with copper(II). That this is the *only* change, with minimal change in bond angles, is consistent with the requirements for fast electron transfer, i.e., that the reorganization energy be low,[13] Similarly small geometric changes have been found between the redox-active reduced and oxidized structures of another blue copper electron transfer protein, plastocyanin,[14] and these data support the view that in both proteins the surrounding protein structure provides a copper site that is optimized for biological electron transfer. In azurin the copper ligands are tightly constrained by hydrogen bonding and van der Waals interactions, and the general region of the copper site appears the least flexible part of the molecule.[5] The principal copper ligands (one thiolate S^- and two imidazole N atoms) are a compromise between those favored by copper(I) and copper(II), and the geometry, trigonal with possible weak interactions with two axial groups, is intermediate between geometries favored by copper(I) (trigonal planar) and copper(II) (trigonal bipyramidal).

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Supplementary Material Available: Coordinates for the copper site of reduced azurin from *A. denitrificans* (2 pages). Ordering information is given on any current masthead page.

(13) Marcus, R. A.; Sutin, N. *Biochim. Biophys. Acta* **1985**, *811*, 265-322.
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Rearrangements and Stereochemistry of S_2 Additions to Olefins

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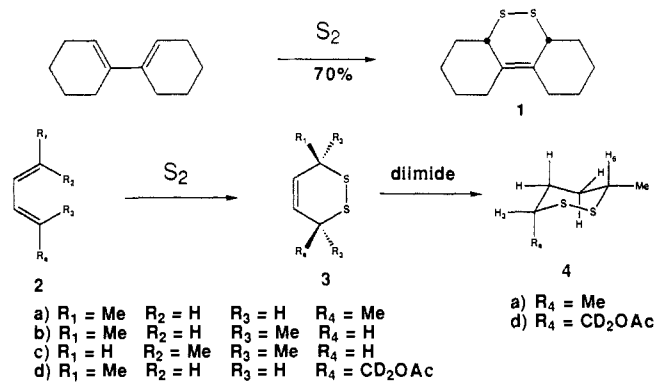
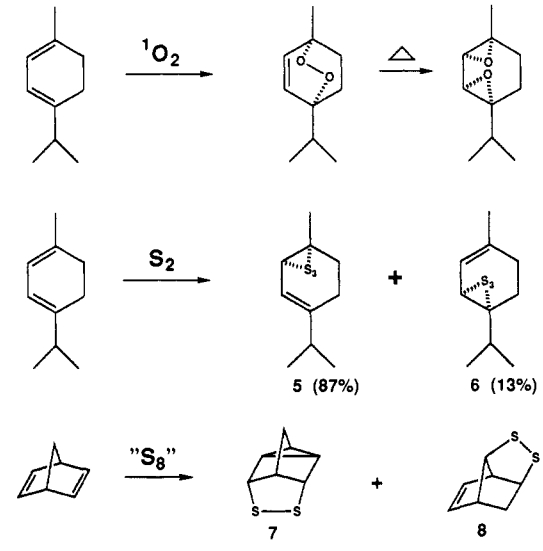
Since we first introduced S_2 chemistry in 1984,[1] several other laboratories have been stimulated to explore this new branch of organosulfur chemistry.[2] From our continuing work in this area, we can now report that the S_2 Diels-Alder type addition to acyclic 1,3-dienes occurs with stereochemical control that is consistent with the Woodward-Hoffmann rules.[3] Evidence is derived from the following expeirmental results. S_2 addition[1] to 1,1'-bicyclohexenyl (Scheme I) gives (70% yield) only the syn adduct **1** and to 2(*E*),4(*E*)-hexadiene (**2a**), the adduct **3a** (52% yield), also with 100% syn stereochemistry. The stereochemistry of **3a** was deduced from the 300-MHz ^1H NMR (CCl_2F_2) analysis of the product **4a** obtained (43% yield) from diimide[4] reduction of the double bond, using naphthosylhydrazine in refluxing diglyme. A single doublet (δ 1.34, J = 6.9 Hz) for the methyls is seen at 25 °C while at −25 °C (coalescence temperature of −10 °C, 12 kcal/mol barrier[5]) the presence of two doublets (δ 1.12 and 1.56) for the required axial, equatorial disposition of the methyls is confirmed.

Similarly, diimide reduction of the S_2-derived deuterated dithiin derivative **3d** yields (50%) only stereoisomer **4d**, in which the room-temperature 300-MHz ^1H NMR ($CDCl_3$) coupling constants (irradiation of the methyl signal at δ 1.4) for the two H_6 doublets (9.7 and 2.7 Hz) and for the two H_3 doublets (5.4 and 5.4 Hz) are consistent only with an equatorial methyl and axial acetoxy substituted deuterated methylene arrangement.[6] Although 2(*E*),4(*Z*)-hexadiene (**2b**) also affords (20%) only the syn adduct **3a** in an apparent violation of the Woodward-Hoffmann rules, a mechanism involving double-bond isomerization similar to the one proposed by O'Shea and Foote[7] (first proposed by Gollnick and Griesbeck[8]) for the analogous addition of $^1O_2$ to this diene is thought to be operative and is based on our observations from the S_2 additions to reactive olefins and cyclic 1,3-dienes described below.

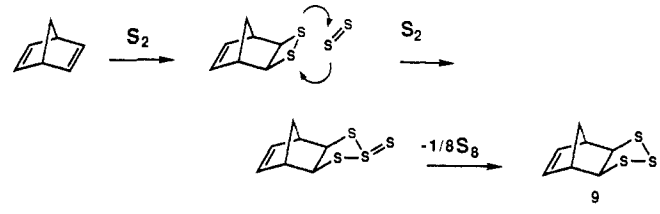
Scheme I



Scheme II



Scheme III



(1) (a) Steliou, K.; Gareau, Y.; Harpp, D. N. *J. Am. Chem. Soc.* **1984**, *106*, 799. (b) Steliou, K.; Salama, P.; Brodeur, D.; Gareau, Y. *J. Am. Chem. Soc.* **1987**, *109*, 926.
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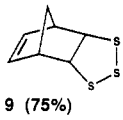
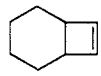
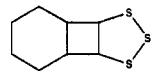
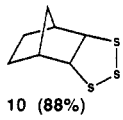
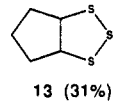
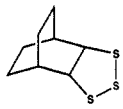
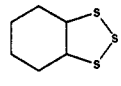
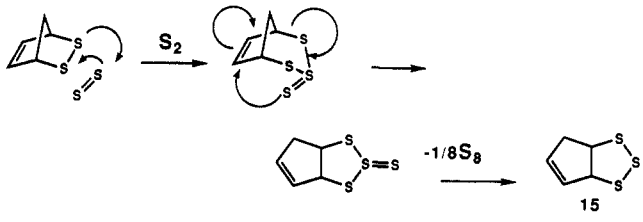
Table I. S_2 Additions to Strained Olefins

Ene	Product (% yield)	Ene	Product (% yield)
	 9 (75%)		 12 (18%)
	 10 (88%)		 13 (31%)
	 11 (15%)		 14 (0%)

Scheme IV

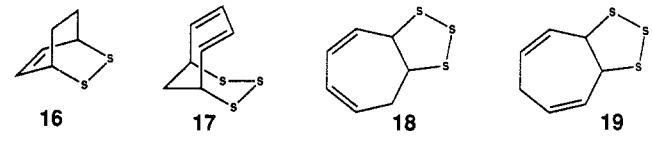


Bicyclic bridged disulfides such as gliotoxin have recently been found to be potent immunomodulating agents.[9] In principle, synthetic entry into this class of compound should be accessible via the addition of S_2 to cyclic 1,3-dienes. We have carried out this type of addition, and the ultimate products obtained, with a single exception, are not the expected bicyclic bridged disulfides but a novel class of allylic epitrisulfide (**5** and **6**, Scheme II) which was difficult to characterize and required us to exclude, by independent syntheses, episulfide formation[10] before we could disclose our findings with some certainty. The allylic epitrisulfide products formed are in striking difference to the products obtained by analogous singlet oxygen chemistry,[11] and we propose an S_2 mechanistic pathway, unavailable to $^1O_2$, to account for it.

Bartlett and Ghosh[12] have reported that norbornadiene reacts with activated elemental sulfur to give [4 + 2] type adduct **7** and its rearranged isomer **8**. We find that S_2 addition, instead, results in the exclusive formation of epitrisulfide **9**[13] (Table I) and that this type of reaction with S_2 appears to be unique to reactive olefins since unstrained olefins, like cyclohexene, are recovered unchanged.

The epitrisulfide products **9-14** (Table I) are formed as a consequence of sulfur deposition from an insertion[15] of a second mole of S_2 to the highly strained S-S bond of the corresponding dithietane precursor intermediates as shown in Scheme III. A similar insertion process followed by a [3,3] sigmatropic rearrangement (Scheme IV) is put forth to account for the allylic epitrisulfide products formed with the cyclic 1,3-dienes.

Although it may be argued that epitrisulfide **15** (Scheme IV) can be derived from cyclopentadiene via a reaction pathway analogous to that for norbornadiene (Scheme III), the [3,3] sigmatropic route is favored from the following two experimental observations. 1,3-Cyclohexadiene reacts with S_2 to give the highly volatile, crystalline Diels-Alder adduct **16** (8% yield) as the sole sulfurated product. Similarly, cycloheptatriene affords only crystalline adduct **17** (20% yield). No trace of the possible dithetane-derived adducts **18** or **19** could be noted.



16 17 18 19

Diels-Alder adduct **16**[13] is the only example of a bicyclic bridged disulfide that we have been able to prepare from S_2 additions.[16] The extreme volatility of this compound, which makes it very difficult to isolate from the reaction medium, is probably also the cause for its being protected from the subsequent and more competitive S_2 insertion into the strained S-S bond. Although the cyclopentadiene adduct should similarly be volatile, the S-S bond in this adduct is much more strained and therefore more susceptible to the S_2 insertion reaction.[15]

Acknowledgment. We thank Professor David N. Harpp for sharing with us unpublished results and for the many stimulating discussions on S_2 chemistry. We are also grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Natural Sciences and Engineering Research Council of Canada as well as the Government of the Province of Quebec for financial support.

Supplementary Material Available: Selected spectral data (^1H NMR, ^{13}C NMR, and HRMS) and selected NMR spectra (6 pages). Ordering information is given on any current masthead page.

(9) Waring, P.; Eichner, R. D.; Mullbacher, A. *Med. Res. Rev.* **1988**, *8*, 499.

(10) Allylic episulfides were synthesized via the methodology of Bombola and Ley (Bombola, M. U.; Ley, S. V. *J. Chem. Soc., Perkin Trans. I* **1979**, 3013). Spectral data are provided as supplementary material.

(11) Singlet oxygen addition to cyclic 1,3-dienes usually affords the expected bicyclic bridged peroxides. This type of peroxide can be thermally induced to rearrange into its corresponding syn bis(epoxide). See references cited in ref 1a. See also: *Singlet Oxygen Chemistry*; Wasserman, H. H., Murray, R. W., Eds.; Academic Press: New York, 1979.

(12) Bartlett, P. D.; Ghosh, T. *J. Org. Chem.* **1987**, *52*, 4937.

(13) All S_2 additions were carried out according to the procedure described in ref 1, and isolated compounds were fully characterized. Spectral data are provided as supplementary material.

(14) Fritz, H.; Weis, C. D. *Tetrahedron Lett.* **1974**, 1659.

(15) Sulfur insertion into strained sulfur-sulfur bonds is well-known. See ref 12, and also see: Murdock, K. C. *J. Med. Chem.* **1974**, *17*, 827. For sulfur deposition, see: Williams, R. C.; Chew, W.; MacDonald, J. G.; Harpp, D. N. *Tetrahedron Lett.*, submitted. Harpp, D. N. *Perspectives in the Organic Chemistry of Sulfur*; Zwanenberg, B., Klunder, A. J. H., Eds.; Elsevier: Amsterdam, 1987.

(16) Harpp and MacDonald[2a] have also prepared this compound using S_2 chemistry.

Ruthenium-Catalyzed Oxidation of Amides and Lactams with Peroxides

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The oxygenation of C-H bonds adjacent to nitrogen of amides with metal complex catalysts is of importance in view of the xenobiotic metabolism of amino compounds[2] and is one of the most attractive strategies for the synthesis of biologically active nitrogen compounds.[3] Cytochrome P-450 enzymes catalyze specific ox-

(1) (a) Osaka University. (b) Takasago Research Institute Inc.

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