Recent advances in chemistry of dithiirane and small ring compounds containing two chalcogen atoms

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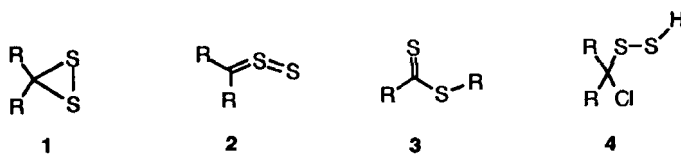
Abstract. Sulfurization of nonenolizable dicarbonyl compounds affords a series of bicyclic 1,3-dithietanes by intramolecular head-to-tail dimerization of the resulting dithiocarbonyl compounds. Oxidative hydrolysis of these 1,3-dithietanes leads to the first synthesis of rather thermally stable, isolable, and nicely crystalline dithiiranes. Oxidation of 1,3-dithietane *S*-oxides or the dithiiranes produces the corresponding dithiirane oxides. Properties of the dithiiranes and their *S*-oxides, including X-ray crystal structure, are discussed. Intramolecular head-to-tail dimerization between thiocarbonyl and carbonyl groups leading to 1,3-oxathietanes is also described in some detail.

We have recently succeeded in the preparation of the first isolable dithiiranes. The present account is concerned with the preparation and properties of these dithiiranes and chemistry of the related small ring compounds containing two chalcogen atoms.

The smallest cyclic disulfides, dithiiranes (**1**), are isomers of thiocarbonyl *S*-sulfides (**2**) and dithioesters (**3**). Although dithioesters **3** are generally thermally stable, no isolable, stable dithiiranes **1** or thiocarbonyl *S*-sulfides **2** were known until we report the first synthesis of the former species (1,2). In 1979, Senning proposed the formation of **1** or **2** by dehydrochlorination of **4** with a base (3). A full paper followed in 1985 (4). In the years 1985-89, a total of 11 papers by other groups, which dealt with different approaches to the system, appeared. Among them, the most important work is probably the formation of thiocarbonyl *S*-sulfide by sulfur transfer from tetraphenyl-1,2,4-trithiolane to thiobenzophenone (5). In this case, the thiocarbonyl *S*-sulfide (**2**: R = Ph) is trapped by 1,3-dipolar cycloaddition with dimethyl acetylene-dicarboxylate (DMAD). Since then, more than 10 papers including those from our laboratories have appeared as reviewed very recently by Senning (6).
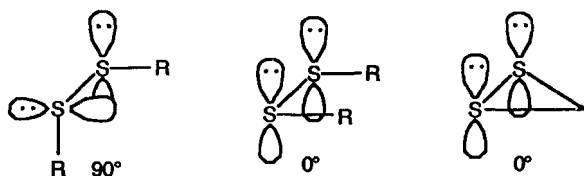

The nature of the disulfide linkage is significantly altered by changes in the dihedral angle between the two carbon-sulfur bonds. As this angle is reduced from 90° to 0°, the destabilizing interactions between lone pair electrons on adjacent sulfur atoms become larger (7). Thus, as to dithiiranes where the dihedral angle is 0° of necessity, the largest factor that makes these molecules unstable would come from sulfur-sulfur lone pair interactions, and then large strains of the bond angles might follow.

In 1990 we reported the sulfurization of nonenolizable diketones (**5**) by Lawesson's reagent (LR) and boron trisulfide. This has been undertaken to know how two thiocarbonyl groups interact with each other depending on the length of the methylene chain; we expected the formation of 1,2-dithietanes (**7**) by head-to-head dimerization in a system with an appropriate chain length (**8**). In every case, disappointingly, the resulting dithiocarbonyl compounds underwent the intramolecular head-to-tail dimerization to give 1,3-dithietanes (**6**) as the principal product. However, we could have put forward the following important proposals. For example, in the case of n = 0, the sulfurization with LR at 50 °C affords the disulfide **8a** (23%), the trithiolane **9a** (7%), and the 1,3-dithietane **6a** (70%), while the reaction in refluxing benzene increased the yield of **8a** to 80% yield at sacrifice of the formation of **6a**; **9a** still formed in 13% yield. Actually, heating **6a** in refluxing benzene gives **8a** quantitatively. This observation could be best explained by assuming the equilibrium between **6a** and the head-to-head dimer **10a** via the dithiocarbonyl compound. The ring-opening of **10a** would give rise to **8a**. We have also pointed out the presence of the equilibrium between the monothiocarbonyl compound **11a** and the 1,3-oxathietane **12a**. This stems partly from the observation that the expected characteristic coloration due to **11a** does not develop during the reaction. We also proposed that the trithiolane **9a** is the result of the intramolecular 1,3-dipolar cycloaddition of the thiocarbonyl sulfide and thiocarbonyl groups of **13a** (the precursor compound of which might be its isomer, dithiirane **14a**) which was formed by thionation. Although the rigid evidence for the first proposal still remains as an open question, we have now succeeded in giving the rigid evidences for the second and third proposals as described below.
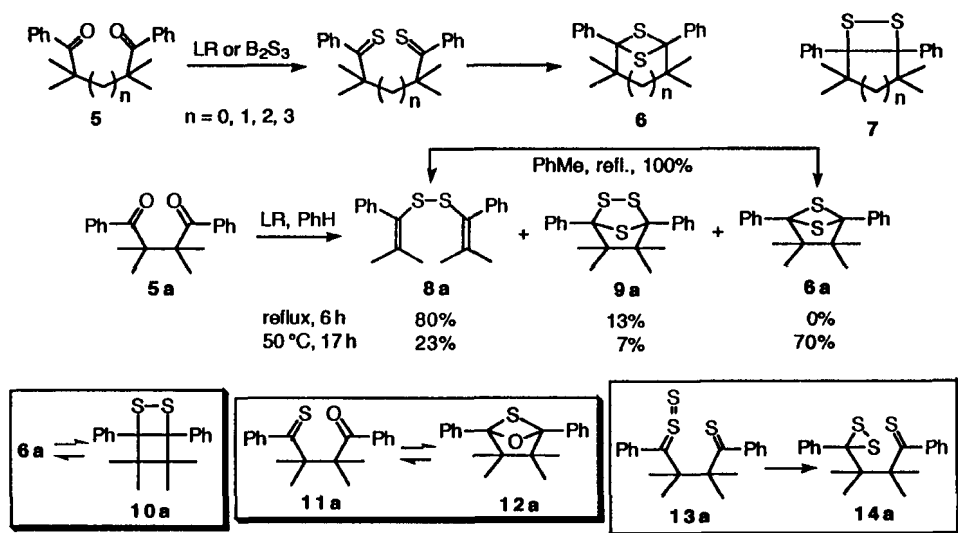

The formation of the thiocarbonyl *S*-sulfide **18b** or its isomer dithiirane is also probable in the reaction of the monohydrazone **15** with S_2Cl_2. The reaction affords the oxadithiolane **16b** in 56% yield, which should be formed via **18b**. This observation is in harmony with the proposal that the formation of thioketones by treatment of hydrozones with S_2Cl_2 proceeds via thiocarbonyl *S*-sulfides (11). Interestingly, the reaction of **15** with Se_2Cl_2 affords the oxadiselenolane **17** in 21% yield, the formation of which is indicative of the intermediacy of the selenocarbonyl *Se*-selenide **19** (9,10). Treatment of **16b** with $P(NMe_2)_3$ or PPh_3 affords a mixture of the 1,3-oxathietane **12b** and the thione **11b**. The both compounds are not isolable in pure form by column chromatography because of the equilibrium between them. This is the first observation of the [2+2] cycloaddition of the thiocarbonyl and carbonyl in a head-to-tail manner and provides the rigid evidence for our second proposal. Treatment of **17** with $P(NMe_2)_3$ affords the 1,3-oxaselenetane **20** in 17% yield along with other products. The compound **20** also isomerizes to the selenoketone **21** when heated, which is chemically trapped by cycloaddition with DMAD.
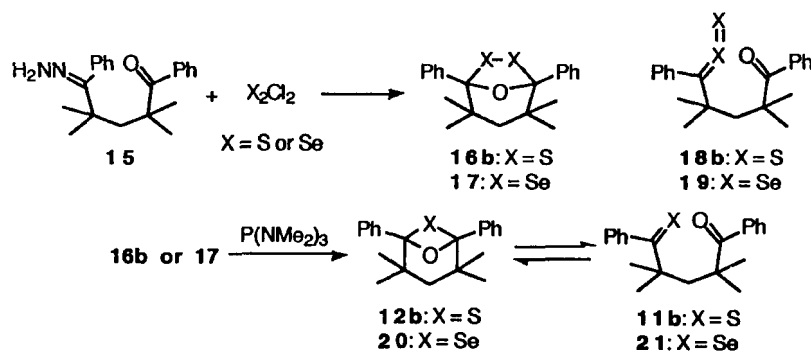
In another study, the bis-hydrazone **22** was treated with Se_2Cl_2, which afforded compounds **23-25** in 25%, 20%, and 12% yields, respectively. The formation of **24** is again indicative of the formation of the selenocarbonyl *S*e-selenide **26** (12).
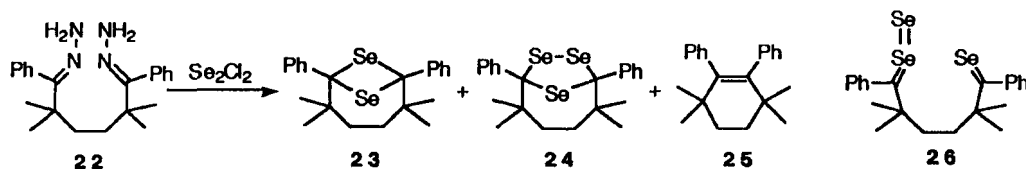

Until here we have given the rather indirect evidences for the intermediacy of the thiocarbonyl *S*-sulfides and selenocarbonyl *Se*-selenides or their three membered-ring isomers. Next are given much more direct evidences for these species with emphasis being placed on the first isolation of stable, nicely crystalline dithiiranes. In our continuing interest in the stereochemical course of the oxidation of bicyclic 1,3-dithietanes (13), we have examined oxidation of **6b** with MCPBA, which furnishes sulfoxides **27b-exo** (35%) and **27b-endo** (57%). Further oxidation of **27b-exo** with OXONE®, to our surprise, gave a 57% yield of the dithiirane oxide **28b-cis**, mp 124-125 °C (dec), by oxidative hydrolysis along with the sulfine **29b** and the diketone **5b**. Structure of **28b-cis** was unambiguously determined by spectroscopic means, chemical transformations, and X-ray single crystal structure analysis. Similarly oxidation of **27b-endo** afforded a mixture of the dithiirane oxides, **28b-trans** and **28b-cis**, in 2% and 16% yields, respectively.
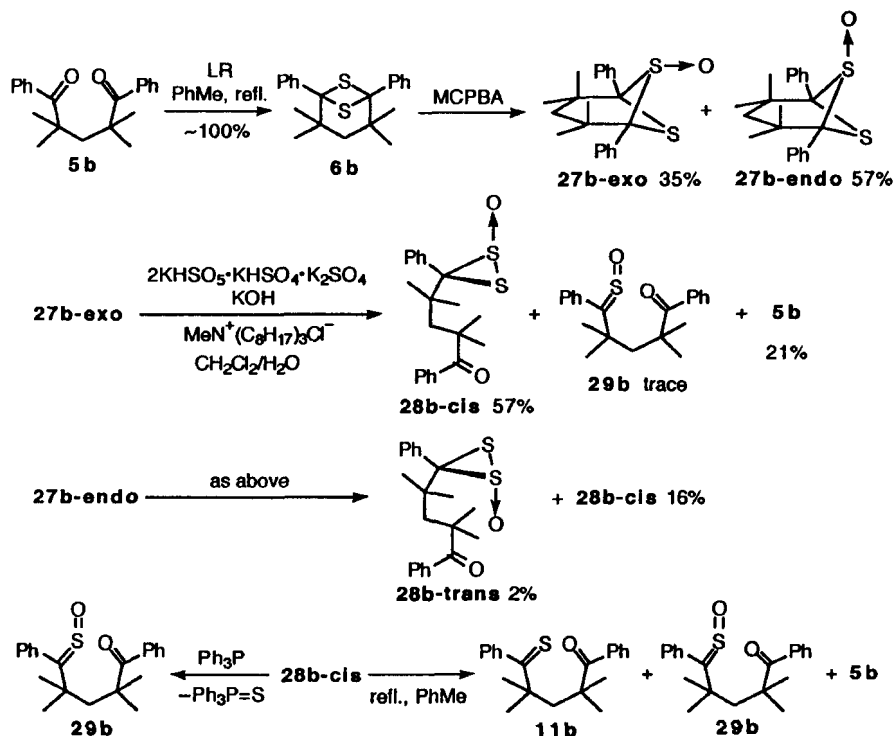
Treatment of **28b-cis** with Ph₃P in CH₂Cl₂ at room temperature gives the sulfine **29b** in 79% yield, while heating in refluxing toluene produces the thioketone **11b** (48%) and the sulfine **29b** (14%) with loss of sulfur monooxide and sulfur, respectively, in addition to the ketone **5b** (38%) which formed by further decomposition of former compounds.

Successful isolation of dithiirane oxides **28b** encouraged us to prepare isolable, stable dithiiranes. However, attempted preparation by reduction of **28b** was unsuccessful. We could find out finally that the oxidative hydrolysis of the 1,3-dithietane **6b** with OXONE® again gives the dithiirane **30b** in 20% isolated yield along with **28b-cis**, **27b-endo**, and **5b**. The dithiirane **30b** is a nicely crystalline compound with mp of 68-75 °C (dec) (we give this vermilion-colored compound (λ_{max} 452 nm) a conventional name, *dithiavermilione*, after its color and structure containing two sulfur atoms and a carbonyl group; remind also that vermilion (cinnabar) is also a sulfur compound (HgS)). The structure of **30b** was unambiguously determined by spectroscopic means, chemical transformations, and X-ray single crystal structure analysis. Oxidation of **30b** with 1 equiv of MCPBA affords **28b-cis** (87%), **28b-trans** (7%), **29b** (2%) with 4% recovery, while treatment with Ph₃P at room temperature gives the thioketone **11b** quantitatively. The ratio of the products arising from the thermolysis of **30b** much depends on the concentration and polarity of the solvents. Thus, heating a dilute 1,2-dichloroethane solution of **30b** gives the oxadithiolane **16b** (94%) and a mixture of **11b** and **12b** (5.3%), while heating a benzene solution gives only a 27% yield of **16b** with an increased yield of a mixture of **11b** and **12b** (73%). The formation of **16b** is well explained by the initial formation of the thiocarbonyl *S*-sulfide **18b**, which undergoes an intramolecular dipolar cycloaddition to give **16b** as the final product. The formation of the polar species **18b** would be
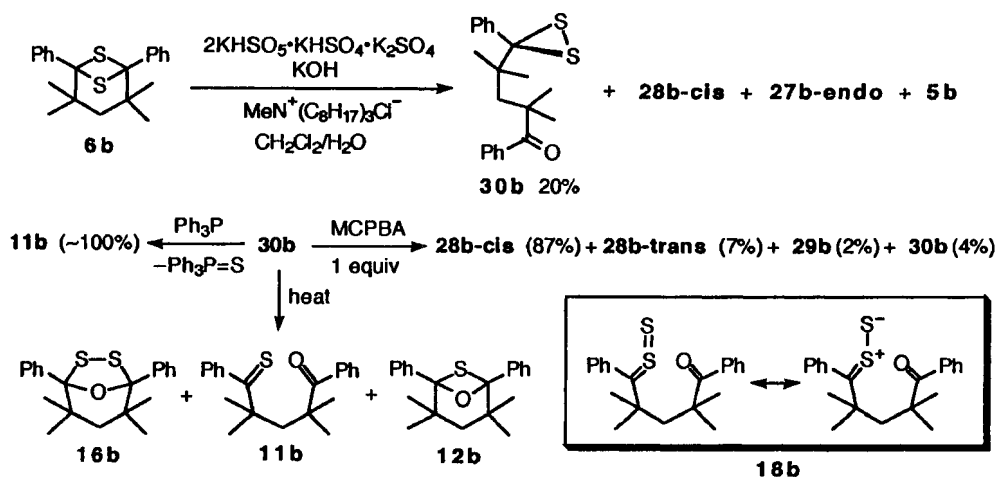

accelerated in polar solvents to give an increased yield of **16b** and also thermolysis in dilute solutions where bimolecular reaction pathways leading to the desulfurization product **11b** and **12b** are retarded gives a better yield of **16b**. Thus, we could provide more rigid evidence for the third proposal, the presence of thiocarbonyl *S*-sulfide **18b** as an intermediate, with a large bonus of isolation of the crystalline, stable dithiirane **30b**.

The X-ray structure analysis reveals that no unusual bond lengths and angles are observed in the dithiirane ring of **30b**. The S-S bond length (2.073 Å) corresponds to the mean value (2.070 Å) of S-S bond lengths found in disulfides in which the dihedral angles between C-S bonds are constrained to 0-20° and the two C-S bond lengths (1.821 and 1.814 Å) are very similar to that of the parent thiirane (1.815 Å).

Oxidation of **6a** with OXONE® also produces the corresponding dithiiranes **30a** in 10-20% yields, which could not be isolated in pure form because of their susceptibility to heat and bases. However, they

could be converted to the corresponding thioketones **11a** and dithiirane oxides **28a-cis** by treatment with Et₃N and MCPBA, respectively (14). On the other hand, oxidation of **6c** did not give the corresponding dithiiranes in any amounts, but gave the dithiirane oxides **28c-cis** in 9-18% yields along with other compounds. In order to know much more about the properties of dithiiranes, preparation of more simple dithiiranes is desirable. However, attempts to prepare more simple dithiiranes **31** by oxidation of 1,3-dithietanes **32** (R = H, Me, Et) unfortunately gave the ketones **33** in high yields.
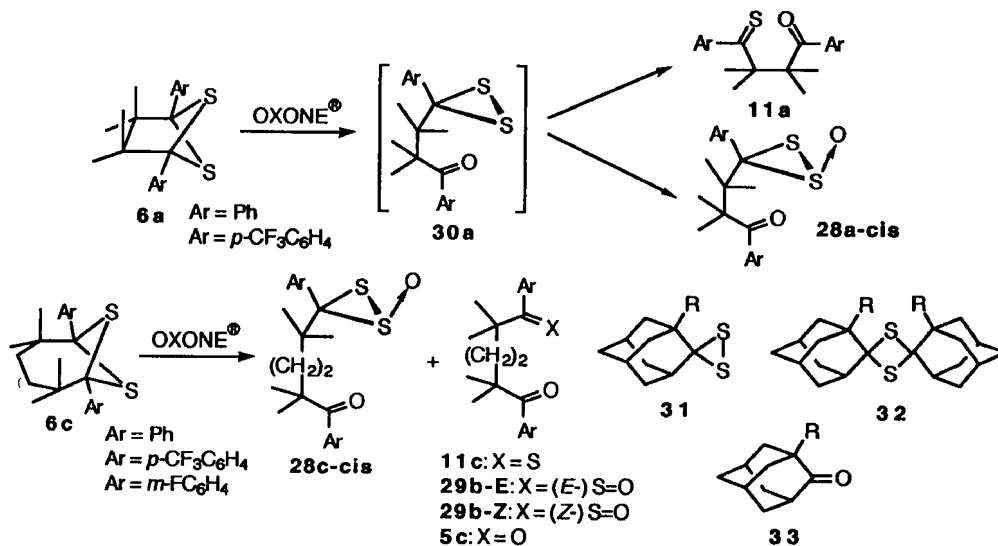
Generally speaking, oxidation of **6a-c** with OXONE® is sluggish and often requires nearly one week for completion. This prompted us to search for more convenient oxidation reagents. As a result, we have found that oxidation with HOCl or NaOCl proceeds more quickly and completes in 30 min to give better yields of dithiiranes. For example, oxidation of **6b** with NaOCl (1.4 equiv) in the presence of a perchlorate salt such as LiOCl₄ completes in 30 min to give a <u>54% yield</u> of **30b** along with other products such as **27b-endo** and **34** in small amounts (15). A plausible mechanism for the formation of these compounds is given below (oxidation with OXONE® will also proceed in similar pathways).
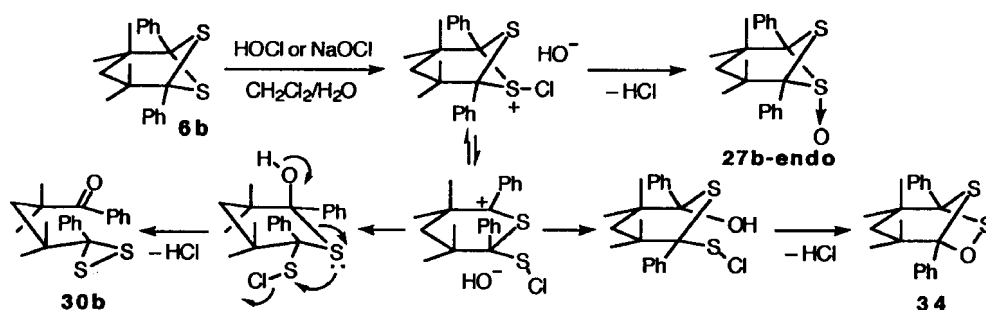
Finally we would like to refer to the fact that reaction of the ynediamine **35** with elemental sulfur affords the inner salt **38** in an excellent yield (16). The reaction may involve the dithiiranes such as **36** and **37** as intermediates. The salt **38** is an isomer of the dithiirane **37**.
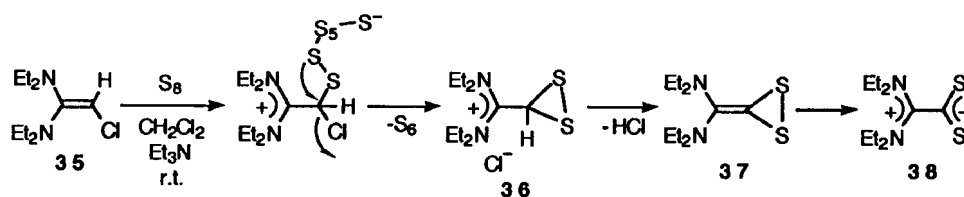
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