that the positive Brønsted deviations for the BCA-catalyzed hydration and hydrolysis of methyl pyruvate are even more pronounced than those for the corresponding hydroxide ion catalyzed processes. Interestingly, for the hydration of methyl pyruvate, the enzymatic rate coefficient, $k_{BCA}{}^{max}$, is similar to that for the hydration of aliphatic aldehydes.[21] Indeed, for the reversible hydration reactions included in Table II, the positive Brønsted deviations are of comparable magnitude. It will be noted that for the hydrolysis of methyl pyruvate, the positive deviation of $k_{BCA}{}^{max}$ from Brønsted behavior is second only to that for the hydration of CO_2.

The hydrolysis reaction exhibits a greater sensitivity toward general-base catalysis but a smaller relative deviation of k_{OH^-} from the extrapolated Brønsted slope. The hydration reaction, on the other hand, exhibits a smaller sensitivity toward general-base catalysis but a larger relative deviation of k_{OH^-} from the extrapolated Brønsted slope. The deviation of the enzymatic coefficient, k_2/K_m, is much larger for hydrolysis than for hydration. The above observations imply that there are general-base components in the enzymatic mechanism of carbonic anhydrase. This is in accord with the fact that the vast majority of carbonic anhydrase catalyzed reactions either require proton transfer as part of the stoichiometry of the reaction (e.g., hydrolysis) or include proton-transfer steps in their most reasonable mechanistic portrayals (e.g., hydration).[28,30] Since the concentrations of hydronium or hydroxide ions are too low at neutral pH values to permit sufficiently high rates of turnover, general catalysis is almost certainly operative in many, if not all, of these reactions.

Indeed, due to the presence of zinc-bound water (or OH^-) and of a proton-transfer group (imidazole), the catalytic site of carbonic anhydrase would be expected to show, inter alia, the characteristics of a general-base and a nucleophilic catalyst. Through catalytic versatility studies,[3-12] we note that the best substrates of the enzyme prove to be compounds, the reactions of which are catalyzed by general bases and which also have at least a tendency toward nucleophilic catalysis.

Acknowledgment. Helpful discussions with Dr. Simo Sarkanen have significantly improved this paper.

Registry No. Methyl pyruvate, 600-22-6.

---

[30] Pocker, Y.; Deits, T. L.; Tanaka, N. In "Advances in Solution Chemistry"; Bertini, I., Lunazzi, L., Dei, A., Eds.; Plenum: New York, 1981; pp 253–274.

Reaction of a Benzvalene with Sulfur Dioxide. A Chemical Cascade[1]

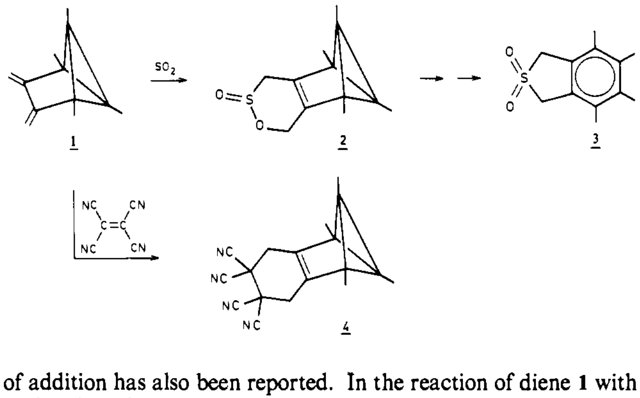
H. Hogeveen* and L. Zwart

Contribution from the Department of Organic Chemistry, University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands. *Received September 30, 1981*

Abstract: The reaction between benzvalene derivative **4** and sulfur dioxide has been investigated in the temperature range −95 to +80 °C and found to follow a cascade-type pathway. The first step in the reaction leading to dipolar ion **5** is thought to be a charge-controlled attack of SO_2 at the central bond of the bicyclobutane moiety. Rearrangement and ring closure subsequently lead to isomeric sulfones **7** and **8** and sultine **9**. The latter compound readily extrudes sulfur monoxide, affording cyclopentadiene **10**. Both the facile sulfone–sultine rearrangement and the loss of sulfur monoxide occur at exceptionally low temperatures.

Sulfur dioxide has been known as a reagent in organic chemistry for almost a century,[2] and in recent years an avalanche of research about its chemical properties has appeared in literature.[3] Most studies of organic reactions of sulfur dioxide concern its behavior toward (di)enes. Sulfur dioxide has been reported to give π complexes with alkenes,[4] and quite recently has been found to induce the "ene" reaction.[5] The cheletropic reaction of sulfur dioxide with dienes, a $(2 + 4)(n + \pi\pi)$ type of reaction, has been known for a long time,[6] and recently[7] the $(2 + 4)(\pi + \pi\pi)$ mode of addition has also been reported. In the reaction of diene **1** with sulfur dioxide, a strong interaction between the bicyclobutane moiety and the unsaturated sites in the remaining part of the skeleton probably plays a role. This interaction induces some interesting facts. For example, diene **1** reacts in Diels–Alder reactions with a rate comparable to that of cyclopentadiene.[8] On

Scheme I



---

[1] With chemical cascade we imply a reaction involving a series of observable consecutively formed isomeric products. See also ref 9.

[2] As an example: the reaction of sulfur dioxide with alkenes was reported in 1888 by W. Solonina. In 1935 Staudinger and Ritzenthaler proved the product to be a polymer. See: Staudinger, H.; Ritzenthaler, B. *Ber.* **1935**, *68*, 455 and references cited therein.

[3] Haase, V.; Heibel, B.; Kirschstein, G.; Kubny, A.; Rogler-Ditten, H. J.; Horn, H. G.; Steudel, R. "Gmelin Handbuch der Anorganischen Chemie"; Springer-Verlag: Berlin, 1980; Erg. Bd. 3 Schwefeloxide pp 70–234.

[4] Booth, D.; Dainton, F. S.; Ivin, K. J. *Trans. Faraday Soc.* **1959**, *55*, 1293.

[5] Rogić, M. M.; Masilamani, D. *J. Am. Chem. Soc.* **1977**, *99*, 5219; **1978**, *100*, 4634.

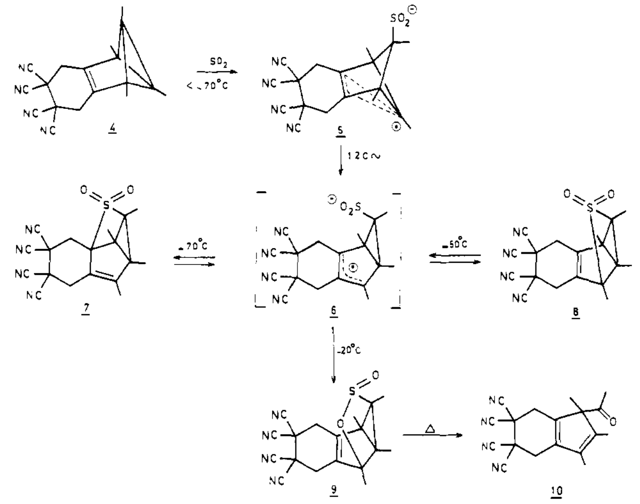
[6] de Bruin, G. *Proc. K. Ned. Akad. Wet.* **1914**, *17*, 585. See also: Turk, S. D.; Cobb, R. L. "1,4-Cycloaddition Reactions"; Hamer, Ed.; Academic Press: New York, 1976; Chapter 2.

[7] Heldeweg, R. F.; Hogeveen, H. *J. Am. Chem. Soc.* **1976**, *98*, 2341.

[8] Hogeveen, H.; Huurdeman, W. F. J.; Kok, D. M. *J. Am. Chem. Soc.* **1978**, *100*, 871.

0002-7863/82/1504-4889$01.25/0

Scheme II



reaction of sulfur dioxide[7] (Scheme I) an intermediate sultine (**2**)—the $(2 + 4)(\pi + \pi\pi)$ addition product—can be observed before rearrangement to the final product **3**.

In the present paper the reaction of sulfur dioxide with the substituted benzvalene **4** is reported. A spectroscopic study performed at various temperatures has revealed the intimate details of the reaction path, showing an example of a chemical cascade.[9] The last step is a quantitative loss of sulfur monoxide; therefore the oxidation of the organic substrate **4** and the reduction of the sulfur dioxide are the net result of the overall reaction.

At present one can only speculate whether such a reaction in generalized form

$$\text{substrate} + SO_2 \rightarrow \text{substrate·oxide} + [SO]$$

plays a role in sulfur dioxide being a serious environmental problem.[10]

Results

At −95 °C compound **4** reacted with sulfur dioxide,[11] and zwitterion **5** was formed. The reaction was followed by ^1H NMR spectroscopy (SO_2ClF solution): compound **4** slowly disappeared, and **5** was formed in at least 70% yield. Obtaining more detailed information at this temperature was hampered by the broadening of the signals in the spectrum. Warming this solution to −80 °C resulted in the formation of a precipitate. Similar precipitate formation occurred in methylene chloride, even in 0.01 M solutions. Only with sulfur dioxide (mp −72 °C) as solvent[11] was a suitable concentration for ^{13}C NMR measurements obtained. Then, at −70 °C, the presence of products **5** (50%) and **7** (20%) was observed. These compounds disappeared on warming the solution to −50 °C in favor of compounds **8** (60%) and **9** (30%). At −20 °C a conversion of **8** into **9** was observed, and at room temperature (the SO_2 solvent was replaced by methylene chloride) **8** completely disappeared in favor of **9**. This sequence of reactions is summarized in Scheme II. Compound **9** was isolated in 74% yield, and its structure was determined by X-ray analysis.[12] During the purification of sultine **9** another reaction was observed: a quantitative conversion into ketone **10** took place on warming compound **9** in solution slightly above room temperature.

Structural Assignment of Compounds 5, 7, 8, 9, and 10. The structural assignments of the low-temperature products **5**, **7**, and **8** are based largely on their ^{13}C NMR spectra. ^{13}C NMR spectroscopy offered the best information because it usually indicates most clearly whether the bicyclobutane fragment is still present or not.[13] ^1H NMR spectroscopy was informative, but signals between 1.0 and 1.6 ppm were often found to coincide at the low temperatures.

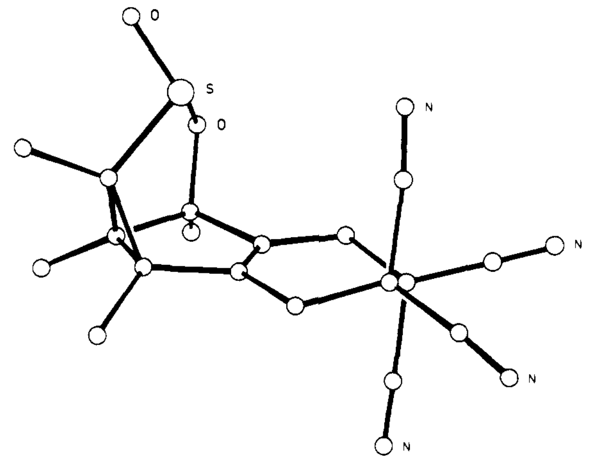
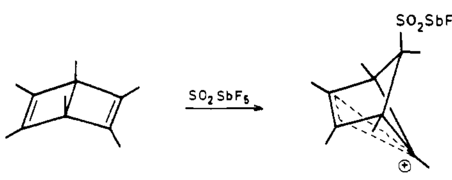


Figure 1. X-ray computer drawing of compound **9**.

The structure of the zwitterion **5** is based on a comparison of the NMR data with those of **11**:[14] ^1H NMR data of **11** 1.62, 1.74, 2.04, 2.28 ppm; ^1H NMR data of **5**: 1.40 (s, 6 H), 1.65 (s, 3 H), 2.08 (s, 3 H), 3.40 (m, 4 H) ppm. See Table I for ^{13}C NMR data. The observed symmetry and the absence of ^1H NMR signals for methyl groups at a $C{=}C$ bond (expected at ca. 2.3 ppm) indicate the position of the annulated six-membered ring.



11

The structure of sulfone **7** is based on its ^{13}C NMR absorptions (Table I). Indicative of the double-bond position exocyclic with respect to the six-membered ring (C-4/C-6) is the large difference (114.3 and 146.1 ppm) between the peaks of the sp^2 C atoms; for similar compounds, see ref 15. The chemical shifts of the signals for the heteroatom bound at C-1 and C-5 (60.9 and 83.3 ppm, respectively) show that this compound is a sulfone. In a sultine both absorptions are expected to be at approximately 15 ppm lower field (compare with **9**). The quaternary atoms C-2 and C-3 absorb at positions indicative of bridgehead positions of the bicyclo[3.1.0]hexenyl system.[16]

---

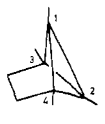
[9] Another example of a cascade reaction has been presented by: Cornelis, A.; Laszlo, P. *J. Am. Chem. Soc.* **1975**, *97*, 244.

[10] Human activities cause a yearly release of 60–80 Mton of sulfur dioxide in the atmosphere. Jaeschke, W.; Stauff, J. *Ber. Bunsenges. Phys. Chem.* **1978**, *82*, 1180.

[11] It was found that the amount of sulfur dioxide used in this reaction is not important; using 1 or 20 equiv (SO_2 used as solvent) gives the same sequence of reaction products.

[12] Kindly performed by F. van Bolhuis, Department of Chemical Physics, University of Groningen.

[13] The bicyclobutane moiety in methyl-substituted tricyclo[3.1.0.0^{2,6}]hexanes has a very regular absorption pattern in ^{13}C NMR measurements. The absorptions for C-1 and C-2 are found at high field: 17–32 ppm, the absorptions for C-3 and C-4 at 37–51 ppm. Also the methyl groups show regularity in the ^{13}C NMR chemical shift values: those at C-1 and C-2 absorb between 1.5 and 4 ppm and those at C-3 and C-4 between 4 and 9 ppm. The exceptional behavior of benzvalenes is due to strong electronic interaction between the double bond and the bicyclobutane moiety: the absorptions for the quaternary bicyclobutane atoms are shifted considerably (~30 ppm) downfield.

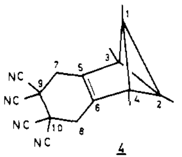
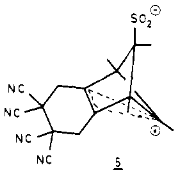
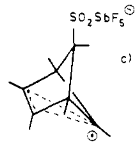
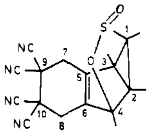
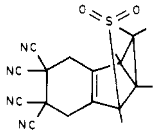
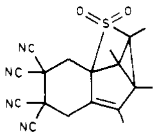


1

[14] Hogeveen, H.; Jorritsma, H.; Kwant, P. W. *Tetrahedron. Lett.* **1975**, 1795.

[15] Huurdeman, W. F. J. Ph.D. Dissertation, Groningen, 1976.

Table I. ^{13}C NMR Chemical Shifts of Compounds 4, 5, 7, 8, 9, and 11[a]

compound	CH_3	C_1	C_2	C_3	C_4	C_5	C_6	$C_{7,8}$	$C_{9,10}$	CN
 4 a)	4.4, 7.1	45.9		64.3		134.5		32.2	38.8	110.8
 5 b)	1.5 (2x), 2.2, 5.2	89.4	42.4	61.9		131.3		37.1	43.9	109.5–110.0
 11 c)	0.3, 5.9 (2x), 9.6 (2x), 20.6	81.0	41.3	66.9		124.2				
 9 d)	6.8, 7.5, 9.4, 17.5	73.4	45.3/47.2		99.3	131.6/133.8		29.4, 31.3	39.8, 39.9	110.5–112
 8 e)	1.4, 2.1, 5.3, 7.6	61.3	44.6/45.6		89.4	126.4/133.4		28.0, 29.2	37.1, 37.1	108–110
 7 f)	6.7, 8.2, 10.4, 14.2	60.9	42.4/46.1		114.3	83.3	146.1	25.2, 28.3	37.8, 38.2	108–110

[a] (a) In $CDCl_3$ at room temperature; (b) in SO_2 at -70 °C; (c) in SO_2 at -70 °C, ref 14; (d) in acetone-d_6 at room temperature; (e) in SO_2 at -20 °C; (f) in SO_2 at -70 °C.

Compound **8**, which can be isolated as a solid by addition of pentane to the reaction mixture at –50 °C, shows infrared absorptions at 1160 and 1310 cm^{-1}, indicative of a sulfone group. In the ^{13}C NMR spectrum absorptions due to two quaternary sp^2-hybridized C atoms are observed; according to the ^1H NMR spectrum the carbon–carbon double bond is not methyl substituted. The positions of the quaternary C-2 and C-3 absorptions are indicative of the bicyclo[3.1.0]hexenyl system.

The structure of compound **9** is elucidated unambiguously by an X-ray analysis[12] (Figure 1). The spectral data also show the presence of the sultine group (IR and ^{13}C NMR) and the bicyclo[3.1.0]hexenyl system (^{13}C NMR).

Compound **10** shows an infrared absorption at 1720 cm^{-1} and gives a positive haloform test (acyl group). Comparison of the NMR spectral data with those of the permethylated parent compound[17] confirms the structure.

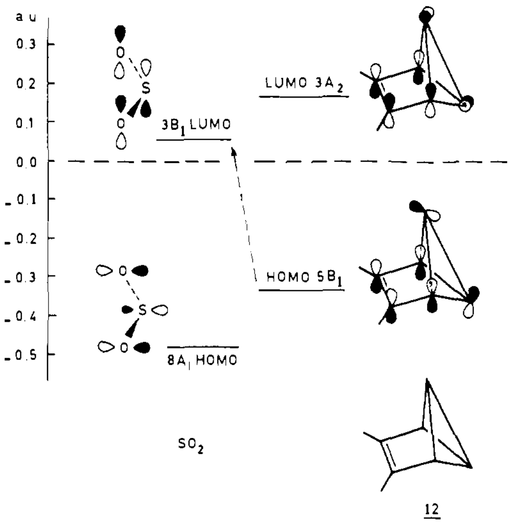


Figure 2. Orbital representation of SO_2 and model compound **12**.

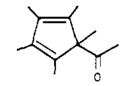
Mechanistic Aspects of the Reaction of Benzvalene Derivative 4 with Sulfur Dioxide

The Intial Attack. Quantum Mechanical Considerations. The formation of the initial zwitterion **5** in the reaction between **4** and sulfur dioxide implies attack by sulfur dioxide at the bicyclobutane functionality rather than at the double bond. To obtain more

---

(16) The ^{13}C NMR absorptions of the quaternary bridgehead atoms in bicyclo[3.1.0]hexanes are usually found between 40 and 50 ppm (excluding heteroatom effects).

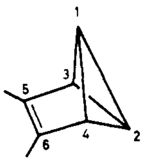
(17) Spectral data for the permethylated parent compound II are as fol-



11

lows: ^1H NMR 1.07 (s, 3 H), 1.54 (s, 3 H), 1.65 (s, 6 H), 1.80 (s, 6 H), ppm; ^{13}C NMR 9.8 (CH_3, 2x), 11.0 (CH_3, 2x), 14.2 (CH_3), 22.3 (CH_3), 71.1 (C), 136.7 (sp^2 C, 2x), 139.1 (sp^2 C, 2x), 207.7 (C=O) ppm.

Table II. Electron Distribution and $5B_1$ Orbital Coefficients of Compound **12**[20]



12

atoms	electron excess	coeff of $5B_1$
1 + 2	0.38	0.52
3 + 4	0.58	0.15
5 + 6	0.08	1.10

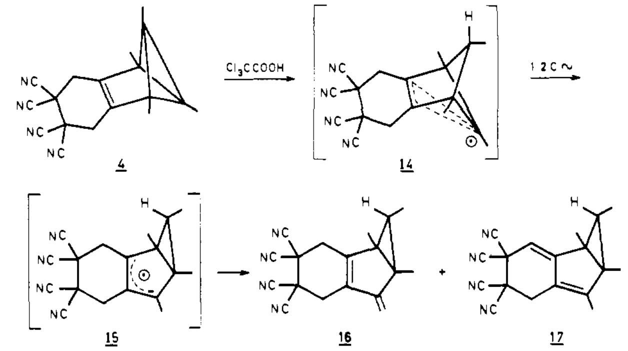
insight into why this is the preferred pathway we have considered the frontier orbital interactions.[18] The energies and symmetries of the HOMO and LUMO orbitals of sulfur dioxide[19] and of model compound **12**[20] are depicted in Figure 2. An important mechanistic feature that has to be dealt with is the concerted or stepwise character of the reaction. For a concerted process to occur, a more or less synchronous interaction between the occupied bonding orbitals (HOMO's) with the empty antibonding orbitals (LUMO's) has to take place. Because of the symmetry-imposed barriers,[21,22] bonding orbitals can only mix with antibonding orbitals of the same symmetry. Figure 2 shows that one interaction ($3B_1$–$5B_1$) is allowed. The other interaction ($8A_1$–$3A_2$) is not allowed; moreover, the large energy difference (405 kcal/mol) between these orbitals makes interaction less likely.

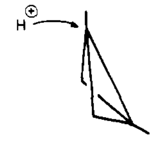
Thus a concerted cycloaddition of sulfur dioxide to the central bond of the bicyclobutane moiety or to the carbon–carbon double bond is not the expected process of the initial addition step. More likely is a reaction in which sulfur dioxide reacts as a Lewis acid in a donor–acceptor-type, stepwise process. In this case we can distinguish two kinds of reaction types: a charge-controlled reaction and an orbital-controlled reaction. Klopman[23] has argued that if an energy gap exists between the interacting orbitals (here, of course, $3B_1$ and $5B_1$), the reaction will be charge controlled. In case of model compound **12** and sulfur dioxide (Figure 2), the energy difference amounts to 167 kcal/mol, and as a consequence a charge-controlled process seems most likely. In such a case the nature of the product is determined by the interaction between the donor center carrying the highest electronic density and the acceptor with the lowest electronic density.

Calculations on model compound **12**[24] performed by van Duijnen and van der Ploeg[20] reveal this molecule to carry highest electron density at the bicyclobutane part whereas the $5B_1$ orbital has the highest coefficient on the double bond (Table II).

Calculations on sulfur dioxide[19] indicate the sulfur atom to be positively charged (electron excess −1.133). In fact, according to these data the sulfur atom should react at C-3/C-4, but in the actual compound **4** this is probably prevented by the methyl substituents (also the very small coefficient at C-3/C-4 probably plays a role). A theoretical study of Lehn and Wipff[25] confirms that proton attack of 1,3-dimethylbicyclobutane should occur at the back side of the central bond, which has extremely high p character.[26] This is depicted in **13**, corresponding to attack at the 1,2 position of **12**.

Scheme III



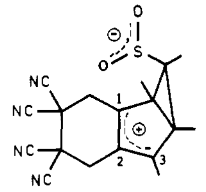


13

According to Klopman,[23] protons are suitable acceptors for a charge-controlled process, and, indeed, the results obtained on reaction of **4** with trichloroacetic acid[27] can be explained in the same way[28] (Scheme III).

To conclude, the formation of **5** is thought to be the result of a charge-controlled attack of sulfur dioxide at the back side of the central bond of the bicyclobutane moiety in **4**.

Formation of Sulfones 7 and 8 and Sultine 9. The products formed after the initial attack of sulfur dioxide on **4** are derived from the bicyclo[3.1.0]hexenyl intermediate **6**. This zwitterionic particle—which has not been observed—is probably formed from **5** by means of a 1,2-carbon shift (Scheme II). Ring closure of **6** can lead to several isomeric structures, due to the ambient character of both the anionic and the cationic part.



6

Three of the possible isomers have indeed been observed: compounds **7**, **8**, and **9**. The disappearance of **7** and **8** on warming the mixture above −70 °C shows the reactions **6** → **7** and **6** → **8** to be reversible. Sulfone **8** is thermodynamically more stable than the isomeric sulfone **7**, due to the carbon–carbon double bond being more stable if incorporated in two rings (as in **8**) as compared to one ring (as in **7**). Both sulfones rearrange above −20 °C to sultine **9**. The kinetic preference for sulfone formation at low temperatures can be explained by the HSAB principle: the soft S rather than the hard O of the RSO_2^- group reacts with the soft allylic cationic centers.[29] At higher temperatures the larger ring strain in the sulfones (four-membered ring) as compared to

---

[18] See, e.g.: Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976.

[19] Huzinaga, S.; Yoshimine, M. *J. Chem. Phys.* **1978**, *68*, 4486.

[20] We are greatly indebted to P. van der Ploeg for providing detailed information: van Duijnen, P. Th.; van der Ploeg, P.; Hogeveen, H.; Huurdeman, W. F. J. *Tetrahedron Lett.* **1975**, *573*. See also ref 8 (the numbering **5**, **6**, **7**, and **8** in Figure 3 of this reference has to be replaced by **8**, **7**, **5**, and **6**, respectively).

[21] Pearson, R. G. "Symmetry Rules for Chemical Reactions: Orbital Topology and Elementary Processes"; Wiley: New York, 1976.

[22] Jorgensen, W. L.; Salem, L. "The Organic Chemist's Book of Orbitals"; Academic Press: New York, 1973.

[23] Klopman, G. "Chemical Reactivity and Reaction Paths"; Wiley: New York, 1974; pp 59–67.

[24] For the present discussion it is unfortunate that no quantum-mechanical calculations are available for the permethylated benzvalene, because a compound with four methyl groups on the bicyclobutane moiety would have been a much better model for comparison with compound **4**.

[25] Lehn, J. M.; Wipff, G. *J. Chem. Soc., Chem. Commun.* **1973**, 747.

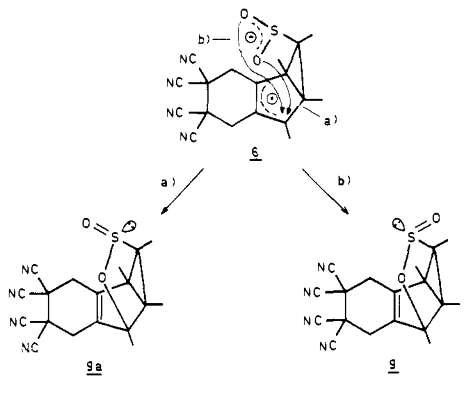
[26] Calculations indicate the central bond of the bicyclobutane functionality to be sp[24]; Newton, M. D.; Schulmann, J. M. *J. Am. Chem. Soc.* **1972**, *94*, 767.

[27] Hogeveen, H.; Huurdeman, W. F. J. *J. Am. Chem. Soc.* **1978**, *100*, 860.

[28] Because compound **14** is not observed, an alternative mechanism involving attack at the edge bond to form **15** directly cannot be excluded.

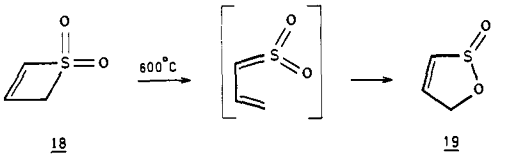
[29] In relation to the general perturbation theory, one might say that attack via S is orbital controlled and via O is charge controlled (ref 26, pp 67–72).

Scheme IV



the sultine (five-membered ring) makes the latter thermodynamically more favorable.

The rearrangement of a sulfone (**8**) into a sultine (**9**) is a rarely encountered process[30] and has been observed so far only at elevated (≳400 °C) temperatures, e.g.:[31]

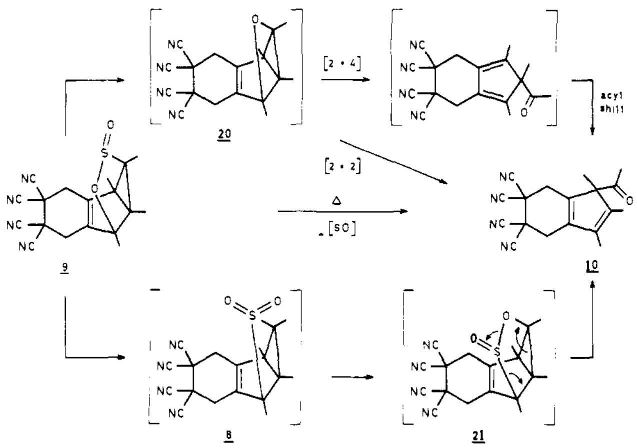


The conversion **18** → **19** has been rationalized in terms of a mechanism involving a sulfene intermediate that is formed and reacts in a concerted manner, with the release of ring strain providing the driving force.[31] We do not suppose the conversion **8** → **9** occurs via such a sulfene intermediate but prefer to propose a mechanism via **6**. The fact that no methanol adduct is formed[32] on carrying out the reaction in methanol solution can be reconciled with the intermediacy of **6** when the intramolecular ring-closure reaction **6** → **9** is assumed to be fast in comparison with the intermolecular trapping reaction involving methanol.[32]

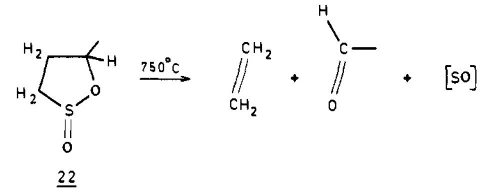
Ring closure **6** → **9** can in principle lead to two stereoisomeric products, depending on the S=O position. The X-ray data (Figure 1) have shown that only the stereoisomer **9** is formed. If in intermediate **6** a maximal Coulombic interaction between the positive and negative charges would have determined the stereochemistry of the sultine, then reaction via path a leading to the isomer **9a** would have been more likely (Scheme IV). It seems therefore that other factors determine the stereochemical outcome of the reaction product. A likely factor could be a stereoelectronic repulsion in **9a** between the double-bonded O atom and the axial CN group on the six-membered ring (Figure 1).

Sulfur Monoxide Extrusion from Sultine 9. During the purification of sultine **9**, we observed a quantitative conversion of **9** to ketone **10** on slightly warming a solution of compound **9** (see Scheme V). The mechanism of this reaction is not yet established but will most likely involve a rupture of the original C–O bond in **9**. In Scheme V two possible routes are depicted. The first possibility involves the intermediate oxetane **20**, which via a thermal (2 + 2) cycloreversion,[33] or via a thermal (2 + 4) cycloreversion followed by an acyl shift,[34,35] would yield **10**.

Scheme V



The second possibility involves rearrangement of the SO_2 functionality leading to **21** (possibly via **8**) followed by an extrusion reminiscent to the reaction found on thermolysis of **22**.[36]



We have tried to extrude sulfur monoxide photolytically from **9** in order to observe an intermediate product at room temperature. However, neither sulfur monoxide nor sulfur dioxide extrusion occurred, and **9** was recovered quantitatively after 6 h of irradiation. During the thermal conversion **9** → **10**, we did not observe any ESR signals due to possible radical intermediates or any CIDNP signals (in NMR). The rate of reaction depended slightly on solvent polarity, with the half-lives of **9** being 8, 90, and 65 min in dimethyl sulfoxide (80 °C), acetonitrile (70 °C), and methanol (65 °C), respectively. As a tentative conclusion one might say that reaction **9** → **10** probably does not involve ionic intermediates.

Evidence for the formation of sulfur monoxide was obtained by performing the reaction **9** → **10** in the presence of pyridine *N*-oxide, which afforded pyridine (60%) and sulfur dioxide. This reaction constitutes, according to Maccagnani and co-workers,[37] evidence for the presence of sulfur monoxide. In a reaction of compound **9** with diene **1** in dimethyl sulfoxide solution product **3** was the only sulfur-containing compound formed. Apparently sulfur monoxide abstracts an oxygen atom from dimethyl sulfoxide

---

[30] The reverse reaction—the rearrangement of sultines or sulfinates to sulfones—is a fairly common process; e.g.: Kenyon, J.; Phillips, H. *J. Chem. Soc.* **1930**, 1676. Darwish, D.; McLaren, R. *Tetrahedron Lett.* **1962**, 1231.

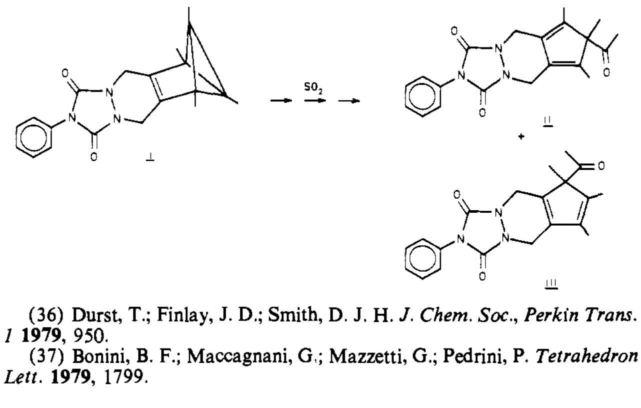
[31] King, J. F.; de Mayo, P.; McIntosh, C. L.; Piers, K.; Smith, D. J. H. *Can. J. Chem.* **1970**, *48*, 3703.

[32] Zwitterionic intermediates can usually be intercepted by methanol (Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 117, 199); however, exceptions to trapping ionic intermediates are known; see, e.g.: Paquette, L. A.; Ward, J. S.; Boggs, R. A.; Farnham, W. B. *J. Am. Chem. Soc.* **1975**, *97*, 1101. Paquette, L. A.; Beckley, R. S.; Farnham, W. B. *Ibid.* **1975**, *97*, 1089.

[33] The thermal (2 + 2) cycloreversion of oxetanes is known to proceed at temperatures above ~400 °C; e.g.: Carless, H. A. J. *Tetrahedron Lett.* **1974**, 3425. Clarke, M. J.; Holbrook, K. A. *J. Chem. Soc., Faraday Trans. 1* **1977**, *73*, 890.

[34] Franck-Neuman, M.; Buchecker, C. *Tetrahedron Lett.* **1972**, 937. Martin, M.; Regitz, M. J. L. *Liebigs Ann. Chem.* **1974**, 1702.

[35] A point in favor of this mechanism over one involving a (2 + 2) cycloreversion is found in the reaction of benzvalene i with SO_2, leading ultimately to a mixture of ketones ii and iii (preliminary results obtained by Dr. W. F. J. Huurdeman).



[36] Durst, T.; Finlay, J. D.; Smith, D. J. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 950.

[37] Bonini, B. F.; Maccagnani, G.; Mazzetti, G.; Pedrini, P. *Tetrahedron Lett.* **1979**, 1799.

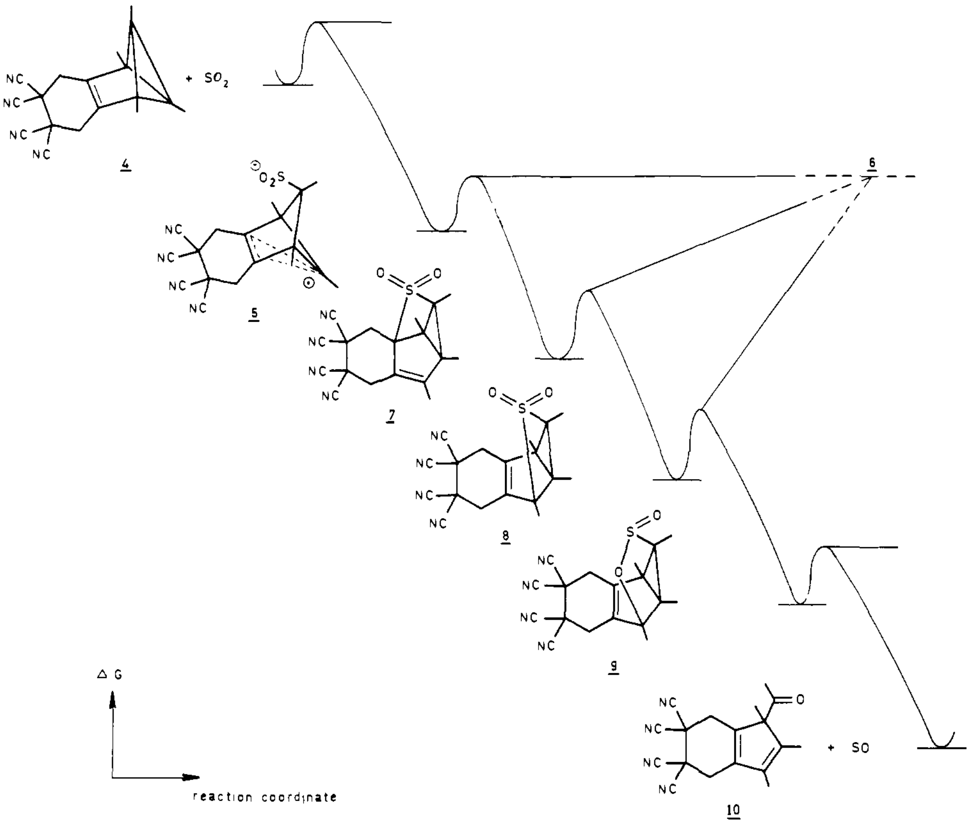
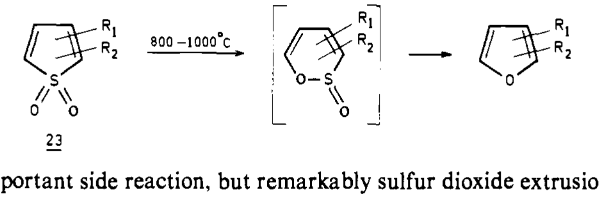
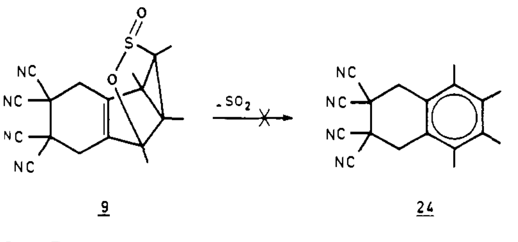


Figure 3. Schematic free-enthalpy diagram for the cascade reaction between 4 and SO_2.

faster than it reacts with the reactive diene **1**; the sulfur dioxide formed reacts with diene **1** to afford sulfone **3**. Usually sulfur monoxide reacts with dienes to yield 2,5-dihydrothiophene 1-oxides.[38]

The extrusion of sulfur monoxide from sultines is rarely encountered. In the pyrolysis (temperatures between 600 and 1000 °C) of sulfones proceeding with loss of sulfur monoxide, a mechanism via sultines is proposed. The work of van Tilborg and Plomp,[39] who pyrolyzed a series of substituted 1,1-dioxythiophenes (**23**), is illustrative. Usually extrusion of sulfur dioxide is an important side reaction, but remarkably sulfur dioxide extrusion from compound **9** to yield the aromatic product **24** has not been observed.





Concluding Remarks

The reaction between **4** and sulfur dioxide has been shown to follow a cascade-like pathway, which is shown schematically in a free-enthalpy diagram (Figure 3). Each of the structures shown is detectable and/or isolable (except **6**). The first step in the overall reaction has been deduced to be a charge-controlled attack at the central bond of the bicyclobutane fragment of benzvalene **4**, giving **5**. Thermodynamic and kinetic factors have been shown to play a role in the reversible conversions of the tetracyclic derivatives **7**, **8**, and **9**. Especially, the facile sulfone–sultine rearrangement (**8** → **9**) constitutes a rarity in organic chemistry. The same exceptional behavior is observed in the last step (**9** → **10**), in which sulfur monoxide is extruded at about 60 °C, which is extraordinary for sultines.

Experimental Section

General Remarks. Melting points (uncorrected) were determined on a Reichert apparatus by the Kofler method or in a silicon oil bath. Elemental analyses were performed in the analytical section of our department. Mass spectra were obtained on an AEI MS-902 spectrometer. Infrared spectra were recorded on a Unicam SP200 spectrometer (liquids and oils neat, solids in Nujol). Proton magnetic resonance (^{1}H NMR) spectra were recorded on a 60-MHz Hitachi, Perkin-Elmer, or a JEOL C-60 HL spectrometer. Carbon 13 magnetic resonance (^{13}C NMR) spectra were recorded on a 100-MHz Varian XL-100 spectrometer. Low-temperature ^{13}C NMR spectra were recorded on a Bruker HX 360 spectrometer by K. Dijkstra. The chemical shifts are given in ppm downfield from internal tetramethylsilane, and unless otherwise stated deuteriochloroform ($CDCl_3$) was used as solvent. Splitting patterns are designated as follows: in ^{1}H NMR, s for singlet, d for doublet, t for triplet, q for quartet, and m for multiplet; in ^{13}C NMR, the indication C, CH, CH_2, CH_3 indicates the number of coupling protons in the coupled spectrum. Sulfur dioxide was dried over phosphorus pentoxide (siccapent) before use.

Reaction of Benzvalene 4 with Sulfur Dioxide in SO_2ClF at −95 °C. A ^{1}H NMR tube containing 20 mg of **4** was cooled to −120 °C. SO_2ClF (0.3 mL) (containing approximately 10% SO_2) was introduced into the tube under a nitrogen atmosphere. The sample was warmed to −95 °C in the ^{1}H NMR cavity; compound **4** reacted slowly, and ion **5** was formed. Integration of the ^{1}H NMR spectrum (signal at 2.08 ppm compared to the other signals) showed at least 70% conversion of **4** into **5**. The spectral data for **5** are reported below.

Reaction of Benzvalene 4 with Sulfur Dioxide from −70 to −20 °C. A NMR tube containing an appropriate amount of **4** (20 mg) was cooled to −120 °C. Under a nitrogen atmosphere 0.3 mL of sulfur dioxide, which solidified at once, was introduced into the tube. In the (^{1}H and ^{13}C) NMR cavity the sample was warmed to its melting point (ca. −75

---

[38] Chao, P.; Lemal, D. M. *J. Am. Chem. Soc.* **1973**, *95*, 920, 922.

[39] van Tilborg, W. J. M.; Plomp, R. *Recl. Trav. Chim. Pays-Bas* **1977**, *46*, 282.

°C) and measured at once. The starting material had completely disappeared; the mixture consisted of 50% of the symmetric ion **5** and 20% of compound **7** (and contained further small quantities of compounds **8** and **9**) according to the spectra.

Spectroscopic data for ion **5**: ^{1}H NMR (SO_2) 1.40 (s, 6 H), 1.65 (s, 3 H), 2.08 (s, 3 H), 3.40 (m, 4 H) ppm. See Table I for ^{13}C NMR data.

The ^{1}H NMR (SO_2) absorptions of **7** (partly coinciding with those for **8** and **9**) are found at 1.30 (s, 3 H), 1.32 (s, 3 H), 1.55 (s, 3 H), and 1.58 (s, 3 H) ppm. See Table I for ^{13}C NMR data.

On further warming of the sample to −50 °C, compounds **5** and **7** readily disappeared, and compounds **8** (60%) and **9** (30%) were formed. Spectroscopic data for **8**: ^{1}H NMR (SO_2) 1.28 (s, 3 H), 1.33 (s, 6 H), 1.48 (s, 3 H), 2.56 (d, J = 15 Hz, 1 H), 3.07 and 3.35 (AB q, J_{AB} = 3 Hz, 2 H), 3.61 (d, J = 15 Hz, 1 H) ppm. See Table I for ^{13}C NMR data; additional data for **8** are reported below.

Further warming of the sample to −20 °C gave a slow conversion of **8** into **9**. The spectroscopic data for **9** are reported below; the ^{13}C NMR data in sulfur dioxide as compared to those in acetone-d_6 are all shifted slightly (2–3 ppm) upfield.

Isolation of Sulfone 8. A solution of 1.00 g (3.5 mmol) of compound **4** in 20 mL of methylene chloride was cooled to −80 °C. Under a nitrogen atmosphere, sulfur dioxide was bubbled through the stirred solution for 20 min. After warming to −60 °C, 40 mL of pentane was added, and a precipitate was formed. The solution was stirred for 20 min and allowed to warm to −40 °C, after which the solid was filtered on a glass-sintered funnel (under nitrogen). The product (800 mg, 2.3 mmol, 65%) **8** was obtained as a white solid, which was not completely pure because it contained ~10% **9**, mp 124–130 °C dec: IR 1160 and 1310 cm^{-1} (sulfone), 2300 cm^{-1} ($C{\equiv}N$); MS, parent peak at m/e 352, 100% peak at 304 (352 − SO); exact mass (−SO) m/e 304.135; calcd for $C_{18}H_{16}N_4O$ 304.132.[40] Compound **8** is hardly soluble in the common organic solvents. In a deuteriochloroform/dimethyl-d_6 sulfoxide mixture, the conversion **8** → **9** was followed by ^{1}H NMR spectroscopy. Due to solvent-induced shifts the ^{1}H NMR is slightly changed compared to that in sulfur dioxide solution (see above), and the methyl groups are all observed separately (at 1.18, 1.27, 1.42, and 1.49 ppm).

Compound **8** is stable as a solid at −20 °C for at least 1 month. On stirring suspensions of **8** in chloroform, methylene chloride, or ether, we found that it converted quantitatively into **9**.

Synthesis of Sultine 9. A solution of 900 mg (3.1 mmol) of compound **4** in 20 mL of methylene chloride was cooled to −70 °C. Under a nitrogen atmosphere sulfur dioxide was bubbled for 20 min through the stirred solution. The solution was warmed to room temperature (the excess sulfur dioxide boiled out of the solution) and stirred overnight. Compound **9** was precipitated by addition of pentane, and 821 mg (2.3 mmol, 74%) were obtained as a white solid, analytically pure after recrystallization from acetone: mp 152–154 °C dec. Anal. Calcd for $C_{18}H_{16}N_4SO_2$: C, 61.4; H, 4.6; N, 15.9; S, 9.1. Found: C, 61.1; H, 4.5; N, 16.0; S, 9.0.

Spectroscopic data for **9**: IR 1120 cm^{-1} (sultine), 2290 cm^{-1} (very weak $C{\equiv}N$); MS, parent peak at m/e 352, 100% peak at 304 (352 − SO); ^{1}H NMR 1.26 (s, 6 H), 1.41 (s, 3 H), 1.59 (s, 3 H), 3.15 (s, 4 H) ppm. See Table I for ^{13}C NMR data.

Conversion of 8 to 9 in Methanol. In a nitrogen atmosphere 30 mg of sulfone **8** (90% pure) was stirred in 5 mL of methanol. After 10 min the suspension became a clear solution. The solvent was evaporated after 30 min. According to ^{1}H NMR spectroscopy the crude product did not contain a methoxy group.

Product **9** was isolated in 63% yield by precipitation with pentane from the methylene chloride solution.

Extrusion of Sulfur Monoxide from 9. Synthesis of Ketone 10. In a sublimation apparatus 900 mg (2.6 mmol) of compound **9** was warmed to 120 °C. When vacuum (0.05 mmHg) was applied, compound **10** sublimated as a yellow solid. After two recrystallizations from methylene chloride/pentane, 430 mg (1.4 mmol, 55%) of **10** was obtained. Compound **10** was analytically pure after crystallization from methanol, mp 205.5–206.5 °C. Anal. Calcd for $C_{18}H_{16}N_4O$: C, 71.0; H, 5.3; N, 18.4. Found: C, 70.6; H, 5.4; N, 18.6.

Spectroscopic data for **10**: IR 1720 cm^{-1} ($C{=}O$); MS, parent peak at m/e 304; ^{1}H NMR 1.20 (s, 3 H), 1.69 (s, 3 H), 1.75 (s, 3 H), 1.90 (s, 3 H), 3.2 (m, 4 H) ppm; ^{13}C NMR 10.2 (CH_3), 10.5 (CH_3), 14.3 (CH_3), 23.4 (CH_3), 31.1 (CH_2), 31.6 (CH_2), 38.3 (C), 38.4 (C), 71.1 (C), 109.5–111 (4CN's), 132 (sp^2 C), 135.1 (sp^2 C), 136.5 (sp^2 C), 144.1 (sp^2 C), 203.5 ($C{=}O$) ppm. **10** gave a positive haloform test.[41] The conversion **9** → **10** proceeded also in solution and was followed by ^{1}H NMR spectroscopy in Me_2SO-d_6 at 80 °C, $t_{1/2}$ = 8 min; in CD_3CN at 70 °C, $t_{1/2}$ = 90 min, and in CD_3OD at 65 °C, $t_{1/2}$ = 65 min. In these solvents the reaction was observed to proceed quantitatively.

Attempted Photolysis of 9. A solution of 30 mg of compound **9** in methylene chloride was irradiated at room temperature in a quartz apparatus by using a high-pressure mercury arc (Hanau Q81). After 6 h of irradiation no reaction had occurred, and compound **9** was recovered quantitatively by evaporation of the solvent.

Attempted ESR Measurements of the Extrusion Reaction. In a Varian E4 spectrometer equipped with a Varian A-1268 variable temperature controller, 0.2 M solutions of **9** in acetonitrile or 1,2-dichloroethane were heated to 70 and 80 °C, respectively (temperature checked with a copper constantan thermocouple). No absorptions were found during the reaction **9** → **10**.

Sulfur Monoxide Trapping with Pyridine *N*-Oxide. A dimethyl-d_6 sulfoxide solution of 30 mg (0.08 mmol) of **9** in 0.3 mL was heated with a threefold excess of pyridine *N*-oxide (23 mg, 0.24 mmol) to 80 °C. After 30 min the conversion of **9** to **10** was complete. Integration of the ^{1}H NMR peaks of pyridine and pyridine *N*-oxide showed 20% of the oxide had been converted to pyridine. Thus 60% of the generated sulfur monoxide had reacted with the pyridine *N*-oxide.

Sulfur Monoxide Trapping with Diene 1. A dimethyl sulfoxide solution of 20 mg (0.13 mmol) of diene **1** and 66 mg (0.19 mmol) of sultine **9** was heated to 80 °C for 1 h. The reaction was followed by ^{1}H NMR spectroscopy. After extractive workup (methylene chloride/water) the mixture of products **3** and **10** was isolated and identified as such by spectroscopic (IR, ^{1}H NMR) comparison with an authentic sample.

Registry No. 1, 50590-86-8; **3**, 59339-91-2; **4**, 50590-87-9; **5**, 82190-36-1; **7**, 82065-48-3; **8**, 82080-51-1; **9**, 82080-52-2; **10**, 82065-49-4; sulfur dioxide, 7446-09-5.

---

[40] Under mass spectroscopic conditions, **8** reacts fast to form **9**, and as a consequence the MS peaks observed may be due to the latter.

[41] Vogel, A. "Textbook of Practical Organic Chemistry", 4th ed.; Longman, Inc: New York, 1978.