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Communications to the Editor

Diatomic Sulfur Transfer from Stable Alkoxy Disulfides

Sylvie L. Tardif, Charles R. Williams, and David N. Harpp*

Department of Chemistry, McGill University
Montreal, Quebec, Canada H3A 2K6

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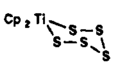
Diels−Alder reactions involving heteroatoms have been given considerable attention in recent years not only because of their fundamental importance but also as to their role in synthesis.[1] Of particular interest is the use of diatomic sulfur in such processes. Since the first publication of a synthetically useful procedure to generate and transfer S_2 by Steliou in 1984,[2a] there have been a number of reports of a diverse set of precursors to carry out this task with moderate success.[2] The best isolated yields to date (60−85%) of adducts like **1** result from Steliou's elegant biphenyl dithione approach (Scheme 1).[2b]

Our own efforts in this area[2e,i−k] have involved four different molecules (**2**−**5**) which have been shown to deliver diatomic sulfur units to dienes in modest yield.



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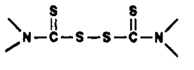

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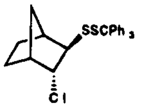

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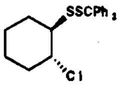

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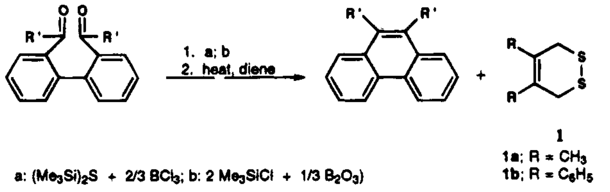
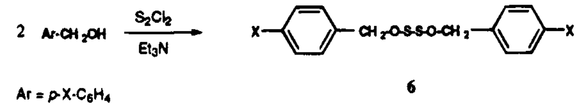
We now report a novel method for the effective delivery of diatomic sulfur from stable precursors, alkoxy disulfides **6**. This unusual class has been given little attention since its discovery in 1895.[3] In 1965 Thompson[4] prepared some aliphatic examples and discussed their ready decomposition. We have synthesized a series of them by a modified procedure in overall isolated yields of *ca.* 85% (Scheme 2, Table 1).[5]

Scheme 1



Scheme 2



Scheme 3

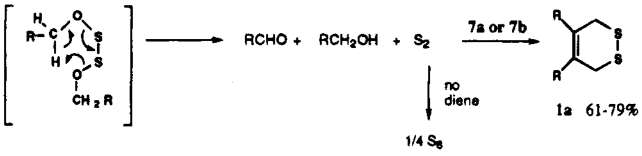


Table 1. Preparation of 4-Substituted Dibenzyloxy Disulfides **6**

ROSSOR **6**	X	yield (%)[a]	mp (°C)
a	H	88	50−51
b	NO_2	90	92−93
c	Cl	86	45−47
d	OMe	62[b]	34−36
e	Me	82	liquid

[a] Isolated yields after flash chromatography and recrystallization; **6a**−**d** are solids while **6e** is a liquid. [b] **6d** was very unstable on silica gel.

These substituted benzyl derivatives are conveniently stored with no detectable decomposition for months at −15 °C. Nitro derivative **6b** is stable in toluene to *ca.* 70 °C. At this temperature it begins to decompose, delivering elemental sulfur, benzyl alcohol, and benzaldehyde in high isolated yield. The likely mode of decomposition is displayed in Scheme 3 and suggests the possibility of loss of singlet diatomic sulfur.

We have found by appropriate trapping experiments with dienes **7a** (R = Me) and **7b** (R = Ph) that diatomic sulfur is effectively transferred in good isolated yield. The reaction is solvent and temperature dependent as is summarized in Table 2. In previous reports dealing with diatomic sulfur transfer, yields of trapped product (disulfide **1**) are generally not very high, ranging from unreported[2d] or "low" [2h] to a high average of 73%[2b] in trapping experiments with dienes.

By using an excess of reagent **6** to diene,[6] *isolated yields of up to 79% of trapped disulfide 1 are obtained.* We find that the trapped disulfide and diene are comparably competitive for the S_2 transfer reagents **6**. As a consequence, tetrasulfide **8** is observed in all of the experiments. Adduct **8** is of special interest as it is formed in many of our trapping experiments in variable yield. Concern has been expressed[1b] that diatomic sulfur transfer (as opposed to "activated" elemental sulfur) is not taking place when other than two sulfur atoms are transferred

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(1) (a) Suarez, D.; Sopordo, T. L.; Sordo, J. A. *J. Am. Chem. Soc.* **1994**, *116*, 763. (b) Steliou, K. *Acc. Chem. Res.* **1991**, *24*, 341. (c) Boger, D. L.; Weinreb, S. N. *Hetero Diels-Alder Methodology in Organic Synthesis*; Academic Press: San Diego, CA, 1987.

(2) These references are the sum of known diatomic sulfur transfer reactions where diene trapping experiments were carried out; average yields of isolated, trapped cyclic disulfide/tetrasulfide are in brackets: (a) Steliou, K.; Gareau, Y.; Harpp, D. N. *J. Am. Chem. Soc.* **1984**, *106*, 799 [35%/0%]. (b) Steliou, K.; Salama, P.; Brodeur, D.; Gareau, Y. *J. Am. Chem. Soc.* **1987**, *109*, 926 [73%/0%]. (c) Schmidt, M.; Görl, U. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 887 [48%/unreported]. (d) Ando, W.; Sonobe, H.; Akasaka, T. *Tetrahedron Lett.* **1987**, *28*, 6653 [unclear]. (e) Harpp, D. N.; MacDonald, J. G. *J. Org Chem.* **1988**, *53*, 3812 [28%/51%]. (f) Nicolaou, K. C.; DeFrees, S. A.; Hwang, C.-K.; Stylianides, N.; Carroll, P. J.; Snyder, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 3029 [25%/28%]. (g) Sato, R.; Satoh, S.; Saito, M. *Chem. Lett.* **1990**, 139 [55%/unreported]. (h) Gilchrist, T. L.; Wood, J. R. *J. Chem. Soc., Chem Commun.* **1992**, 1460 ["low"/detected]. (i) Chew, W.; Harpp, D. N. *Sulfur Letters* **1993**, *16*, 19 [9%/28%]. (j) Abu-Youssef, I. A.; Harpp, D. N. *Tetrahedron Lett.* **1993**, *34*, 4289 [detected/4%]. (k) Abu-Youssef, I. A.; Harpp, D. N. *Tetrahedron Lett.* **1994**, *35*, 7167 [0%/38%]. It appears that S_2 is of astronomical importance being detected in Jupiter's recent collision with Comet Shoemaker-Levy 9; see: (l) Noll, K. S.; McGrath, M. A.; Trafton, L. M.; Atreya, S. K.; Caldwell, J. J.; Weaver, H. A.; Yelle, R. V.; Barnet, C.; Edgington, S. *Science* **1995**, *267*, 1307.

(3) Legfeld, F. *Chem. Ber.* **1895**, *28*, 449.

(4) Thompson, Q. E.; Crutchfield, M. M.; Dietrich, M. W.; Pierron, E. *J. Org. Chem.* **1965**, *30*, 2692.

(5) For the *p*-nitro derivative, the yield can be optimized to 90% (after isolation by column chromatography) by using a solvent mixture of CH_2Cl_2−Et_2O (1:1) during the reaction; the observed increase in yield is related to a higher degree of solubility of reagents. It is of note that each of the alkoxy disulfides displays an AB quartet in the ^1H NMR spectrum perhaps more consistent with a thionosulfite structure (ROS(=S)OR). The X-ray structures of **6b** and **6c** have been determined, and the molecules are clearly R−O−S−S−O−R. This interesting system is being examined and will be the topic of a future publication.

(6) It also appears that each of the alkoxy disulfides **6** is similarly efficient in transferring diatomic sulfur, although **6b** appears superior.

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Table 2. Trapping Experiments with **6b** in the Presence of Dienes

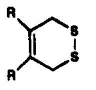
6b:diene[a]	solvent	time (h)	**1a** (%)[b]			**8a** (%)[b]	
3:1.0	toluene	24		(43)	[75]		(36)
3:1.0	(100–102 °C)[c]	36	32	(31)	[72]	47	(45)
5:1.0		24		(18)	[75]		(63)
1:3.0		24	31	(28)	[36]	19	(17)
1:3.0[d]		24	26	(24)	[31]	18	(15)
3:1.0[d]		24	34	(35)	[79]	48	(49)
1:1.2	ClC_6H_5	1.2	1[f]			25	
1:2.0	(130–135 °C)	1.2	1[f]			22	
1:3.0		1.2	1[f]			51	
6b:diene[a]	solvent	time (h)	**1b** (%)[e]			**8b** (%)[e]	
1:1.0	ClC_6H_5	2	26	(13)	[39]	30	(28)
3:1.0		2	48	(26)	[54]	34	(31)
5:1.0		2	50	(33)	[61]	35	(31)

[a] Typical amounts of **6b**:diene in the case of the 3:1 ratio are 600 mg (1.63 mM):44.6 mg (0.54 mM) in 7 mL of solvent. In addition, for each mole of **6** used, 1 mol of MgO is added and the reactions are carried out until reagent **6** is depleted (tlc). [b] ^1H NMR yields using an internal standard are listed; brackets indicate isolated yield after flash chromatography (silica gel–CCl_4); square brackets indicate isolated yield after treatment of either **8a** or **8b** with triphenylphosphine to give respectively **1a** and **1b**. This reaction is reliably carried out in 90 ± 2% isolated conversion (see footnote 8). [c] The temperature of the oil immersion bath must not exceed 110 °C. [d] **6c**:diene. [e] Flash chromatography for this system was 4% diethyl ether–petroleum ether on silica gel. [f] Evaluated by ^1H NMR (200 MHz) in $CDCl_3$.

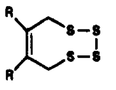
to the diene.[7] Adduct **8** has been reported in most of the instances[2e,f,h–k] where S_2 has been implicated in trapping experiments with dienes.

These cases have involved precursors **2**,[2e] **3**,[2i] **4**,[2j] **5**,[2k] **9**,[2f] and **10**.[2h] It appears particularly likely that S_2 is directly involved in the decomposition of dithiatopazine **9** as well as the bicyclic disulfide **10** (chelotropic reversion process). Further, in our hands treatment of elemental sulfur with diene **7a** in the presence of the final thermal decomposition products of **2**–**5**, **6a**–**e**, in no case gave sulfurated products.

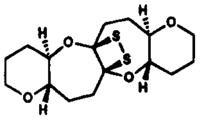
The tetrasulfides **8a** and **8b** are conveniently converted back to the disulfide in 90 ± 2% isolated yield.[8] In our 1988 paper[2e] we did not correctly identify **8a**. *We find that disulfide **1a** is slowly converted to tetrasulfide **8a** by heating in various solvents (toluene, 100 °C; C_6H_5Cl, 135–140 °C).* Evidently, **1** undergoes a cycloreversion process to diatomic sulfur and the diene. The diatomic sulfur apparently adds to **1a** giving **8a** (Scheme 4). We have also found that with the addition of 1 molar equiv of MgO for each mole of **6** used, consistent results are obtained. The reaction is sensitive to acids [9] causing loss of disulfide and the formation of more complex mixtures.[9]



1a; R = CH_3
1b; R = C_6H_5



8a; R = CH_3
8b; R = C_6H_5



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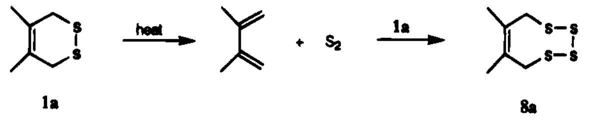
Scheme 4



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Supporting Information Available: Analytical data for compounds **6a**–**e** as well as ^{13}C and ^1H NMR spectra (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(7) S_3 transfers have been reported from different types of reagents; see ref **2g** as well as the following: Bartlett, P. D.; Ghosh, T. *J. Org. Chem.* **1987**, *52*, 4937.

(8) In cases where both **1** and **8** are formed (Table 2), we have found that treatment of the crude product mixture with triphenylphosphine quantitatively (NMR) converts **8** to **1**; for instance, for the 6th entry in Table 2, where the diene is the limiting reagent and **8a** = 49% isolated yield, we have 49% x 0.90 = 44% conversion to **1a** by triphenylphosphine. Since **1a** = 35% isolated yield, the combined isolation is 79%. Cf.: Williams, C. R.; Harpp, D. N. *Tetrahedron Lett.* **1994**, *32*, 7651.

(9) Alkoxy disulfides **6** decompose quickly in the presence of Lewis acids to sulfites, sulfinates, and elemental sulfur. Kobayashi, M.; Minato, H.; Shimada, K. *Int. J. Sulfur Chem.* **1971**, *1*, 105.