mediately attacked the epoxy compounds.

These data can be combined in the thermochemical cycle of Scheme I. From this the overall heats of reaction for the dimethyl and trimethyl series are −59.94 and −53.14 kcal/mol, respectively. The latter value is almost that predicted for reaction 1, but clearly substitution, solvation, and cationic effects make such good agreement partly fortuitous. In any case, the spontaneous oxygenation of the model generates more than enough energy to accomplish the base strength amplification required for the deprotonation reaction.

These data provide powerful support for the proposed mechanism of Dowd and Ham.[2] Not only is the unprecedented use of the biochemical reaction with oxygen demonstrated to be easily able to supply the large energetic demands of the base strength amplification mechanism, but the detailed thermochemical predictions which are specific to this proposal are also closely confirmed.

The mechanism of action of vitamin K represents a prime example of an energy transduction reaction in which the energy made available from oxidation is employed to effect acid–base chemistry.

Acknowledgment. We are grateful for the support from the National Science Foundation to the research efforts of E.M.A. (CHE-8821554) and P.D. (CHE-9014322).

(5) (a) Arnett, E. M.; Moriarity, T. C.; Small, L. E.; Rudolf, J. P.; Quirk, R. P. *J. Am. Chem. Soc.* **1973**, *95*, 1492. (b) Arnett, E. M.; Small, L. E. *J. Am. Chem. Soc.* **1977**, *99*, 808. (c) Arnett, E. M.; Venkatasubramaniam, K. G. *J. Org. Chem.* **1983**, *48*, 1569.

Hetero-Diels–Alder Addition of Sulfur Dioxide to 1,3-Dienes. Suprafaciality, Regioselectivity, and Stereoselectivity

Brigitte Deguin and Pierre Vogel*

Section de Chimie de l'Université, 2, rue de la Barre CH 1005 Lausanne, Switzerland

Received June 12, 1992

The cheletropic reaction $(_\omega 2_s + {_\pi}4_s)^1$ of SO_2 with 1,3-dienes to give 2,5-dihydrothiophene 1,1-dioxides (sulfolenes) has been known since 1914.[2,3] Although selenium dioxide,[4] N-sulfenyl-amines[5] (RN=S=O), and sulfines (RR′C=S=O),[6,7] which have considerable structural analogy to SO_2, readily take part in hetero-Diels–Alder additions,[8] the $[_\pi 4_s + {_\pi}2_s]$-cycloaddition of SO_2 to 1,3-dienes is a rare reaction which has been reported in only two cases. The first case involves the highly reactive diene 1, which adds to SO_2 below 20 °C to give adduct 2 reversibly.[9] In the

(1) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970; pp 152.

(2) de Bruin, G. *Proc. K. Ned. Akad. Wet.* **1914**, *17*, 585. See also: Backer, H. J.; Strating, J. *Recl. Trav. Chim. Pays-Bas* **1934**, *53*, 525.

(3) For a review, see: Turk, S. D.; Cobb, R. L. In *1,4-Cycloaddition Reactions*; Hamer, J., Ed.; Academic Press: New York, 1967; pp 13.

(4) Mock, W. L.; McCausland, J. H. *Tetrahedron Lett.* **1968**, 391.

(5) (a) Wichterle, O.; Rocek, J. *Chem. Listy* **1953**, *47*, 1768; *Collect. Czech. Chem. Commun.* **1954**, *19*, 282. Mock, W. L.; Nugent, R. M. *J. Am. Chem. Soc.* **1975**, *97*, 6521, 6526. (b) See also: Dittmer, D. C.; Hoey, M. D. In *The Chemistry of Sulphinic Acids, Esters and their Derivations*; Patai, S., Ed.; J. Wiley & Sons Ltd.: New York, 1990; Chapter 9, pp 239. (c) Bell, S. I.; Parvez, M.; Weinreb, S. M. *J. Org. Chem.* **1991**, *56*, 373.

(6) Zwanenburg, B.; Thijs, L.; Broens, J. B.; Strating, J. *Recl. Trav. Chim. Pays-Bas* **1972**, *91*, 443. Porskamp, P. A. T. W.; der Liij, M. V.; Lammerink, B. H. M.; Zwanenburg, B. *Ibid.* **1983**, *102*, 100. Porskamp, P. A. T. W.; Haltiwanger, R. C.; Zwanenburg, B. *Tetrahedron Lett.* **1983**, *24*, 2035.
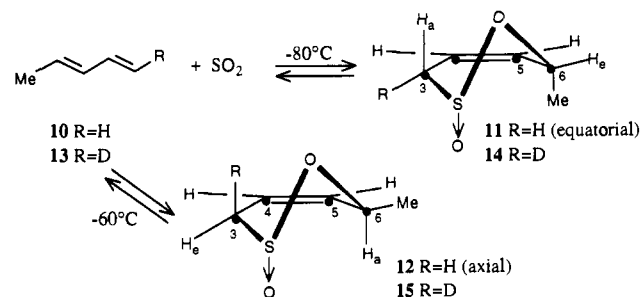
(7) See also the reaction of S_2 to 1,3-dienes: Steliou, K.; Gareau, Y.; Milot, G.; Salama, P. *J. Am. Chem. Soc.* **1990**, *112*, 7819. Gilchrist, T. L.; Wood, J. E. *J. Chem. Soc., Perkin Trans. 1* **1992**, 9.

(8) See also the reactions of sulfur dioxide bis(imides): Natsugari, H.; Whittle, R. R.; Weinreb, S. M. *J. Am. Chem. Soc.* **1984**, *106*, 7867 and references cited therein.
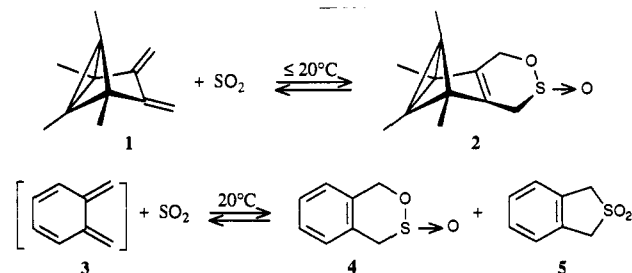
Scheme I
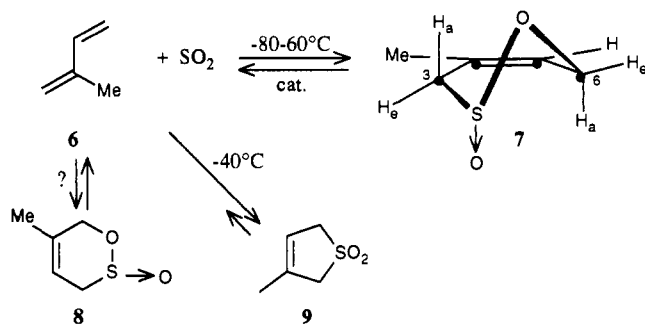
Scheme II

second case, *o*-quinodimethane (3) adds to SO_2, giving a 9:1 mixture of sultine 4 and sulfolene 5.[10]

Previous attempts to generate 3,6-dihydro-1,2-oxathiin 2-oxides (sultines) derived from penta-1,3-diene and 1-phenylbutadiene via an indirect method suggested that monocyclic sultines undergo fast cycloreversions at 0 °C.[11] On lowering of the temperature, the entropy contribution to the free energy of the equilibrium 1,3-diene + SO_2 ⇌ sultine is expected to be reduced; thus the chances of observing a sultine in equilibrium with SO_2 and the corresponding diene should increase, provided the hetero-Diels–Alder addition is not too slow and can be made to occur faster than the concurrent and more exothermic cheletropic reaction diene + SO_2 → sulfolene. We report here that such conditions have been found for simple dienes such as isoprene (6) and (*E*)-piperylene (10). We shall also show that the hetero-Diels–Alder addition of SO_2 to (*E,E*)-1-deuteriopiperylene (13) is suprafacial for the diene and that it follows the Alder (endo) rule.[12]

When a 0.2 M solution of 6 in CD_2Cl_2/SO_2, 2/3 v/v, was allowed to stand for several hours between −80 and −60 °C (5-mm sealed NMR tube), no reaction was observed. However, upon addition of 0.5–1 equiv of CF_3COOH or $BF_3\cdot Et_2O$, the sultine 7 began to form. At −60 °C, the equilibrium 6 + SO_2 ⇌ 7 was reached in ca. 6 h and an equilibrium constant $K \cong 3 \times 10^{-2}$ mol^{-1} dm^3 was evaluated (toluene as internal reference). The regioi-

(9) Heldeweg, R. F.; Hogeveen, H. *J. Am. Chem. Soc.* **1976**, *98*, 2341.

(10) Durst, T.; Têtreault-Ryan, L. *Tetrahedron Lett.* **1978**, 2353.

(11) Jung, F.; Molin, M.; Van Den Elzen, R.; Durst, T. *J. Am. Chem. Soc.* **1974**, *96*, 935.

(12) Alder, K.; Stein, G. *Angew. Chem.* **1937**, *50*, 510. Woodward, R. B.; Katz, T. J. *Tetrahedron* **1959**, *5*, 70. Hoffmann, R.; Woodward, R. B. *Acc. Chem. Res.* **1968**, *1*, 17. Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779. Ginsburg, D. *Tetrahedron* **1983**, *39*, 2095. Gleiter, R.; Böhm, M. C. *Pure Appl. Chem.* **1983**, *55*, 237. Stephenson, L. M.; Smith, D. E.; Current, S. P. *J. Org. Chem.* **1982**, *47*, 4170.

someric sultine **8** was not detected even after prolonged standing at −60 °C. At −40 °C, the sulfolene **9** was formed. The structure of **7** was deduced from its ^{1}H- and ^{13}C-NMR spectra.[13] The homoallylic coupling constants $^5J_{H,H}$ between the methylene protons at C(3) and C(6)[14] and the $^3J_{H,H}$ coupling constants between the olefinic proton at C(5) and the vicinal H_a and H_e protons at C(6) were consistent with the half-chair conformation shown in Scheme I.

When a 0.3 M solution of **10** in CD_2Cl_2/SO_2, 2/3 v/v, containing 0.2 M CF_3COOH was allowed to stand at −80 °C, the sultine **11** was formed. At −60 °C, **11** was decomposed to **10** and SO_2 and the more stable sultine **12** was generated (equilibrium constant $K \cong 4 \times 10^{-3}$ mol^{-1} dm^3 after ca. 6 h). When CF_3COOD (0.5–1 equiv) was used as the catalyst, no deuterium incorporation in either **11** or **12** was detected, thus demonstrating that the $[_\pi 4_s + _\pi 2_s]$-cycloaddition of SO_2 to **10** does not require the protonation of the diene to engender an allylic carbocation intermediate that would react with SO_2. The structures of sultines **11** and **12** (Scheme II) were elucidated from their NMR spectra.[15,16] The δ_H and δ_C values of the C(6) methylene groups[17] were consistent with the expected axial position of the S→O moiety.[18]

These results demonstrate that the hetero-Diels-Alder addition of SO_2 to **10** obeys the Alder (endo) rule as the less stable sultine **11** (with the S→O and Me groups in axial positions) is formed more rapidly than the thermodynamically more stable isomer **12** (axial S→O, equatorial Me–C(6)). When (*E,E*)-1-deuteriopiperylene (**13**)[19] was allowed to react with SO_2 under identical conditions, the sultine **14** was obtained at −80 °C, and the isomeric adduct **15** was formed at −60 °C. Less than 5% of any other isomeric compounds was detected (360-MHz ^{1}H-NMR), thus demonstrating the suprafaciality of the acid-catalyzed cycloadditions of (*E*)-piperylene to SO_2.

Under the above conditions (0.2 M CF_3COOH, CD_2Cl_2/SO_2, −80 to 50 °C), butadiene, (*Z*)-piperylene, and (*E,Z*)-hexa-2,4-diene did not give the expected sultines. The lack of an electron-releasing methyl group in butadiene makes its cycloaddition to SO_2 too slow. In the case of (*Z*)-piperylene and (*E,Z*)-hexa-2,4-diene, the acid-catalyzed hetero-Diels-Alder addition of SO_2, which is probably a concerted (nearly synchronous) process,[20] is

(13) Data of **7**: ^{1}H-NMR (360 MHz, CD_2Cl_2/SO_2, −60 °C) δ_H 5.58 (H-5), 4.48 (H-6$_a$), 4.38 (H-6$_e$), 3.42 (H-3$_a$), 2.89 (H-3$_e$), 1.66 ppm (Me), ^2J(H-6$_a$,H-6$_e$) = 16.0, ^2J(H-3$_a$,H-3$_e$) = 17.0, ^3J(H-5,H-6$_a$) = 2.5, ^3J(H-5,H-6$_e$) = 3.5, ^4J(H-5,H-3$_a$) = 2.5, ^4J(H-5,H-3$_e$) = 1, ^4J(H-5,Me) < 1, ^5J(H-3$_a$,H-6$_a$) = 4.0, ^5J(H-3$_a$,H-6$_e$) = 3.0, ^5J(H-3$_e$,H-6$_a$) = 2.5, ^5J(H-3$_e$,H-6$_e$) < 1 Hz (with irradiation of the methyl signal at δ_H = 1.66 ppm); ^{13}C-NMR (62.9 MHz, −60 °C) δ_C 121.0 (s, C$_4$), 116.0 (d, C$_5$, ^1J(C,H) ~ 170), 59.0 (t, C$_6$, ^1J(C,H) = 150), 48.0 (t, C$_3$, ^1J(C,H) = 135), 23.0 (q, CH$_3$, ^1J(C,H) = 135 Hz).

(14) Barfield, M.; Sternhell, S. J. *J. Am. Chem. Soc.* **1972**, *94*, 1905. Barfield, M.; Karplus, M. *Ibid.* **1969**, *91*, 1. Kowalewski, J. *Progr. Nucl. Magn. Reson. Spectrosc.* **1978**, *9*, 1. Mahaim, C.; Carrupt, P.-A.; Vogel, P. *Helv. Chim. Acta* **1985**, *68*, 2182.

(15) Data of **11**: ^{1}H-NMR δ_H 6.00 (H-5), 5.80 (H-4), 4.60 (H-6$_e$), 3.37 (H-3$_e$) (vanishes in **14**), 3.25 (H-3$_a$), 1.32 (Me), ^2J(H-3$_a$,H-3$_e$) = 16.5, ^3J-(H-3$_e$,H-4) = 7.0, ^3J(H-3$_a$,H-4) = 2.5, ^3J(H-5,H-6$_e$) = 2.0, ^3J(H-4,H-5) = 11.5, ^3J(H-6$_e$,Me) = 7.0, ^4J(H-3$_a$,H-5) = 2.5, ^4J(H-3$_e$,H-5) < 0.5, ^4J(H-4,H-6$_e$) = 3.0, ^5J(H-3$_a$,H-6$_e$) = 3.0, ^5J(H-3$_e$,H-6$_e$) < 0.5 Hz; ^{13}C-NMR δ_C 130 (d, C$_5$, ^1J(C,H) $\cong$ 166), 114 (d, C$_4$, ^1J(C,H) = 175), 74 (d, C$_6$, ^1J(C,H) = 150), 45 (t, C$_3$, ^1J(C,H) = 138), 22.5 (q, CH$_3$, ^1J(C,H) = 128 Hz).

(16) Data of **12**: ^{1}H-NMR δ_H 5.8 (H-5), 5.6 (H-4), 4.65 (H-6$_a$), 3.45 (H-3$_a$) (vanishes in **15**), 2.95 (H-3$_e$), 1.3 (Me), ^2J(H-3$_a$,H-3$_e$) = 17, ^3J(H-4,H-5) = 11.0, ^3J(H-3$_e$,H-4) = 5.5, ^3J(H-5,H-6$_a$) = 1.0, ^3J(H-3$_a$,H-4) = 2.0, ^4J(H-3$_a$,H-5) = 1.5, ^4J(H-3$_a$,H-5) = 2, ^5J(H-3$_a$,H-6$_a$) = 4.0, ^5J(H-3$_e$,H-6$_a$) = 2.5, ^3J(H-6$_a$,Me) = 7.0 Hz; ^{13}C-NMR δ_C 129 (d, C$_5$, ^1J(C,H) $\cong$ 166), 114 (d, C$_4$, ^1J(C,H) = 175), 65 (d, C$_6$, ^1J(C,H) = 150), 45 (t, C$_3$, ^1J(C,H) = 138), 19 (q, Me, ^1J(C,H) = 128 Hz).

(17) Buchanan, G. W.; Sharma, N. K.; de Reinach-Hirtzbach, F.; Durst, T. *Can. J. Chem.* **1977**, *55*, 44. Wood, G.; Buchanan, G. W.; Mislow, M. H. *Ibid.* **1972**, *50*, 521. Buchanan, G. W.; Stothers, J. B.; Wood, G. *Ibid.* **1973**, *51*, 3748.

(18) Juaristi, E.; Cuevas, G. *Tetrahedron* **1992**, *48*, 5019 and references cited therein.

(19) Berson, J. A.; Malherbe, R. *J. Am. Chem. Soc.* **1975**, *97*, 5910.

(20) Berson, J. A.; Dervan, P. B.; Malherbe, R.; Jenkins, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 5937. Dewar, M. J. S.; Pierini, A. B. *J. Am. Chem. Soc.* **1984**, *106*, 203. Dewar, M. J. S. *Ibid.* **1984**, *106*, 1984. Tolbert, L. M.; Ali, M. B. *Ibid.* **1984**, *106*, 3806. Houk, K. N.; Lin, Y.-T.; Brown, F.-K. *Ibid.* **1986**, *108*, 554. Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. *Ibid.* **1986**, *108*, 5571. Gajewski, J. J.; Peterson, K. B.; Kagel, J. R. *Ibid.* **1987**, *109*, 5545.

drastically retarded because the s-cis conformers of these dienes are destabilized through steric repulsions.[21]

Supplementary Material Available: NMR spectra of **7** and **11–15** (14 pages). Ordering information is given on any current masthead page.

(21) Sustmann, R.; Böhm, M.; Sauer, J. *Chem. Ber.* **1979**, *112*, 883. Scharf, H. D.; Plum, H.; Fleischbauer, J.; Schleker, W. *Ibid.* **1979**, *112*, 862.

Extraordinarily Intense Vibrational Circular Dichroism of a Metmyoglobin Cyanide Complex

Junji Teraoka,*,† Keiji Nakamura,† Yumi Nakahara,† Yoshimasa Kyogoku,‡ and Hiromu Sugeta*,‡

*Department of Chemistry, Osaka City University
Sugimoto, Osaka, Japan 558
Institute for Protein Research, Osaka University
Suita, Osaka, Japan 565*

Received April 1, 1992

Vibrational circular dichroism (VCD) has become one of the most powerful means of investigating the structures of chiral molecules in solution.[1,2] This technique has been used to elucidate the structures of polypeptides and proteins and has provided a new insight into their conformations in solution.[3,4] Marcott et al. reported that the antisymmetric stretching vibration of the azide in azidomethemoglobin A at 2025 cm^{-1} gives rise to an extraordinarily strong VCD band with an anisotropy ration, g = 0.02, of 2 orders of magnitude greater than that normally observed for VCD.[5] They suggested that the exceptionally great rotational strength may be due to the presence of the chirally arranged lone pairs of the ligated N_3. Freedman and Nafie tried to explain the great rotational strength of the azide antisymmetric stretching in a chiral environment in terms of vibrationally generated ring currents, originating from the large region of delocalizable electron density in the porphyrin ring and low-lying electronic states.[1,6] However, there is still no experimental evidence for the proposed mechanism. Therefore, we investigated the VCD spectra of azidometmyoglobin (metMbN$_3$) and a reconstituted azidometmyoglobin with an iron-octaethylporphyrin (FeOEP), metMb-(OEP)N$_3$, and a variety of ligands of metMbL (L = SCN$^-$, OCN$^-$, CN$^-$ and CO) in order to clarify the VCD enhancement mechanism of the azide ligand. New interesting observations are presented in this paper. The first is that no VCD band for the

* Authors to whom correspondence should be addressed.
† Department of Chemistry, Osaka City University.
‡ Institute for Protein Research, Osaka University.

(1) Freedman, T. B.; Nafie, L. A. In *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Eds.; John Wiley: New York, 1987; Vol. 17, pp 113–206.

(2) Keiderling, T. A. In *Practical Fourier Transform Infrared Spectroscopy*; Ferraro, J. R., Krishnan, K., Eds.; Academic Press: San Diego, 1990; pp 203–284.

(3) Yasui, S. C.; Keiderling, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 5576–5581.

(4) Pancoska, P.; Yasui, S. C.; Keiderling, T. A. *Biochemistry* **1989**, *28*, 5917–5923.

(5) Marcott, C.; Havel, H. A.; Hedland, B.; Overend, J.; Moscowitz, A. In *Optical Activity and Chiral Discrimination*; Mason, S. F., Ed.; Reidel: Dordrecht, The Netherlands, 1979; pp 289–292. Our g value of metMbN$_3$ determined by measurement of peak area is quite similar to that reported by Asher et al. (ref 8). They also mentioned that the VCD intensity of HbN$_3$ was even reduced by ca. 15% compared to the MbN$_3$. Therefore, the g value reported by Marcott et al. is somehow too large.

(6) Nafie, L. A.; Freedman, T. B. *J. Phys. Chem.* **1986**, *90*, 763–767.