

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.<sup>13</sup> Similarly small geometric changes have been found between the redox-active reduced and oxidized structures of another blue copper electron transfer protein, plastocyanin,<sup>14</sup> 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.<sup>5</sup> The principal copper ligands (one thiolate S<sup>-</sup> 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.

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## Rearrangements and Stereochemistry of S<sub>2</sub> Additions to Olefins

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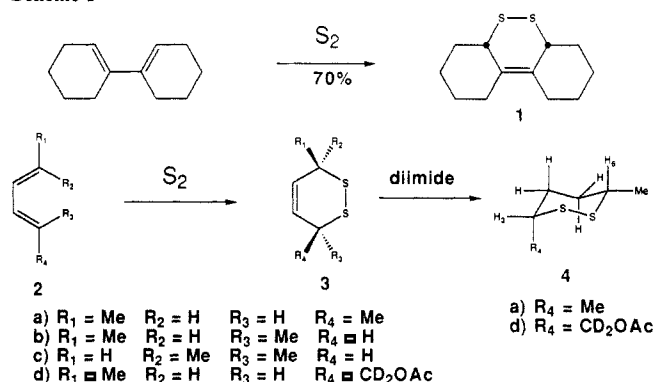
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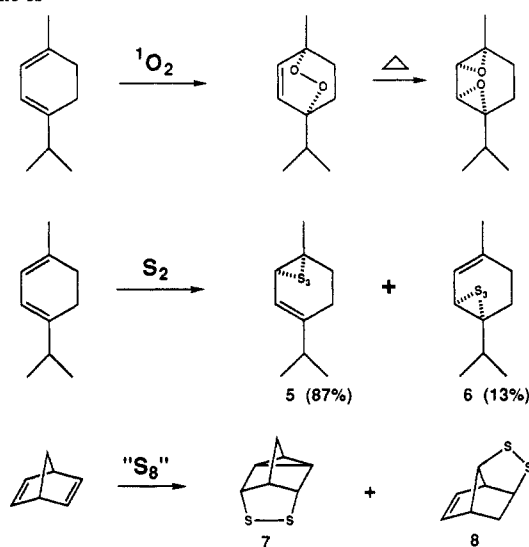
Revised Manuscript Received August 16, 1990

Since we first introduced S<sub>2</sub> chemistry in 1984,<sup>1</sup> several other laboratories have been stimulated to explore this new branch of organosulfur chemistry.<sup>2</sup> From our continuing work in this area, we can now report that the S<sub>2</sub> Diels-Alder type addition to acyclic 1,3-dienes occurs with stereochemical control that is consistent with the Woodward-Hoffmann rules.<sup>3</sup> Evidence is derived from the following experimental results. S<sub>2</sub> addition<sup>1</sup> 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 <sup>1</sup>H NMR (CCl<sub>2</sub>F<sub>2</sub>) analysis of the product **4a** obtained (43% yield) from diimide<sup>4</sup> 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

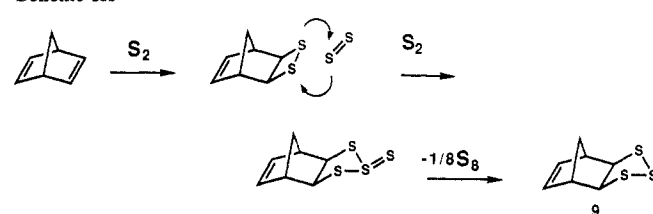
Scheme I



Scheme II



Scheme III



barrier<sup>5</sup>) 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<sub>2</sub>-derived deuterated dithiin derivative **3d** yields (50%) only stereoisomer **4d**, in which the room-temperature 300-MHz <sup>1</sup>H NMR (CDCl<sub>3</sub>) coupling constants (irradiation of the methyl signal at δ 1.4) for the two H<sub>6</sub> doublets (9.7 and 2.7 Hz) and for the two H<sub>3</sub> doublets (5.4 and 5.4 Hz) are consistent only with an equatorial methyl and axial acetoxy substituted deuterated methylene arrangement.<sup>6</sup> 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<sup>7</sup> (first proposed by Gollnick and Griesbeck<sup>8</sup>) for the analogous addition of <sup>1</sup>O<sub>2</sub> to this diene is thought to be operative and is based on our observations from the S<sub>2</sub> additions to reactive olefins and cyclic 1,3-dienes described below.

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
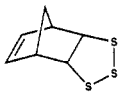

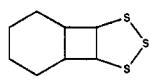

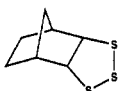

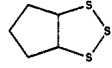

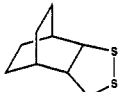

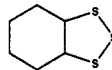
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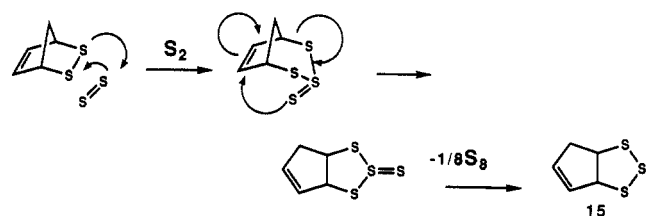
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Table I. S<sub>2</sub> Additions to Strained Olefins

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

Scheme IV



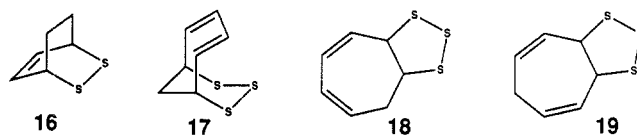
Bicyclic bridged disulfides such as gliotoxin have recently been found to be potent immunomodulating agents.<sup>9</sup> In principle, synthetic entry into this class of compound should be accessible via the addition of S<sub>2</sub> to cyclic 1,3-dienes. We have carried out this type of addition, and 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<sup>10</sup> 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,<sup>11</sup> and we propose an S<sub>2</sub> mechanistic pathway, unavailable to <sup>1</sup>O<sub>2</sub>, to account for it.

Bartlett and Ghosh<sup>12</sup> 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<sub>2</sub> addition, instead, results in the exclusive formation of epitrisulfide **9**<sup>13</sup> (Table I) and that this type of reaction with S<sub>2</sub> 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<sup>15</sup> of a second mole of S<sub>2</sub> 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 rear-

angement (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<sub>2</sub> 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 dithietane-derived adducts **18** or **19** could be noted.



Diels–Alder adduct **16**<sup>13</sup> is the only example of a bicyclic bridged disulfide that we have been able to prepare from S<sub>2</sub> additions.<sup>16</sup> 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<sub>2</sub> 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<sub>2</sub> insertion reaction.<sup>15</sup>

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**Supplementary Material Available:** Selected spectral data (<sup>1</sup>H NMR, <sup>13</sup>C NMR, and HRMS) and selected NMR spectra (6 pages). Ordering information is given on any current masthead page.

(16) Harpp and MacDonald<sup>2a</sup> have also prepared this compound using S<sub>2</sub> 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<sup>2</sup> and is one of the most attractive strategies for the synthesis of biologically active nitrogen compounds.<sup>3</sup> Cytochrome P-450 enzymes catalyze specific ox-

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