should be clarified by careful comparison of it with Cu^{II}OEP oxidized by different methods.

Further investigations with other copper porphyrins and copper chlorophyll are under way. The detailed results and discussions will be presented in a full paper.

Registry No. Cu^{II}OEP, 14409-63-3; [Cu^{II}OEP]$^{+\cdot}$, 74891-14-8.

An Unusually Facile Thioallylic Rearrangement: Stereochemical Evidence for a Free-Radical Chain Mechanism

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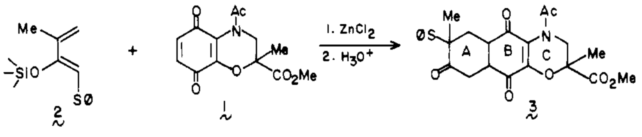
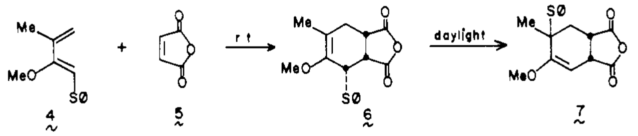
In the course of our efforts to synthesize the rubradirin antibiotics,[1] we had the occasion to study the Diels–Alder reaction of 2-alkoxy-1-phenylthio-1,3-butadienes with various dienophiles. We noticed that when the quinone **1** was reacted with 3-methyl-1-(phenylthio)-2-[(trimethylsilyl)oxy]-1,3-butadiene (**2**)[2] in the presence of zinc chloride, a facile rearrangement of sulfur apparently took place during the Diels–Alder reaction as evidenced by the appearance of the A-ring methyl group as a singlet in the ^{1}H NMR spectrum of the hydrolyzed product.[3]



To provide confirmatory evidence for this notion, we decided to investigate the reaction of the simpler dienophile maleic anhydride with 2-methoxy-3-methyl-1-phenylthio-1,3-butadiene (**4**).

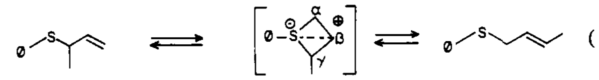


These materials reacted rapidly at room temperature to deliver the expected cycloadduct **6** in nearly quantitative yield provided the reaction flask was properly concealed from light (the flask was simply wrapped with aluminum foil). When a deuterochloroform solution of the crystalline cycloadduct (mp 95.5–96.5 °C) was allowed to stand for 1.5–2 days exposed to the laboratory lighting or ordinary daylight (an NMR tube of the sample was simply taped to the window!), a remarkably facile and essentially quantitative rearrangement took place. The same transformation could be effected thermally, but in poorer yield, by refluxing a toluene solution of **6** in the dark for several hours. The new product was clearly that of a 1,3 thio shift, for an olefinic proton was now visible at δ 4.78 (d, J = 3.6 Hz), and the methyl group appeared as a sharp singlet at higher field strength (δ 1.37). (In **6** the methyl group appeared as a broad singlet at δ 1.71.) Additionally, the doublet that appeared at δ 4.27 (J = 5.8 Hz) in the 300-MHz ^{1}H NMR spectrum of the starting material, which is ascribable to the proton on the carbon bearing the phenylthio substituent, was now absent.

The cycloadduct derived from *N*-phenylmaleimide and 3-methyl-1-(phenylthio)-2-[(trimethylsilyl)oxy]-1,3-butadiene was also observed to undergo ready thioallylic rearrangement under similar conditions. Here, however, hydrolysis of the enol silyl ether was observed to occur concurrently with the 1,3 sulfur shift, thus complicating the isolation.[4]

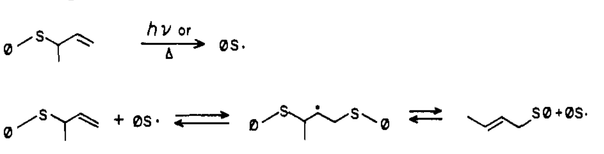
While thioallylic rearrangements are themselves certainly not uncommon, we felt that our particular example provided an excellent opportunity to investigate the stereochemical consequences of this process. To our knowledge, most thioallylic rearrangements have been studied previously in acyclic systems with no attempt having been made to ascertain their precise stereochemical characteristics.[5]

Two different proposals have been put forth regarding the mechanism of the thioallylic rearrangement reaction. Kwart has provided *conclusive* evidence for an associative mechanism when the substituent on sulfur is an electronegative phenyl group in which an intermediate is generated with the sulfur atom assuming a hypervalent state through electron donation from the allylic double bond to create a trigonal-bipyramidal (TBP or equivalent) structure (see eq 1).[6] Secondary deuterium isotope effects appear to indicate some degree of bonding between the central β-carbon atom and sulfur. Kwart has moreover suggested that "the photocatalyzed isomerization travels a path which is parallel to that of the thermal reaction".[7]



(1)

Other workers have argued that the thioallylic rearrangement reaction (both thermal and photochemical) occurs by a radical chain mechanism. The heat or light initiates the reaction by bringing about cleavage of the allyl–sulfur bond. In the next step, the phenylthio radical so produced adds to the double bond of the allyl sulfide, leading to a new radical which now loses the resident phenylthio group to generate the rearranged isomer.[5] Krusic and Kochi have, in fact, detected by ESR spectroscopy the presence of the symmetrical radical formed when dimethyl disulfide is photolyzed in the presence of allyl methyl sulfide.[8] While such a radical pathway is accessible to alkyl allyl and allyl aryl sulfides, the failure of alkyl allyl sulfides to undergo thermal thioallylic isomerization is in keeping with Kwart's proposed TBP configuration for the thioallylic intermediate (aryl is needed to stabilize the TBP).[6a] The associative mechanism does thus appear to be quite well established for the rearrangement of allyl phenyl sulfides (see eq 2).



(2)

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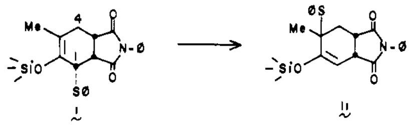
[1] Kozikowski, A. P.; Sugiyama, K.; Springer, J. *J. Org. Chem.* **1981**, *46*, 2426.

[2] The preparation and utilization of this new diene will be described separately: Kozikowski, A. P.; Huie, E. *J. Am. Chem. Soc.*, accepted for publication.

[3] Sugiyama, K., unpublished results.

[4] For the primary cycloadduct i the methyl group is present as a broad



singlet at δ 1.66 and the proton on C_1 as a doublet at δ 4.11 (J = 5.7 Hz). Upon rearrangement a new doublet for the olefinic proton appears at δ 5.08 (J = 3.7 Hz), and a sharp methyl resonance is found at δ 1.30.

[5] Brownbridge, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2125 and references cited therein.

[6] (a) Kwart, H.; Johnson, N. A. *J. Am. Chem. Soc.* **1970**, *92*, 6064. (b) Kwart, H.; Johnson, N. A. *Ibid.* **1977**, *99*, 3441. (c) Kwart, H.; Stanulonis, J. J. *Ibid.* **1976**, *98*, 4009. (d) Kwart, H.; Johnson, N. A. *J. Org. Chem.* **1977**, *42*, 2855.

[7] Kwart, H.; George, T. J. *J. Am. Chem. Soc.* **1977**, *99*, 5214.

[8] Krusic, P. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 846.

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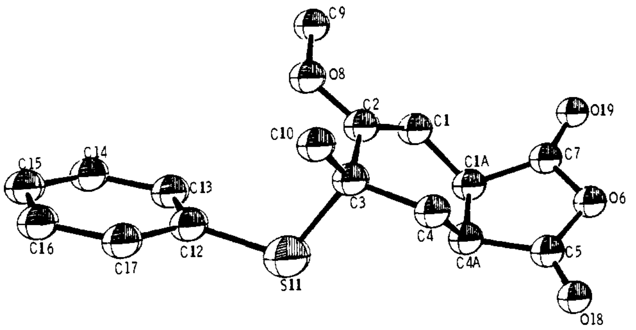
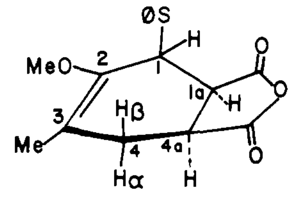


Figure 1. A perspective drawing of 7 with hydrogens omitted for clarity.

Kwart has moreover provided further evidence for his proposed thiacyclobutane intermediate by demonstrating that 4,4-dimethyl-2-cyclohexenyl phenyl sulfide fails to rearrange under the usual thioallylic isomerization conditions, a fact attributed to the strain involved in attaining the four-membered ring intermediate.[6b] Under more forcing conditions, thermal reorganization does occur, but this entails a symmetry-forbidden 1,3 migration of hydrogen rather than sulfur rearrangement. Since the rearrangement of **6** to **7** through the associative mechanism would face a similar dilemma, it became of considerable interest to see whether this exceedingly facile process did, in fact, involve a departure from the normal mechanism. As long as we carefully define the stereochemistry of the starting cycloadduct **6** and we ascertain with a high level of certainty the stereochemistry of the rearrangement product **7**, then a definitive conclusion about the mechanism of our particular class of thioallylic rearrangement reactions can be reached.

The stereochemistry of the primary cycloadduct **6** was readily ascertained by examination of its 300-MHz ^{1}H NMR coupling constants. A slightly deformed version of an extended boat conformation was apparent for this molecule.[9]

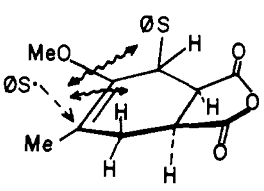


6

The H_1 proton at δ 4.27 is coupled in a gauche fashion with H_{1a} ($J_{1,1a}$ = 5.8 Hz). The ring-fusion proton H_{1a} appears at δ 3.59 as a doublet of doublets ($J_{1,1a}$ = 5.8 Hz, $J_{1a,4a}$ = 10.0 Hz). The H_{4a} proton is strongly coupled to $H_{4\alpha}$ as a consequence of their "eclipsed-like" relationship ($J_{4a,4\alpha}$ = 10.4 Hz) and only moderately coupled to $H_{4\beta}$ due to a more "gauche-like" interaction ($J_{4a,4\beta}$ = 5.8 Hz). The doublet of doublets for the $H_{4\beta}$ proton, which is strongly coupled geminally to $H_{4\alpha}$ ($J_{4\alpha,4\beta}$ = 17.5 Hz), shows some slight broadening due to interaction with the C_3 methyl group.[10] The stereochemistry of this product thus reveals that the cycloaddition reaction of **4** + **5** does adhere to the Alder endo rule.[11]

With the conformation of **6** in hand, we can now make some predictions. On the basis of the associative mechanism proposed by Kwart, rearrangement through a thiacyclobutane intermediate would require naturally that sulfur remain on the β face of the molecule during the migration process. The product should thus bear the phenylthio substituent opposite the ring-fusion hydrogens.

For the free radical chain process, however, it would seem that the incoming phenylthio group would add to the α face of **6**, opposite the bulky resident phenylthio group. Additionally, by adding to the bottom face, the thio group avoids a serious eclipsing interaction with the neighboring vicinal hydrogen.[12] These interactions, which are indicated in structure I, should presumably guarantee that the product of the free radical chain process differ from that expected for the associative mechanism.



I

To secure the structure of **7** beyond any question of a doubt, we resorted to an X-ray analysis. Crystals of **7** formed with symmetry $P2_12_12_1$ and dimensions a = 6.512 (1) Å, b = 8.332 (2) Å, and c = 27.603 (3) Å. Of the 1233 unique reflections measured with Cu radiation, 1137 were observed ($I \geq 3\sigma(I)$). The structure was solved by using direct methods and refined by using a full-matrix least-squares technique by minimizing $\sum w(|F_o| - |F_c|)^2$ with $w = 1/(F_o)^2$. The final unweighted residual was 0.057.[13] Figure 1 is a perspective drawing of **7**, while Tables I, II, and III in the supplementary material contain the final fractional coordinates, temperature parameters, bond distances, and bond angles.

Clearly, the phenylthio group has journeyed from one face of the six-membered ring to the other during its 1,3 shift, a result in line with a free radical chain mechanism. The alternate chain mechanism must thus be made more favorable for these Diels–Alder-derived allyl phenyl sulfides through the presence of the polar methoxy (or silyloxy) substituent. The associative mechanism cannot operate here for the aforementioned reasons of ring strain.

Whereas our detection of such exceedingly facile thiaallylic rearrangements may not be so exceptional, we do believe that it is exceedingly important to call attention to the possible incursion of such secondary processes when heteroatom-substituted 1-phenylthio-1,3-butadienes are employed in cycloaddition reactions. While these sulfur-substituted dienes do seem to be acquiring greater acceptance in natural-product total synthesis,[14] their proper utilization may require that in some instances the laboratory practitioner take additional precautions in achieving intended transformations.

Acknowledgment. We are indebted to the Sloan Foundation and the National Institutes of Health for partial support of this work. We thank the referees for valuable comments.

Registry No. 2, 81027-64-7; **4**, 77270-57-6; **5**, 108-31-6; **6**, 81027-65-8; **7**, 81027-66-9; i, 81027-67-0; ii, 81027-68-1; *N*-phenylmaleimide, 941-69-5.

Supplementary Material Available: Listings of atomic coordinates, temperature parameters, bond distances, and bond angles (3 pages). Ordering information is given on any current masthead page.

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[9] Very similar conclusions have been recorded for the conformation of the Diels–Alder product derived from the reaction of maleic anhydride with 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene: Danishefsky, S.; Yan, C.-F.; Singh, R. K.; Gammill, R. B.; McCurry, P. M.; Fritsch, N.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 7001. Also see: Overman, L. E.; Freerks, R. L.; Petty, C. B.; Clizbe, L. A.; Ono, R. K.; Taylor, G. F.; Jessup, P. J. *J. Am. Chem. Soc.* **1981**, *103*, 2816.

[10] Sternhell, S. *Rev. Pure Appl. Chem.* **1964**, *14*, 15.

[11] The product of the reaction of methyl vinyl ketone with (*Z*)-2-methoxy-1-phenylthio-1,3-butadiene had been shown previously to be exclusively that of endo addition: Cohen, T.; Mura, Jr., A. J.; Shull, D. W.; Fogel, E. R.; Ruffner, R. J.; Falck, J. R. *J. Org. Chem.* **1976**, *41*, 3218. Cohen, T.; Ruffner, R. J.; Shull, D. W.; Daniewski, W. M.; Ottenbrite, R. M.; Alston, P. V. *Ibid.* **1978**, *43*, 4052.

[12] Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2436. Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *Ibid.* **1981**, *103*, 2438.

[13] The following library of crystallographic programs was used: MULTAN 78, University of York, York, England, 1978; Structure Determination Package V17.0, Enraf-Nonius Corp., Delft, Holland, 1980; ORTEP-II, Oak Ridge National Laboratory, Oak Ridge, TN, 1970.

[14] For an up-to-date review on heteroatom-substituted 1,3-dienes, see: Petrzilka; M., Grayson, J. I. *Synthesis* **1981**, 753.