comparison with computed spectra. In the case of tetramethylcyclobutanone 1,2,4-trithiolane, the thermal formation of the dithiolactone was observed. Pyrolysis of the (dichloro)tetramethylcyclobutane derivative resulted only in the formation of a mixture of the thiosulfine and dithiirane. In this case, conversion into the corresponding dithiolactone could be achieved photochemically. The dispirodiadamantane derivative gave a mixture of the respective thiosulfine and dithiirane but no dithiolactone could be detected in the mixture.

Introduction

Thiocarbonyl *S*-sulfides **1** (thiosulfines) belong to the class of so-called S-centered 1,3-dipoles that have only been described as elusive intermediates and have, in contrast to the relatively stable thiocarbonyl *S*-oxides (sulfines),[1] never been isolated.[2] Structures of type **1** can be trapped in solution through the reaction with dipolarophiles (C=C, C≡C, C=S) to give the corresponding five-membered sulfur heterocycles.[2] Thiosulfines **1** can be generated by various methods; the most representative include (a) formal elimination of acetyl chloride from α-chloro-substituted acetylated disulfanes in the presence of morpholine ("unzipping reaction"),[3] (b) sulfur transfer from reactive three-membered heterocycles (intermediate formation of thiaziridines,[4] oxathiiranes,[5] or thiiranes[6,7]) to thioketones, and (c) thermal [2+3] cycloreversion of 1,2,4-trithiolanes.[6–8] The latter is the most general and most widely applied approach. In pioneering work on the chemistry of thiosulfines, Senning et al. postulated that in situ generated thiosulfines **1** (method a) equilibrate with dithiiranes **2**, which subsequently undergo isomerization to dithioesters **3** through 1,3-migration of the R^2 substituent.[3a]



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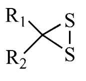

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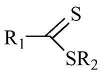

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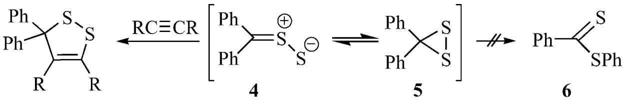
Reactions of thiobenzophenone *S*-sulfide (**4**) were extensively studied by Huisgen and Rapp.[6] They generated **4** in solution by thermal [2+3] cycloreversion of 3,3,5,5-tetraphenyl-1,2,4-trithiolane (method c) and trapped it with activated acetylene derivatives or cycloaliphatic thioketones.[6] The equilibrium between thiosulfine **4** and dithiirane **5** was postulated but evidence for the formation of phenyl dithiobenzoate (**6**) through migration of the Ph group could not be found (Scheme 1).



Scheme 1. Postulated equilibrium of thiosulfine **4** ⇆ dithiirane **5** system.

In recent years, Ishii and Nakayama reported the syntheses and reactions of several dithiiranes, which were isolated as stable compounds.[9] On the one hand, the ring opening of dithiirane **7** to the corresponding thiosulfine **8** was proven by intramolecular [2+3] cycloaddition with the C=O group, which led to the corresponding 1,3,4-oxadithiolane **9**, but on the other hand, no rearrangement through migration of the phenyl or aliphatic group to give dithioester **10** was observed[9a] (Scheme 2).

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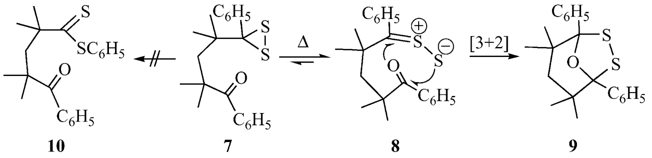
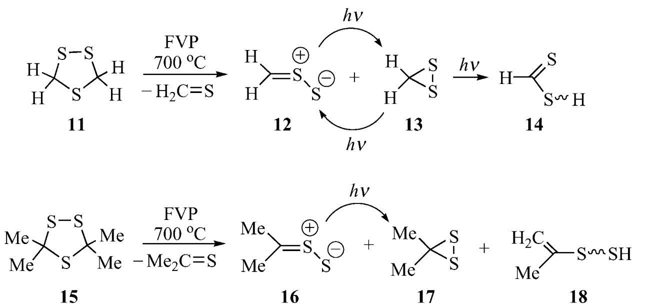


Scheme 2. Formation of 1,3,4-oxadithiolane **9**.

Our recent studies employed matrix isolation techniques for the spectroscopic characterization of products formed after gas-phase flash-vacuum pyrolysis (FVP) of the parent 1,2,4-trithiolane (**11**)[8a] and its 3,3,5,5-tetramethyl derivative **15**[8b] (Scheme 3). Subsequently, we studied the reactivity of the matrix-isolated products by irradiation with UV light or by annealing of the matrix.



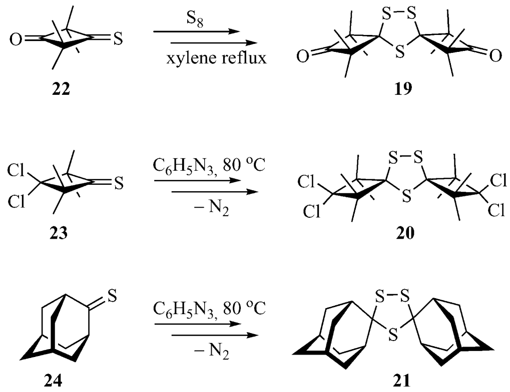
Scheme 3. Transformations of 1,2,4-trithiolanes **11** and **15**.

In the case of **11**, we observed the formation of comparable amounts of both thioformaldehyde *S*-sulfide (**12**) and isomeric dithiirane (**13**). Upon irradiation with $\lambda = 570$ nm light, parent thiosulfine **12** isomerized to **13** and further into dithioformic acid (**14**).[8a] Gas-phase thermolysis of **15** led to the formation of the product resulting from a [1,4] H-shift, identified as vinyldisulfane **18** (Scheme 3). Along with thioacetone, the presence of thioacetone *S*-sulfide (**16**) and dimethyldithiirane (**17**) was proven on the basis of spectroscopic evidence (UV and IR spectra).[8b] Neither photolysis nor thermal conversion of the pyrolysate led to methyl dithioacetate as the product of the Me-group migration. These results showed that the rearrangement of the thiosulfine/dithiirane system into dithioacid and its derivatives is unlikely to occur under thermal conditions.

In this paper, we describe new results on the gas-phase thermolysis of 1,2,4-trithiolanes **19**–**21** bearing dispirodicycloaliphatic substituents at C-3 and C-5. These systems were chosen because isomerizations of the initially formed thiosulfines by [1,4] H-shifts are not likely and other photochemical or thermal reactions of dithiiranes can be revealed.

Results and Discussion

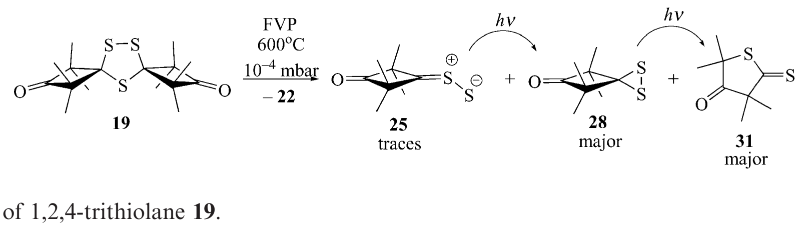
1,2,4-Trithiolanes **19**–**21** are crystalline, stable compounds that are accessible by sulfur-transfer reactions by using the parent thioketones, that is, 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**22**),[10] 3,3-dichloro-2,2,4,4-tetramethylcyclobutanethione (**23**),[11] or adamantanethione (**24**),[12] respectively (Scheme 4). Reactions are postulated to occur via the in situ generated thiosulfines, which subsequently undergo regioselectively the [2+3] cycloaddition with the C=S bond to yield heterocyclic products **19**–**21**.



Scheme 4. Preparation of trithiolanes **19**–**21**.

Gas-phase thermolysis of 1,2,4-trithiolanes **19**–**21** was performed under high-vacuum (≈10^{-4} mbar) conditions by using an empty quartz tube that was heated up to 700 °C. A stream of the reaction products was condensed on a CsI window cooled to ca. 10 K together with a large excess of argon. The pyrolysate collected in the matrix was probed by recording the UV and IR spectra. The observed bands were compared with those of authentic samples of the corresponding thioketones **22**–**24** as well as with computed (see details below) spectra of expected thiosulfines **25**–**27** and dithiiranes **28**–**30**.

Two FVP experiments at 500 and 600 °C of **19** (Scheme 5) were aimed at immediate trapping of the products with an excess amount of argon on a CsI window at 10 K. Decomposition of **19** was almost complete, and monothione **22** was easily identified as one of the reaction products (comparison of IR with the authentic matrix spectrum of **22**). Because **22** undergoes further conversion under the pyrolysis conditions, small bands of the decomposition products dimethylketene, dimethylthioketene, CO, and propene were also detected. Together with these compounds, small amounts of thiosulfine **25**, which is easily detectable by its UV band around 400 nm,[8] dithiirane **28**, and dithio-



Scheme 5. Transformation of 1,2,4-trithiolane **19**.

lactone **31** were also identified. The latter two were formed as main products in approximately 1:1 ratio (Figure 1). At 600 °C, the yield of **31** was higher than that of **28** at 500 °C, which indicates that **31** forms via **28**. Upon irradiation of the matrix-isolated pyrolysis products with λ = 366 nm, which corresponds to the absorption of the thiosulfine system, **25** quickly converts into **28** (10 min.). Like other dithiiranes, **28** displays a very weak – and therefore undetectable – UV absorption around 500 nm; it slowly isomerized into **31** by irradiation of the matrix with visible light ($\lambda >$ 395 nm, Figure 2). Dithiolactone **31** shows a prominent UV absorption at λ_{max} = 304 nm. This photoisomerization was monitored by the respective difference IR spectrum, which also allows the unambiguous identification of both compounds **28** and **31** by comparison with their computed [B3LYP/6-311+G(d,p)] IR spectra (Figure 3).

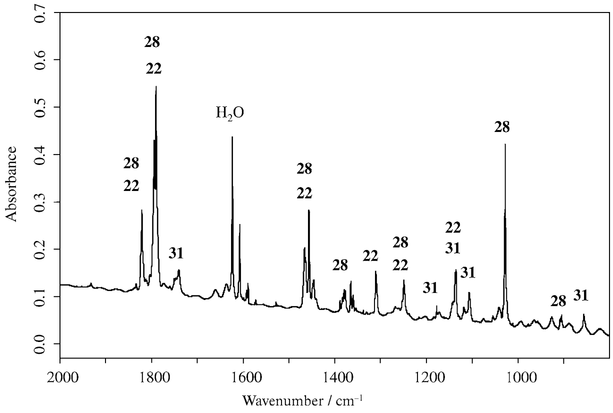


Figure 1. IR spectrum of the matrix-isolated products taken after FVP of **19**.

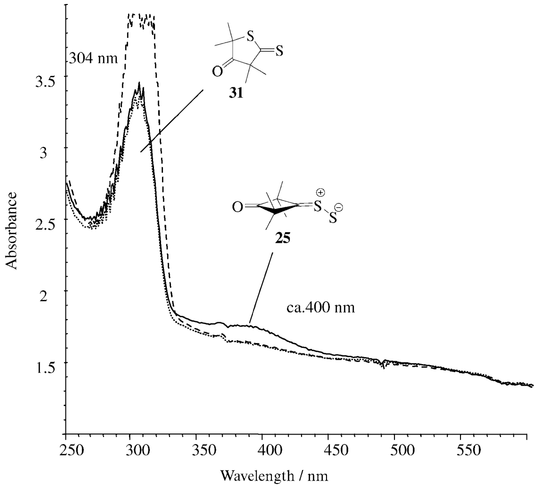


Figure 2. Photoisomerization of thiosulfine **25** into dithiolactone **31** via dithiirane **28**. Solid line: argon matrix of pyrolysis products, unirradiated; dotted line: matrix after 10 min irradiation with 366 nm light; dashed line: after irradiation with $\lambda >$ 395 nm light.

Independently, FVP of **19** was carried out on preparative scale at 450 °C and 10^{-2} mbar. The crude reaction mixture was washed from the cold finger (–78 °C) and analyzed by ^{1}H NMR spectroscopy, which showed the presence of singlets located at δ = 1.35 and 1.62 ppm (attributed to **31**) and at 1.33 ppm (attributed to **22**). Both reaction products were formed in a ca. 1:1 ratio. However, repetition of the experiment at 700 °C (10^{-2} mbar) gave **31** as the only product. Under these conditions, thioketone **22** undergoes a [2+2] cycloreversion to yield dimethylketene and dimethylthioketene, which cannot be trapped at –78 °C. Dimethylketene and dimethylthioketene were also observed among the products identified in the matrix by IR spectroscopy. Both compounds showed characteristic absorptions at 2127 cm^{-1} for dimethylketene and at 1798 cm^{-1} for dimethylthioketene. This type of conversion is known for analogs of **22** such as 2,2,4,4-tetramethylcyclobutane-1,3-dithione.[13]

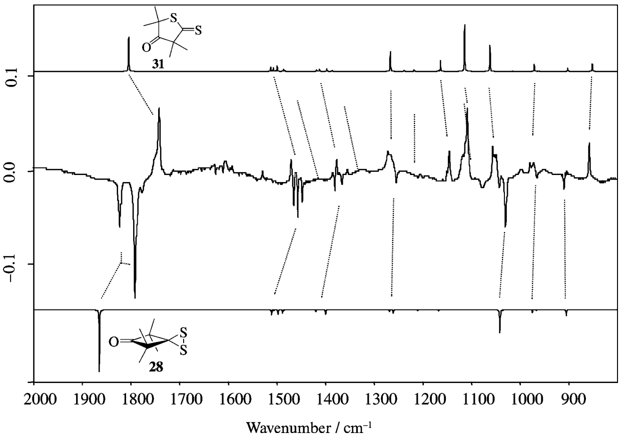
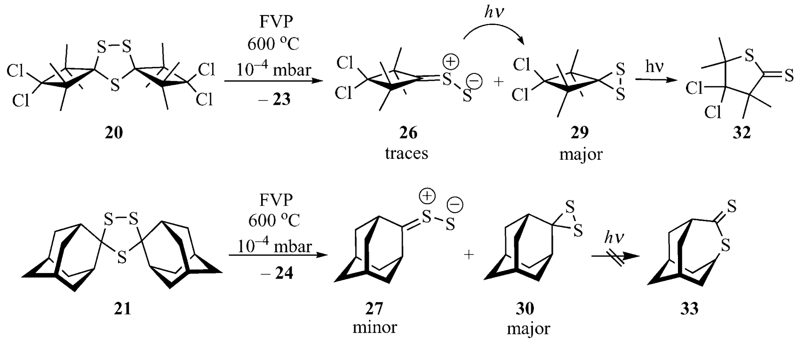


Figure 3. Middle: difference IR spectrum, before and after 4 h irradiation with visible light ($\lambda >$ 395 nm) showing the photoisomerization of dithiirane **28** (negative bands) into dithiolactone **31** (positive bands). Bottom and top: computed [B3LYP/6-311+G(d,p)] IR spectra of **28** and **31**.

In comparison with **19**, thermolysis of **20** at 600 °C led to a different composition of products formed in the pyrolysate at 10 K (Scheme 6). In this case, trace amounts of thiosulfine **26** were identified on the basis of its weak absorption in the UV spectrum around 390 nm. Irradiation of this matrix with λ = 366 nm light resulted in the disappearance of this maximum after 10 min. Unlike the experiment with **19**, the matrix obtained after thermolysis of **20** did not contain the expected dithiolactone **32**, as evident from the lack of the characteristic absorption at ca. 300 nm. In contrast, the IR spectrum of the crude pyrolysate showed the absorption bands of thioketone **23** and dithiirane **29** located at positions predicted by the computations. On the basis of the comparison of the intensities of calculated and registered absorption bands, it is likely that both compounds appeared in comparable amounts (Figure 4). Longer irradiation of the matrix with visible light ($\lambda >$ 395 nm) led to rearrangement of **29** into dithiolactone **32**. Absorption bands in the UV (λ_{max} = 304 nm) and IR spectra characteristic for **32** grew during the reaction.

Finally, 1,2,4-trithiolane **21** was thermolyzed under conditions comparable to those described for **19** and **20**. The analysis of the UV spectrum of the crude pyrolysate showed an absorption band at 384 nm characteristic of thiosulfine



Scheme 6. Transformations of trithiolanes **20** and **21**.

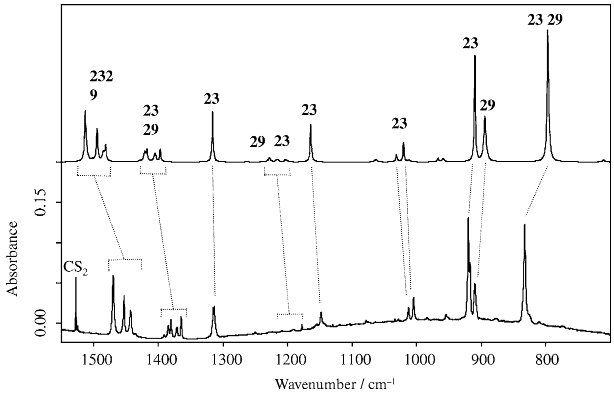


Figure 4. Bottom: IR spectra of pyrolysis products (600 °C) of **20** (Ar matrix, 10 K); top: computed [B3LYP/6-311+G(d,p)] IR spectrum of a 1:1 mixture of thioketone **23** and dithiirane **29**.

27. There was no absorption near 300 nm, excluding the formation of the corresponding dithiolactone **33**. In analogy to **25** and **26**, short irradiation with λ = 366 nm light led to complete disappearance of **27**. However, even longer irradiation times did not, in contrast to **25** and **26**, afford the corresponding dithiolactone **33**. A comparison of absorption bands intensities observed in the experimental IR spectrum of the crude pyrolysate with that computed for adamantanethione (**24**) and dithiirane **30** showed that both compounds are formed in approximately equal amounts (Figure 5).

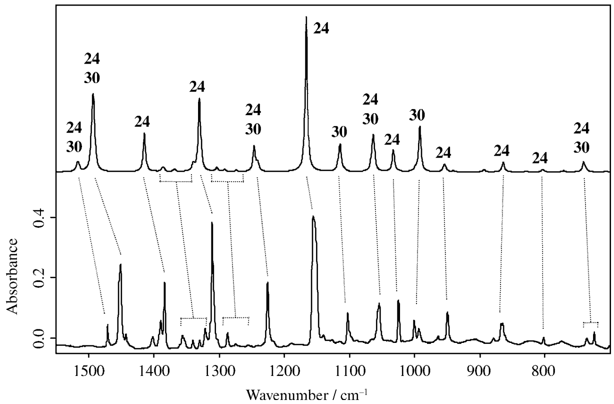
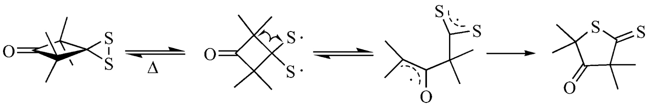


Figure 5. Bottom: IR spectra of pyrolysis products (600 °C) of **21** (Ar matrix, 10 K); top: computed [B3LYP/6-311+G(d,p)] IR spectrum of a 1:1 mixture of thioketone **24** and dithiirane **30**.

The present study shows that the flash-vacuum pyrolyses of symmetrically substituted trithiolanes **19**–**21** led in each case to mixtures of variable amounts of the corresponding thiosulfines **25**–**27** and dithiiranes **28**–**30**. Photolyses of matrix-isolated thiosulfines **25**–**27** result in complete conversion into the corresponding dithiiranes **28**–**30** after short irradiation times with monochromatic light at λ = 366 nm. The irreversible thermal conversion into dithiolactone **31** was observed in the gas phase only for the most sterically congested dithiirane **28**. 3,3-Dichloro derivative **29** was isomerized into **32** only in the matrix upon photolysis with visible light $\lambda > 395$ nm. In the case of spiroadamantane derivative **21**, matrix-isolated dithiirane **30** could not be isomerized to the ring-expanded dithiolactone **33** even under photolytic conditions.

A plausible explanation for this isomerization may be that dithiirane **28** readily forms the corresponding diradical **34**, which opens the cyclobutane ring to form the more stable diradical **35**. Subsequent ring closure leads to five-membered dithiolactone **31** (Scheme 7). The formation of diradical **35** benefits from the release of the strain energy from the four-membered ring and additionally from the stabilization effect of the carbonyl group. A similar stabilization of the diradical intermediate is not possible in the case of dispirodiadamantane derivative **30**, and therefore, the formation of dithiolactone **33** in this system is not observed. Because of the lack of stabilizing effect of the carbonyl group, the formation of the expected dithiolactone **32** occurred only photochemically. The photochemical isomerization into dithiolactone **32** with participation of another diradical formed by alternative S–S bond cleavage is likely.



Scheme 7. Proposed mechanism for the formation of dithiolactone **31** from dithiirane **28**.

It would be desirable to explore the mechanistic proposal outlined in Scheme 7 with computational methods. However, computing the reaction paths involving biradical species such as **35** with expectedly low-lying open-shell singlet and triplet states is a very demanding task, as standard MCSCF and CASSCF methods are not sufficiently accurate to draw firm mechanistic conclusions.[16]

Conclusions

The irreversible conversion of dithiiranes into the corresponding dithiolactones depends on the substitution pattern. Thermal and photolytic isomerizations leading to the ring-enlarged dithiolactone **31** were observed only for strained spiro derivative **28**. The analogous photochemical conversion was observed for matrix-isolated dithiirane **29**, which afforded dithiolane **32**. In this case, thermal isomerization in the gas phase did not take place. Moreover, neither thermal nor photochemical transformation of **30** into **33** was observed.

Experimental Section

Starting Materials: 1,2,4-Trithiolanes used in the study were obtained according to known literature protocols: 1,1,3,3,7,7,9,9-octamethyl-5,10,11-trithiadispiro[3.1.3.2]-undecane-2,8-dione (**19**),[10] 2,2,8,8-tetrachloro-1,1,3,3,7,7,9,9-octamethyl-5,10,11-trithiadispiro-[3.1.3.2]undecane (**20**),[11] and dispiro[adamantane-2,3′-(1,2,4)-trithiolane-5′,2′′-adamantane] (**21**).[12]

Matrix Studies: The cryostat for matrix isolation was a helium closed-cycle refrigeration system (compressor unit RW2 with coldhead base unit 210 and extension module ROK) from Leybold. The matrix IR spectra were measured by using an FTIR instrument IFS 55 from Bruker; the UV/Vis spectra were taken with a Hewlett Packard HP 8453 diode-array spectrophotometer. The light sources used were a mercury high-pressure lamp (HBO 200 from Osram) with a monochromator (Bausch and Lomb) and a mercury low-pressure spiral lamp with a Vycor filter (Gräntzel). For the combination of high-vacuum flash pyrolysis with matrix isolation, a small home-built water-cooled oven directly connected to the vacuum shroud of the cryostat was used. The pyrolysis zone consisted of a completely empty quartz tube (inner diameter 8 mm, length of heating zone 50 mm) resistively heated by a coax heating wire. The temperature was controlled by a Ni/CrNi thermocouple. The precursors were sublimed at 30–40 °C from a storage bulb into the quartz pyrolysis tube. Immediately after leaving the tube, at a distance of ca. 50 mm, the pyrolysis products were cocondensed with a large excess of argon on the surface of the 10 K matrix window.

Computational Methods: IR spectra of structures **25**–**33** were computed by density functional theory method by using the B3LYP functional with the 6-311+G(d,p) basis set as incorporated in the Gaussian package of programs.[15]

FVP of 19: FVP was carried out by using the standard FVP apparatus equipped with 15-cm heating zone without filling and cooling finger (acetone/dry ice) under 10^{-2} mbar.

FVP at 450 °C: Trithiolane **19** (50 mg, 0.135 mmol) was pyrolyzed, and a 1:1 mixture of dithiolactone **31** (^{1}H NMR) and thioketone **22** (^{1}H NMR: $\delta = 1.33$ ppm) was found.

FVP at 700 °C: Trithiolane **19** (200 mg, 0.54 mmol) was pyrolyzed, and only dithiolactone **31** and small amounts of some unidentified products were found in the crude mixture (^{1}H NMR). Dithiolactone **31** was purified by preparative TLC (petroleum ether/$CHCl_3$, 1:3) and subsequently recrystallized from *n*-pentane.

3,3,5,5-Tetramethyl-2-thioxothiolane-4-one (31): Yield 38 % (40 mg, 0.21 mmol). M.p. 36–39 °C (*n*-pentane) (ref.[14] 39–41 °C). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.62$ (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 242.8$ (s, C=S), 216.5 (s, C=O), 63.2 (s, C_q), 61.2 (s, C_q), 28.0 (q, CH_3), 27.7 (q, CH_3) ppm. IR (KBr): $\tilde{\nu} = 1736$ [s (C=O)] cm^{-1}. MS (EI): *m*/*z* (%) = 188 (100) $[M]^+$, 86 (90) $[Me_2C=C=S]^+$.

Acknowledgments

J. R. and G. M. thank the Rector of the University of Lodz for financial support (Grant # 505/712).

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Received: January 9, 2008