ORGANIC LETTERS

2001
Vol. 3, No. 22
3565−3568

A Novel Recyclable Sulfur Monoxide Transfer Reagent

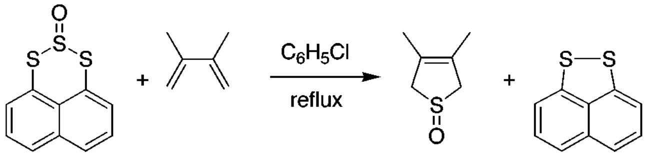
Richard S. Grainger,* Alberto Procopio, and Jonathan W. Steed[†]

Department of Chemistry, King's College London, Strand, London WC2R 2LS, U.K.

richard.grainger@kcl.ac.uk

Received August 31, 2001

ABSTRACT



Trisulfide 2-oxide 11 has been prepared from disulfide 9 via reduction to the corresponding dithiol and subsequent trapping with thionyl chloride. Heating trisulfide oxide 11 in the presence of dienes results in transfer of sulfur monoxide to form cyclic unsaturated sulfoxides 13 in good to excellent yields, along with recovery of disulfide 9. A Pummerer reaction can be used to convert the cyclic sulfoxides into thiophenes.

The search for an effective source of sulfur monoxide has proven to be a challenging problem in organic[1] and inorganic[2] chemistry. Early studies on episulfoxide **1**[3] and thiadiazepin oxide **2**[4] established that small ring sulfoxides fragment upon heating to produce alkenes and sulfur monoxide, although attempts to trap out the S═O released with dienes gave variable yields of dihydrothiophene-oxide adduct.[5] More recently, Harpp has introduced episulfoxides **3** and **4** as stable, convenient sources of sulfur monoxide.[6] Upon heating in toluene, **3** and **4** were found to transfer sulfur monoxide to four different dienes in good yields. The metal complex **5**, itself derived from **1**, has been shown to transfer sulfur monoxide to a diene in low yield,[7,8] and Simpkins has shown that rhodium-catalyzed decomposition of stilbene episulfoxide provides a means to transfer sulfur monoxide to alkenes, although this method is restricted to the highly reactive norbornene and norbornadiene.[9] A recent report by Espenson described the transfer of sulfur monoxide from sultine **6**, an intermediate in the methyltrioxorhenium-catalyzed oxidation of thioketones with 2 equiv of hydrogen peroxide.[10] Yields of trapped adduct were limited by the incompatibility of dienes and sulfur monoxide with the strongly oxidizing conditions under which the trapping experiment was carried out.

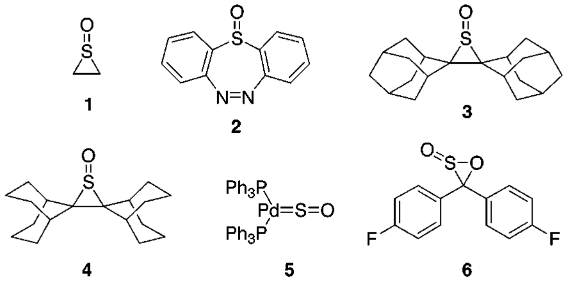


Figure 1. Molecules used to transfer sulfur monoxide to dienes.

[†] To whom correspondence regarding crystal structure should be addressed.

(1) (a) Harpp, D. N. *Phosphorus, Sulfur, Silicon* **1997**, *120/121*, 41. (b) Tardif, S. L.; Rys, A. Z.; Abrams, C. B.; Abu-Yousef, I. A.; Lesté−Lasserre, P. B. F.; Schultz, E. K. V.; Harpp, D. N. *Tetrahedron* **1997**, *53*, 12225.

(2) (a) Schenk, W. A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 98. (b) Huang, R.; Guzei, I. A.; Espenson, J. H. *Organometallics* **1999**, *18*, 5420.

(3) (a) Dodson, R. M.; Sauers, R. *J. Chem. Soc., Chem. Commun*. **1967**, 1189. (b) Dodson, R. M.; Nelson, J. P. *J. Chem. Soc., Chem. Commun*. **1969**, 1159. (c) Anastassiou, A. G.; Chao, B. Y.-H. *J. Chem. Soc., Chem. Commun*. **1971**, 979. (d) Chao, P.; Lemal, D. M. *J. Am. Chem. Soc*. **1973**, *95*, 920. (e) Lemal, D. M.; Chao, P. *J. Am. Chem. Soc*. **1973**, *95*, 922. (f) Grigg, R.; Reimer, G. J.; Wade, A. R. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1929.

(4) Chow, Y. L.; Tam, J. N. S.; Blier, J. E. *J. Chem. Soc., Chem. Commun*. **1970**, 1604. The heterocycle **2** is proposed to close to an episulfoxide prior to sulfur monoxide extrusion.

(5) For transfer of sulfur monoxide from *trans*-2,3-diphenylethene sulfoxide to ylides, see: Bonini, B. F.; Maccagnani, G.; Mazzanti, G.; Pedrini, P.; Piccinelli, P. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1721.

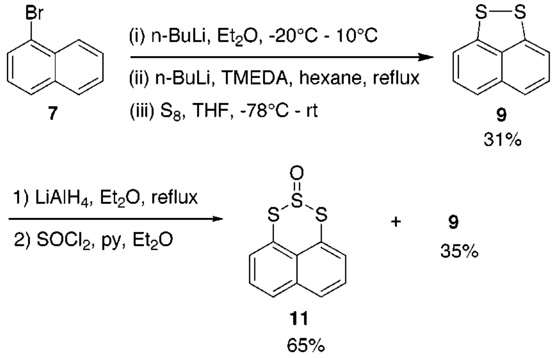
(6) Abu-Yousef, I. A.; Harpp, D. N. *J. Org. Chem.* **1997**, *62*, 8366.

10.1021/ol016678g CCC: $20.00

In searching for alternative structures that may be capable of acting as sources of sulfur monoxide, we were drawn to the unusual reactivity observed in a number of 1,8 (*peri*)-substituted naphthalene ring systems.[11] In particular, transannular interactions between two sulfur atoms in cyclic 1,8-dithiasubstituted naphthalene derivatives have been extensively studied by Glass[12] and Furukawa,[13] and in the latter case this has led to a number of unusual photochemically mediated extrusion reactions. We chose the *peri*-fused trisulfide-2-oxide **11** as our synthetic target.[14]

The synthesis of trisulfide-2-oxide **11** is shown in Scheme 1. The known disulfide **9** appeared to be an ideal precursor to **11**, despite the somewhat laborious methods previously employed in its synthesis.[15] Indeed, reduction of disulfide **9** with lithium aluminum hydride followed by reaction of the air-sensitive dithiol **(10)**[16] with thionyl chloride in the presence of pyridine provided **11** in 65% overall yield after column chromatography.[17] With our subsequent discovery that **11** does indeed act as a source of sulfur monoxide (vide infra), we developed a convenient "one-pot" synthesis disulfide **9** starting from commercially available 1-bromonaphthalene **7**. Hence, lithium−halogen exchange on **7** followed by directed deprotonation[18] and trapping of the resulting 1,8-dilithionaphthalene **(8)** with elemental sulfur[19] provided disulfide **9** in 31% overall yield. Although the yield is only moderate, this reaction allows the rapid preparation of gram quantities of disulfide **9**. The trisulfide oxide **11** is a yellow solid that can be stored refrigerated for months without decomposition.

Scheme 1. Synthesis of Trisulfide-2-oxide **11**



The X-ray crystal structure of **11** highlights a number of interesting structural features (Figure 2). A nonplanar conformation is adopted by the trithiane ring, whereby the central sulfur atom S(2) lies out of the mean least-squares plane of the naphthalene ring and *peri*-sulfur atoms by 1.1708(14) Å (torsion angles C1−S1−S2−S3, 60.1° and C8−S3−S2−S1, 64.6°, respectively). The oxygen atom occupies a pseudoaxial position on the trithiane ring, probably as a result of stabilization of this conformer through stereoelectronic effects.[20,21]

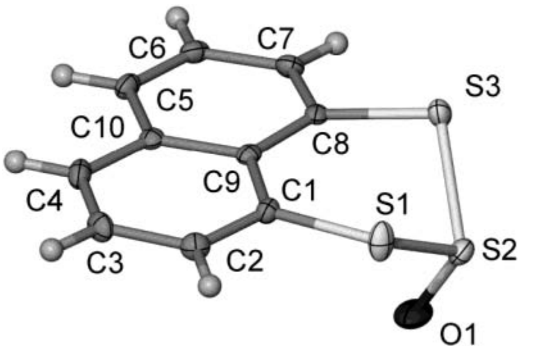


Figure 2. X-ray crystal structure of trisulfide-2-oxide **11**.

Two factors point to the strain in the system. First, the enlargement of the expected bond angles at C(1), C(9), and C(8) (125.7°, 126.6°, and 124.7°) is consistent with the minimization of steric interactions associated with the close proximity of substituents at the 1,8-positions of the naphthalene ring system.[11] Second, whereas S(1) is essentially coplanar with the naphthalene ring, S(3) lies 0.203(4) Å out of the mean least-squares plane, on the opposite side to S(2).

The thermal stability of **11** in the absence of dienes was first investigated. Upon refluxing overnight in chlorobenzene, clean conversion to disulfide **9** was observed, along with the formation of elemental sulfur.[22] Encouraged by this result, we investigated the potential of **11** to act as a source of sulfur monoxide in trapping experiments with dienes and were delighted to find that *refluxing a solution of* ***11*** *in chloro-*

---

(7) Heyke, O.; Neher, A.; Lorenz, I.-P. *Z. Anorg. Allg. Chem.* **1992**, *23*, 608.

(8) For displacement of sulfur monoxide from an iridium complex and trapping with an orthoquinone, see: Schenk, W. A.; Leissner, J. *Z. Naturforsch., B: Chem. Sci.* **1987**, *42*, 799.

(9) Blake, A. J.; Cooke, P. A.; Kendall, J. D.; Simpkins, N. S.; Westaway, S. M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 153.

(10) Huang, R.; Espenson, J. H. *J. Org. Chem.* **1999**, *64*, 6374.

(11) Balasubramaniyan, V. *Chem. Rev.* **1966**, *66*, 567.

(12) Glass, R. S.; Broeker, J. L.; Firouzabadi, H. *J. Org. Chem.* **1990**, *55*, 5739.

(13) For a review see: Furukawa, N. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2571.

(14) For a review of trisulfides and their oxides, see: Clennan, E. L.; Stensaas, K. L. *Org. Prep. Proced. Int.* **1998**, *30*, 553

(15) (a) Zweig, A.; Hoffmann, A. K. *J. Org. Chem.* **1965**, *30*, 3997. (b) Gamage, S. A.; Smith, R. A. J. *Tetrahedron* **1990**, *46*, 2111.

(16) Yui, K.; Aso, Y.; Otsubo, T.; Ogura, F. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 953.

(17) All compounds synthesized exhibited satisfactory spectral data (IR, ^{1}H and ^{13}C NMR, and MS).

(18) (a) Neugebauer, W.; Clark, T.; Schleyer, P. v. R. *Chem. Ber.* **1983**, *116*, 3283. (b) Brandsma, L. *Preparative Polar Organometallic Chemistry*; Springer-Verlag: Berlin, 1987; Vol. 1, pp 195−196.

(19) Meinwald, J.; Dauplaise, D.; Wudl, F.; Hauser, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 255.

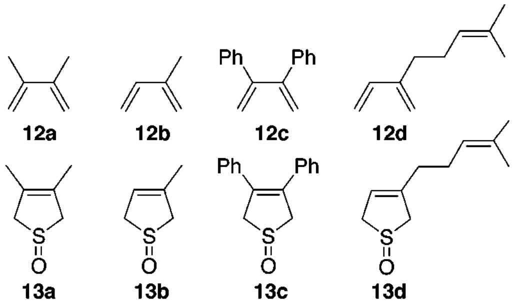
(20) Juaristi, E.; Ordoñez, M. In *Organosulfur Chemistry, Synthetic and Stereochemical Aspects*; Page, P., Ed.; Academic Press: San Diego, CA, 1998; Vol. 2, Chapter 3, pp 63−95.

(21) Pseudoaxial oxygen is also observed in other cyclic trisulfide oxide derivatives for which the X-ray crystal structures are known (all five-membered rings): (a) Ghosh, T.; Bartlett, P. D. *J. Am. Chem. Soc.* **1988**, *110*, 7499. (b) Watson, W. H.; Krawiec, M.; Ghosh, T.; Bartlett, P. D. *Acta Crystallogr.* **1992**, *C48*, 2092. (c) Kimura, T.; Hanzawa, M.; Horn, E.; Kawii, Y.; Ogawa, S.; Sato, R. *Tetrahedron Lett.* **1997**, *38*, 1607.

(22) Presumed to have formed via disproportionation of sulfur monoxide to SO_2 and S_2O, which in turn disproportionates to SO_2 and S_3, a source of S_8.

*benzene with excess 2,3-dimethyl butadiene **12a** resulted in quantitative formation of sulfoxide **13a** and disulfide **9**.*[23] The reaction of trisulfide oxide **11** with dienes **12a**−**d** is summarized in Table 1. Good yields of sulfoxide cycloadducts **13** are obtained when the reaction is run with an excess of diene (entries 1−3 and 5) or an excess of **11** (entry 7). Poorer yields are obtained when a 1:1 ratio of diene to **11** is used (compare entries 3 and 4 and 5 and 6). In all cases the disulfide **9** can be easily recovered in high yield.[24]

Table 1. Reaction of **11** with Dienes **12a**−**d**[a]

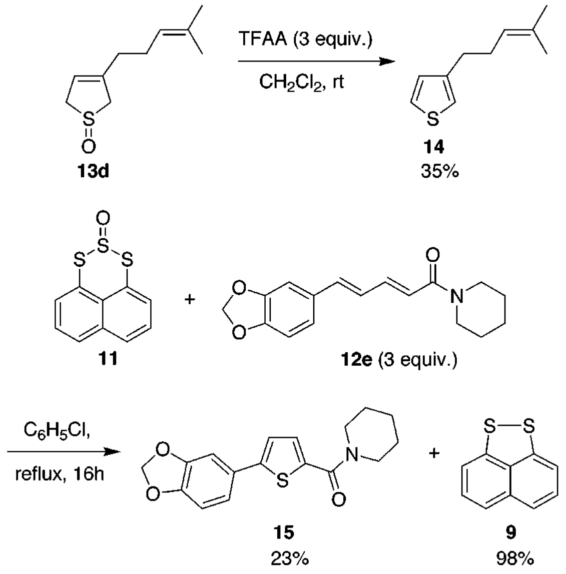


entry	diene	ratio **11**:**12**	time (h)	sulfoxide/yield[b] (%)	recovered **9**[b] (%)
1	**12a**	1:10	14	**13a**/100	99
2	**12b**	1:10	6	**13b**/74	99
3	**12c**	1:2.5	6.5	**13c**/65	100
4	**12c**	1:1	3	**13c**/50	100
5	**12d**	1:2.5	6	**13d**/93	100
6	**12d**	1:1	6	**13d**/38	100
7	**12d**	2.5:1	4.5	**13d**/84	98

[a] Chlorobenzene, reflux. [b] Isolated yield after column chromatography.

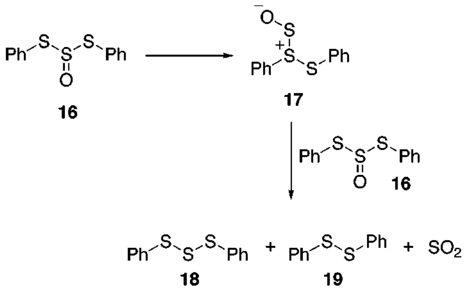
Sulfoxides **13** are potentially useful intermediates in organic synthesis. For example, dehydration of the myrcene-derived cycloadduct **13d** under Pummerer conditions[25] gave thioperillene **14**, a constituent of hop and rose oil (Scheme 2).[26] In the case of reaction of **11** with piperine **12e** the novel thiophene **15** was isolated directly from the reaction mixture.[27]

Scheme 2. Thiophene Synthesis



The thermal decomposition of *acyclic* trisulfide-2-oxides has been investigated in detail by Field and Lacefield.[28,29] In contrast to **11**, thermolysis of acyclic trisulfide-2-oxides gives rise to a mixture of trisulfide, disulfide, and sulfur dioxide (Scheme 3). Interestingly, the proposed mechanism postulates an initial rearrangement to a disulfide-sulfur monoxide adduct **17**, which rapidly reacts with a second molecule of trisulfide oxide **16**. To determine whether sulfur monoxide transfer is common to all trisulfide-2-oxides, we carried out the thermal decomposition of the phenyl derivative **16** in the presence of 2,3-dimethyl butadiene **12a** but did not observe the formation of any sulfoxide **13a**.

Scheme 3. Thermal Decomposition of Acyclic Trisulfide-2-oxides



In summary, the novel trisulfide oxide **11** has been shown to be an effective sulfur monoxide transfer reagent in trapping experiments with dienes. The overall process benefits not only from a convenient source of sulfur monoxide in thionyl chloride but also in the generation of a recyclable byproduct

---

(23) A slower reaction is observed in refluxing toluene; After 26 h a 65% yield of **13a** was obtained.

(24) **Typical Experimental Procedure.** Trisulfide oxide **11** and diene **12** were refluxed in degassed chlorobenzene until TLC analysis showed complete disappearance of **11**. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel. The nonpolar disulfide **9** eluted first (60−80 pet-ether) followed by the sulfoxide **13** upon increasing the solvent polarity (ethanol).

(25) de Lucchi, O.; Miotti, U.; Modena, G. *Org. React.* **1991**, *40*, 157.

(26) (a) Elvidge, J. A.; Jones, S. P.; Peppard, T. L. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1089. (b) Araki, S.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1446. (c) Weyerstahl, P.; Schenk, A.; Marschall, H. *Liebigs Ann. Chem.* **1995**, 1849.

(27) Thiophene **15** could be formed via in situ dehydration of a sulfur monoxide adduct (**13a**), or derived from the reaction of **12e** with other reactive sulfur species (ref 22). For trapping of dienes with S_2O, see: (a) Ishii, A.; Nakabayashi, M.; Nakayama, J. *J. Am. Chem. Soc.* **1999**, *121*, 7959. (b) Ishii, A.; Oshida, H.; Nakayama, J. *Tetrahedron Lett.* **2001**, *42*, 3117. (c) Ishii, A.; Kawai, T.; Tekura, K.; Oshida, H.; Nakayama, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1924.

(28) Field, L.; Lacefield, W. B. *J. Org. Chem.* **1966**, *31*, 3555.

(29) Flash vacuum pyrolysis (>540 °C) of 1,2,3-benzotrithiole 2-oxide results in the loss of sulfur monoxide and the formation of benzodithiete: Breitenstein, M.; Schultz, R.; Schweig, A. *J. Org. Chem.* **1982**, *47*, 1979.

in disulfide **9**. Current efforts include elucidation of the mechanism of transfer of sulfur monoxide from **11** to dienes and application of this design principle to the generation of other reactive intermediates.

Acknowledgment. We thank King's College London for funding this work (studentship to A.P.).

Supporting Information Available: X-ray data in CIF format for compound **11**. This material is available free of charge via the Internet at http://pubs.acs.org. In addition, the author has deposited X-ray coordinates with the Cambridge Crystallographic Data Center (CCDC 171805).

OL016678G