Stereochemistry of the Formation and Hydrolysis of a Dithioether Dication

Richard S. Glass,* Jeffrey L. Broeker, and Habib Firouzabadi†

Department of Chemistry, The University of Arizona, Tucson, Arizona 85721

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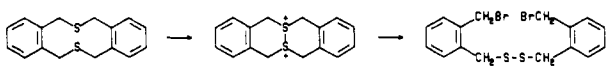
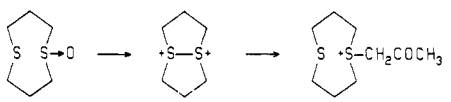
Naphtho[1,8-*bc*]-1,5-dithiocin 1-oxide (**7**) was prepared by oxidation of naphtho[1,8-*bc*]-1,5-dithiocin with sodium metaperiodate in aqueous methanol. The structure and conformation of sulfoxide **7** in the solid state was unequivocally established to be boat **7A** with equatorial sulfoxide by X-ray crystallographic analysis. Sulfoxide **7** crystallizes in the triclinic space group $P\bar{1}$ (no. 2) with a = 8.959 (2), b = 11.313(3), and c = 12.975 (3) Å, α = 64.98 (2)°; β = 81.18 (2)°, γ = 78.67 (2)°, and Z = 4. The structure was solved by direct methods. Full-matrix least-squares refinement led to a conventional R factor of 0.040 after several cycles of anisotropic refinement. Dissolution of sulfoxide **7** in concentrated sulfuric acid produces disulfide dication **8**, which on hydrolysis regenerates the sulfoxide. Deprotonation of sulfoxide **7** with methyllithium followed by treatment with D_2O stereoselectively gives monodeuterated sulfoxide **7** (X = D). ^1H NMR spectroscopic analysis of sulfoxide **7** (X = H) revealed that it is predominantly in chair conformation **7B** with equatorial sulfoxide and the deuterium atom in the monodeuterated derivative is predominantly axial (**7B**, H_a = D). Disulfide dication **8** is deduced to be predominantly in boat conformation **8A** by ^1H NMR spectroscopic analysis and that derived from monodeuterated sulfoxide **7** has the deuterium predominantly axial (**8A**, H_b = D). Hydrolysis of the deuterated disulfide dication regenerates sulfoxide **7** with the deuterium axial. These surprising stereochemical results require retention of configuration at the sulfoxide sulfur both in the formation of disulfide dication **8** and its hydrolysis.

Dithioether dications, $R_2S^+S^+R_2$, formed intramolecularly, have been suggested as intermediates in several reactions. Treatment of 2,5,7,10-tetrahydrodibenzo[*c*,*h*]-1,6-dithiecin (**1**) with bromine gave disulfide **3** presumably



1 **2** **3**

via disulfide dication **2**.[1] Electrochemical oxidation of 1,3-dithioacetals and ketals to give carbonyl compounds and disulfides has also been suggested to occur via a dithioether dication.[2-4] Elemental cyclooctasulfur was also shown to form a dithioether dication by oxidation with arsenic pentafluoride in sulfur dioxide.[5,6] Formation of dithioether dications by oxidation of cyclic and acyclic 1,5- and 1,6-dithioethers appears to be general.[7] In particular, the formation of dithioether dication **5** has been extensively studied. Reaction of 1,5-dithiocane 1-oxide (**4**), with



4 **5** **6**

acetone in the presence of perchloric acid afforded sulfonium salt **6**, by way of dithioether dication **5**.[1,8] Both the reduction of 1,5-dithiocane 1-oxide (**4**) with hydroiodic acid[9] to 1,5-dithiocane and the reverse reaction, i.e., oxidation of 1,5-dithiocane to the corresponding 1-oxide with aqueous iodine[10] were suggested to occur with the intermediacy of dithioether dication **5**. The Pummerer reaction of 1,5-dithiocane 1-oxide with acetic anhydride was also suggested to involve dithioether dication **5** as an intermediate.[11]

Musker and co-workers[7,12] were able to isolate dithioether dication **5** by oxidation of 1,5-dithiocane with nitrosonium tetrafluoroborate in acetonitrile. Electrochemical oxidation of 1,5-dithiocane also afforded dithioether dication **5**.[13,14] Furukawa and co-workers have also been able to obtain crystalline dithioether dication **5** by treatment of 1,5-dithiocane 1-oxide with concentrated sulfuric acid,[15,16] or with trifluoromethanesulfonic anhydride.[17] The crystal structure of this dication as its bis(trifluoromethanesulfonate) salt has been reported.[18] A variety of other cyclic and acyclic 1,*n*-dithioether monosulfoxides provided the corresponding dithioether dications, which were characterized spectroscopically, by reaction with concentrated sulfuric acid.[16,19]

The mechanism for the formation of dithioether dication **5** by the treatment of 1,5-dithiocane 1-oxide with acid involves double protonation of the oxygen and loss of water concomitant with S–S bond formation. Hydrolysis of this dication involves attack by water on sulfur with cleavage of the S–S bond followed by deprotonations to give 1,5-dithiocane 1-oxide. However, the intimate details of these steps are unknown. Owing to the extremely high diastereoselective deprotonation of naphtho[1,8-*bc*]-1,5-dithiocin 1-oxide (**7**, X = H), stereoselectively labeled material (**7**, X = D) was readily prepared, which allowed the

† On leave from the Department of Chemistry, Shiraz University, Shiraz, Iran.

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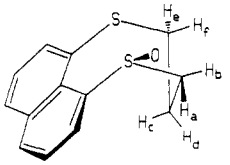
stereochemistry of the formation of dithioether dication 8 and its hydrolysis to be determined. This paper reports the diastereoselective preparation of deuterated sulfoxide 7, X = D, formation and characterization of dithioether dication 8, hydrolysis of this dication, and the stereochemistry of these processes.

Results and Discussion

Sulfoxide 7 was prepared in 92% yield from naphtho[1,8-*bc*]-1,5-dithiocin[20] by oxidation with sodium metaperiodate in aqueous methanol.

The crystal and molecular structure of sulfoxide 7 was determined by X-ray methods. The molecule crystallized in the triclinic space group $P\bar{1}$ (No. 2) with a = 8.959 (2), b = 11.313 (3), and c = 12.975 (3) Å, α = 64.98 (2)°, β = 81.18 (2)°, γ = 78.67 (2)°, and Z = 4. The structure was solved by direct methods. Full-matrix least-squares refinement led to a conventional R factor of 0.040 after several cycles of anisotropic refinement. An ORTEP drawing with the numbering scheme is shown in Figure 1. The conformation of sulfoxide 7 in the solid state is a boat conformation of the eight-membered ring with equatorial oxygen as shown in structure **7A**. The bond distances, bond angles, and selected torsion angles are given in the supplementary material. The nonbonded transannular S···S distance is 3.00 Å and the S···S–O angle is 174°.



Dissolution of sulfoxide 7 in concentrated sulfuric acid gave a red-brown solution from which sulfoxide 7 was recovered by hydrolysis in good yield. In analogy with the work of Furukawa and co-workers,[15,16,19] dication 8 was presumed to be formed on dissolving sulfoxide 7 in concentrated sulfuric acid. The following experiments were performed to prove this supposition. The ^{1}H and ^{13}C NMR spectra of sulfoxide 7 (X = H) dissolved in concentrated D_2SO_4 were measured. These spectra were consistent with

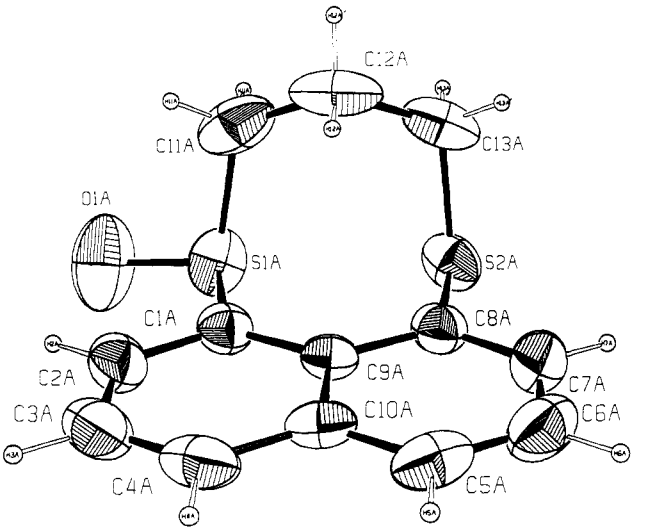
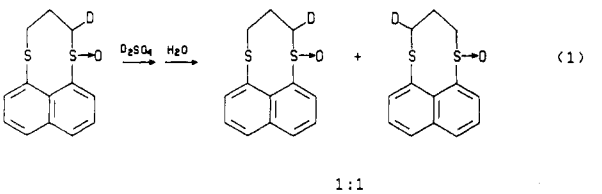


Figure 1. ORTEP drawing of naphtho[1,8-*bc*]-1,5-dithiocin 1-oxide and the labeling scheme. Thermal ellipsoids are drawn at the 50% probability level.

the expected symmetry of dication 8. Specifically, there were only four different aliphatic hydrogen resonances[22] in its ^{1}H NMR spectrum and two different aliphatic and six different aromatic carbon resonances in its ^{13}C NMR spectrum. Sulfoxide 7 (X = H) was deuterated by sequential treatment with methyllithium in tetrahydrofuran and subsequently deuterium oxide. Monodeuterated sulfoxide 7 (X = D) was obtained in approximately 50% yield (90% monodeuterated). Dissolution of monodeuterated sulfoxide 7 (X = D) in concentrated sulfuric acid followed by quenching with water gave a 1:1 mixture of sulfoxide 7 in which the deuterium appeared α to the sulfoxide moiety and α to the sulfide moiety (eq 1). This



(1)

1:1

is consistent with the formation of dication 8 in which attack by water at either sulfur atom is equally likely. ^{18}O-Labeled sulfoxide 7 (X = H) was prepared and studied to prove that the oxygen atom of the sulfoxide moiety in 7 was derived from the water after quenching dication 8. Treatment of an acetic acid solution of naphtho[1,8-*bc*]-1,5-dithiocin with ^{18}O-labeled water and the bromine complex of 1,4-diazabicyclo[2.2.2]octane according to the general method of Oae and co-workers[23] yielded ^{18}O-labeled sulfoxide 7 (X = H). Dissolution of this material in concentrated sulfuric acid followed by quenching with unlabeled water provided unlabeled 7 (X = H) in 77% yield. In this experiment, there is the possibility that the ^{18}O-labeled oxygen of sulfoxide 7 (X = H) exchanged with the unlabeled oxygen atoms of sulfuric acid.[24] The following control experiment was done to preclude this possibility under our reaction conditions. Sulfoxide 7 (X = H) was dissolved in ^{18}O-enriched concentrated sulfuric acid and then quenched with unlabeled aqueous sodium bi-

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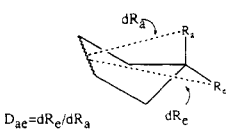
(21) Anet, F. A. L. *Tetrahedron Lett.* In press. Recently Anet has proposed general definitions for substituent positions for tetracoordinated atoms in cyclic compounds. In this definition one considers a five-atom chain in the ring with the substituents in question on the central carbon.



The distance is measured between substituents R_e and R_a and the midpoint of the line joining the terminal atoms (dR_e and dR_a). If the ratio of these distances (D_{ae}) is greater than 1.15 then R_e is distinctly equatorial and R_a is distinctly axial. In either the boat or chair conformers of 7 the ratio D_{ae} is between 1.3 and 1.4 for the proton pairs (H_a, H_b), (H_c, H_d), and (H_e, H_f), and this ratio is 1.4–1.5 for the sulfoxide oxygen and the sulfoxide lone pair. Thus according to the above definition, the aliphatic protons and sulfoxide oxygen can be unambiguously assigned as axial or equatorial.

(22) One expects three different aromatic hydrogen resonances for dication 8. Owing to fortituitous magnetic equivalence two resonances are observed.

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Table I. Aromatic Solvent and Europium-Induced Shift Data for Sulfoxide 7 (X = H)

proton shift, δ	δ($CDCl_3$)	δ(C_6D_6)	δ(C_6D_6)	δ + 0.22 equiv of $Eu(fod)_3$ ($CDCl_3$)	$Eu(fod)_3$-induced rel upfield shift, δ
H_a	3.69	3.11	−0.60	5.22	1.53
H_b	2.54	2.26	−0.23	5.41	2.87
H_c	2.21	1.16	−1.05	2.72	0.51
H_d	1.56	1.03	−0.48	2.45	0.89
H_e	2.61	1.74	−0.90	2.81	0.20
H_f	2.96	2.26	−0.74	3.19	0.23
H_g	8.49	8.95	0.49	11.25	2.76
H_h	7.68	7.32	−0.40	7.92	0.24
H_i	7.92	7.43	−0.52	8.11	0.19
H_j	7.92	7.58	−0.35	8.11	0.19
H_k	7.44	6.97	−0.52	7.63	0.19
H_l	7.84	7.43	−0.44	8.03	0.19

carbonate. The sulfoxide 7 (X = H) recovered in this experiment and did not incorporate ^{18}O. These data clearly show the formation of dication 8 on dissolving sulfoxide 7 in concentrated sulfuric acid.

As already pointed out, sulfoxide 7 (X = H) could readily be deuterated. Brown et al.[25] and Furukawa et al.[16,19] reported that deuteration of 1,5-dithiocane 1-oxide and its derivatives with sodium deuteroxide in deuterium oxide and tetrahydrofuran gave polydeuteration after being heated in a sealed tube. Under comparable conditions sulfoxide 7 (X = H) gave only *mono*deuteration, albeit irreproducibly in modest yield. However, satisfactory yields were reproducibly obtained by successive treatment with methyllithium and deuterium oxide. Monodeuteration occurred with extremely high diastereoselectivity. Having at hand stereoselectivity deuterated sulfoxide 7 provides a unique opportunity to investigate the stereochemistry at the sulfoxide sulfur center of the formation of the dithioether dication and its reverse, i.e., hydrolysis of the dication. This is possible because the stereochemical relationship between the deuterium and the sulfoxide oxygen in 7 and between the deuterium and the S–S bond in 8 can be determined by ^1H NMR spectroscopic analysis. Once this stereochemical relationship is ascertained, the stereochemistry of replacing the S–O bond by S–S and the reverse can be deduced. The conformations of these molecules in solution must be determined and then the spatial orientation of the deuterium at the carbon α to the sulfoxide in order to determine the stereochemical relationship between the deuterium and S–O bond and S–S bond in 7 and 8, respectively. The stereochemistry of the deuteration was established by ^1H NMR spectroscopic analysis as outlined below.

The conformation in solution of sulfoxide 7 (X = H) was determined by ^1H and ^{13}C NMR spectroscopic analysis in combination with lanthanide-induced shifts and aromatic solvent induced[26-28] shifts (Table I). The assignments are given in the Experimental Section. The conformation of 7 in solution is predominantly one conformer. H_b, H_c, and H_f have only one large coupling constant, which is from the geminal hydrogens H_a, H_d, and H_e, respectively. H_a and H_e have two large coupling constants from geminal hydrogens H_b and H_f, respectively, and from trans hydrogen H_d. H_d has three large coupling constants from

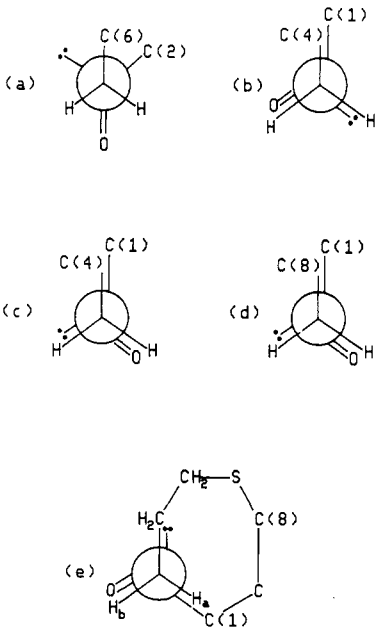
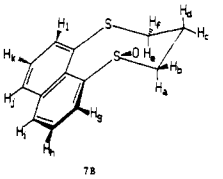


Figure 2. Newman projection viewed down the α-carbon atom–sulfoxide sulfur atom bond in (a) 1,3-dithiane 1-oxide (b) *exo*-2-thiabicyclo[2.2.1]heptane 2-oxide, (c) *endo*-2-thiabicyclo[2.2.1]heptane 2-oxide, (d) 2*H*-naphtho[1,8-*bc*]thiophene *S*-oxide, and (e) naphtho[1,8-*bc*]-1,5-dithiocin 1-oxide (**7B**).

hydrogens H_a, H_e, and H_c. If there were significant contribution of both the boat and chair conformations for 7, then the magnitude of the coupling constants for protons H_a and H_b, protons H_c and H_d, and protons H_e and H_f would become equivalent due to averaging of the boat and chair conformations. However, since there is no such averaging, a single conformation predominates in solution. ^1H and ^{13}C NMR studies on 7 down to 153 K showed no coalescence of protons or carbon atoms. Although this may be due to a low barrier for chair–boat interconversion, this is also consistent with there being only one conformer in solution that is significantly populated. Chair conformation **7B** rather than boat conformer **7A** was deduced to be



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the predominant conformer in solution on the basis of the following observations. (1) There is a relatively small difference (0.7 ppm) in chemical shift between H_c and H_d.[29] (2) The downfield shift induced by $Eu(fod)_3$ is greater for the equatorial[21] α-hydrogen atom (H_b in **7B**) than the axial[21] α-hydrogen atom (H_a in **7B**)—the equatorial α-hydrogen atom and sulfoxide oxygen are eclipsed in chair conformer **7B** but, in the boat conformer **7A**, both axial and equatorial α-hydrogen atoms are gauche to the sulfoxide oxygen atom, thus equal in distance. (3) It is notable

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(29) Kamada, T.; Wasada, N.; Yamamoto, O. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 275. In boat conformations **7A** or **8A**, the distance between the axial hydrogen, H_c, and C(9) on the naphthalene ring is 2.6 Å, while the distance between the equatorial, H_d, and C(9) is 4.5 Å (using molecular models). Using the analysis developed by Kamada, the anisotropic effect of the naphthalene ring on H_c and H_d would give rise to a chemical shift difference of 1.2–1.8 ppm. In chair conformers **7B** and **8B**, the distance between H_c and H_d and C(9) is about 5 Å. At this distance the anisotropic effect is negligible. Thus a much smaller difference in chemical shift between H_c and H_d is expected for chair conformers **7B** and **8B** than boat conformers **7A** and **8A**.

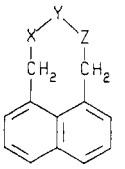
that in the absence of the shift reagent, the α-equatorial hydrogen (H_b in **7B**) absorbs 1.22 ppm upfield of the α axial hydrogen (H_a in **7B**), whereas the γ-equatorial hydrogen (H_f in **7B**) resonates 0.36 ppm downfield of the γ-axial hydrogen (H_e in **7B**). Although the effects of the magnetic anisotropy of a sulfoxide bond are controversial,[30] H(3-exo) in 2-thiabicyclo[2.2.1]heptane 2-*exo*-oxide, which is eclipsed by the sulfoxide moiety, absorbs at 0.8 ppm upfield from H(3-endo) and similarly H(3-endo) in 2-thiabicyclo[2.2.1]heptane 2-*endo*-oxide, which is eclipsed by the sulfoxide moiety resonates 1.2 ppm upfield of H-(3-exo)[27,29,31] as seen in Figure 2. Thus, it seems that protons eclipsed by S–O bonds are shifted considerably upfield. The unusual upfield shift of the α equatorial hydrogen (H_b in **7B**) then could be rationalized if the compound existed in the chair conformer **7B** (Figure 2), since this conformer has the equatorial H_b, eclipsed with the S–O bond.[32] (4) The considerably greater downfield shift of the β-axial hydrogen (H_d in **7B**) over the β-equatorial hydrogen (H_c in **7B**) and over the γ-axial hydrogen (H_e in **7B**) induced by the shift reagent further supports a chair over a boat conformation. In the former, the β-axial hydrogen is about 1.0 and 1.5 Å closer than the β-equatorial or γ-axial hydrogens, respectively, to the sulfoxide oxygen, whereas they are comparable distance in the latter.

Convincing evidence that the sulfoxide oxygen is in the equatorial position as shown in **7B** and not axial is also obtained from the results of the lanthanide-induced shifts. The considerably greater downfield shift induced by Eu(fod)$_3$ for H_a than H_d in conformer **7B** proves that the sulfoxide oxygen is equatorial, not axial. The relatively modest induced shifts for H_e and H_f in **7B** further argue for an equatorial rather than axial sulfoxide oxygen. Finally, the large downfield shift induced in H_g requires an equatorial rather than axial sulfoxide.

The equatorial sulfoxide oxygen is at least 3 kcal/mol lower in energy than the axial counterpart. Flipping chair conformer **7B** to the other chair conformation will flip the equatorial oxygen to an axially disposed oxygen. The energy barrier for this flipping should be about 11 kcal/mol, since the barrier of this process for the sulfone analogue of **7** (that is, naphtho[1,8-*bc*]-1,5-dithiocin 1,1-dioxide) is 10.8 kcal/mol.[33] ^{1}H and ^{13}C NMR variable temperature NMR studies on **7** from 153 to 393 K showed no coalescence of protons or carbon atoms. Since the chair–chair interconversion of **7** should be about 11 kcal/mol, this absence of coalescence is evidence that the chair conformer, with equatorial sulfoxide, is >3 kcal/mol lower in energy than the chair conformer with an axial sulfoxide. In addition, the axial sulfoxide has been determined to be about 8 kcal/mol higher in energy than the equatorial sulfoxide by ab initio calculations on model compounds.[34]

The aromatic induced shifts further support the conclusion that the conformation of the sulfoxide is **7B**. A collision complex is envisioned as being formed between the electron-rich face of benzene and the electron-deficient concave side of the sulfoxide molecule (side opposite protruding oxygen atom and sulfur lone pairs). This results in greater shielding of H_a over H_b, H_c over H_d, H_e over H_f, and deshielding of H_g in conformer **7B**.

Conformational analysis of the parent alkane corresponding to sulfoxide **7**, that is, 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene (**9a**),[35,36] a number of its substituted derivatives,[37,40] and oxygen heterocycle **9b**[35] has



9a, X = Y = Z = CH_2
b, X = Y = CH_2, Z=O
c, X = Z = O, Y = CH_2
d, X = Y = Z = S

shown that the boat conformation predominates and inverts by a pseudorotation via a twist-boat intermediate. An important factor in favoring the boat over the chair conformation is the eclipsing about CH_2–X(CH_2) and (CH_2)Z–CH_2 in the chair, which is absent in the boat conformer. Replacement of the CH_2 groups at positions X and Z by oxygen atoms relieves this strain and heterocycle **9c** and its derivatives preferentially adopt chair conformations.[41,42] In trisulfide **9d** the CH_2–X(CH_2) and (CH_2)Z–CH_2 eclipsing strain is relieved in the chair conformer but nonbonded CH_2(Y) interactions are relieved in the boat conformer. Consequently, these conformers are close in energy with the boat conformer calculated by molecular mechanics methods to be lower in energy by 0.6 kcal/mol.[43] These previous studies present a picture consistent with our conformational analysis of sulfoxide **7**, that is, the boat and the chair forms of **7** with equatorial sulfoxide are lower in energy than the boat or chair conformer of **7** with axial sulfoxide by at least 3 kcal/mol and much lower in energy than the twist conformers (the twist boat conformer for naphtho[1,8-*bc*]-1,5-dithiocin is calculated to be 6.7 kcal/mol higher in energy than the chair or boat conformers by AM1).[33] The interconversion of boat-to-boat or chair-to-chair conformers is approximately 11 kcal/mol. The chair and boat conformers with equatorial sulfoxide are close in energy such that lattice forces favor the boat in the solid state but the chair is favored in solution. On the basis of the analysis of the NMR spectrum of **7** discussed above, the chair conformation predominates in solution. This requires that the chair conformation is at least 1 kcal/mol lower in energy than the boat conformation. Two factors contribute to the preference of the chair conformation for **7** in solution, whereas the parent alkane prefers the boat conformation. Three of the eclipsing interactions in the parent alkane are absent in **7**. The other eclipsing interactions are ameliorated because of the greater C–S than C–C bond length. The conformation in solution of sulfoxide **7** is based in part on the lanthanide-induced shift changes.

(30) Fraser, R. R.; Schuber, F. J.; Wigfield, Y. Y. *J. Am. Chem. Soc.* **1972**, *94*, 8795. Folli, U.; Iarossi, D.; Moretti, I.; Taddei, F.; Torre, G. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1655.
(31) Fraser, R. R.; Wigfield, Y. Y. *J. Chem. Soc., Chem. Commun.* **1970**, 1471.
(32) The presumption is that the chemical shift change caused by the sulfoxide is greater than that caused by the unshared pair of electrons on sulfur. This is important because the lone pair in sulfoxide **7** is directed away from H_a but eclipses an H(3) proton in the 2-thiabicyclo-[2.2.1]heptane 2-oxides.
(33) Glass, R. S.; Broeker, J. L. Manuscript in preparation.
(34) Glass, R. S.; Adamowicz, L.; Broeker, J. L. *J. Mol. Struct. (Theochem)* **1989**, *186*, 273.
(35) Nelsen, S. F.; Gillespie, J. P. *J. Am. Chem. Soc.* **1973**, *95*, 2940.
(36) Kamada, T.; Yamamoto, O. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1159.
(37) Kamada, T.; Yamamoto, O. *Chem. Lett.* **1976**, 843.
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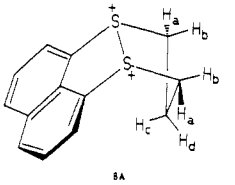
(39) Kamada, T.; Yamamoto, O. *Tetrahedron Lett.* **1977**, 691.
(40) Kamada, T.; Yamamoto, O. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 994.
(41) Litvinov, I. A.; Klimovitskii, E. N.; Yufit, D. S.; Sergeeva, G. N.; Struchkov, Yu. T.; Arbuzov, B. A. *Proc. Acad. Sci. USSR, Chem. Ser. (Engl. Transl.)* **1981**, 115.
(42) Arbuzov, B. A.; Klimovitskii, E. N.; Sergeeva, G. N.; Remizov, A. B.; Chernov, P. P. *J. Gen. Chem. USSR (Engl. Transl.)* **1983**, *53*, 2497.
(43) Guttenberger, H. G.; Bestmann, H. J.; Dickert, F. L.; Jorgensen, F. S.; Snyder, J. P. *J. Am. Chem. Soc.* **1981**, *103*, 159.

This engenders the concern that the lanthanide affects the boat–chair equilibrium;[44] however, it is deemed unlikely that the boat conformation predominates in the absence of the lanthanide shift reagent because the NMR results in the absence of this reagent and also the shifts induced by benzene suggest a predominance of the chair conformation as discussed above.

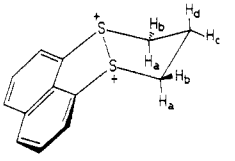
The ddd signal at δ 3.71 with J = 13.1, 12.8, 3.4 Hz in the NMR spectrum of sulfoxide **7** (X = H) greatly diminishes on deuteration. In addition, a large coupling constant of 13.3 Hz is removed from the resonance at δ 2.49. These data are consistent with the assignment of the deuterium at the axial[21] α position (labeled H_a) in the predominant chair conformation of the eight-membered ring with equatorial oxygen as shown in structure **7B**. The deuterium and sulfoxide oxygen are cis to each other. Stereoselective deprotonation of the diastereoisomeric hydrogens α to a sulfoxide group are well-known;[45] however, the factors controlling this selectivity are not well-established. Theoretical calculations on $^-CH_2S(O)H$[46,47] and $^-CH_2S(O)CH_3$[47] reveal nonplanar geometry at the α-carbon atom and conformational preference for the staggered conformer in which the lone-pair orbital on the carbanion is anti to the S–O bond. However, dependence of the stereochemistry of deprotonation on solvent, temperature, cationic complexing agents, and added lithium salts has been reported,[45] which indicates the importance of solution and counterion effects that were not included in the calculations. Conformer **7A** presents a unique geometry of the diastereotopic α-hydrogen atoms relative to the sulfoxide moiety. The chair-like $S(O)CH_2CH_2CH_2S$ fragment in this conformer is different from that in the corresponding fragment in 1,3-dithiane 1-oxides with equatorial sulfoxides.[26,48] With the aid of molecular models it was determined that in conformer **7B** the S–O bond eclipses H_b, whereas the equatorial S–O bond in 1,3-dithiane 1-oxide bisects the HCH angle of the α-carbon atom (see Figure 2). An α-hydrogen atom in *endo*- and in *exo*-2-thiabicyclo[2.2.1]heptane 2-oxide and in 2*H*-naphtho[1,8-*bc*]thiophene *S*-oxide derivatives is eclipsed by the S–O bond, but the other α-hydrogen atom is eclipsed by the lone-pair orbital on sulfur (Figure 2).[26,48] In conformer **7B**, H_a is eclipsed by the S–C(1) bond, not the lone pair orbital on sulfur. In any event the *endo*- and *exo*-2-thiabicyclo[2.2.1]heptane 2-oxides[30] show opposite stereochemistry from that of the 2*H*-naphtho[1,8-*bc*]-thiophene *S*-oxide derivatives[49] on deuterium exchange.

The stereochemistry of the formation and hydrolysis of dication **8** were determined by NMR spectroscopy as follows. The NMR spectra for the dication are listed and assigned in the Experimental Section. On the basis of the coupling constants, the conformation of the dication in solution is predominantly one conformer, either a chair or a boat conformation. That its predominant conformation is boat **8A** is based on the large chemical shift difference between H_c and H_d of 1.37 ppm and small chemical shift



8A

difference (0.16 ppm) between H_a and H_b. The large difference between H_c and H_d chemical shifts is due to the substantial shielding of H_c by the π-ring current of the naphthalene ring.[29,31] If the dication adopted chair conformation **8B**, only a small difference in chemical shift is



8B

anticipated between H_c and H_d as observed for sulfoxide **7**.[29] The comparable chemical shifts of H_a and H_b are expected for boat conformation **8A**, because H_a is shielding by the naphthalene ring and H_b is shielded by being axially disposed relative to H_a. However, in chair conformation **8B** shielding of H_a by the π-ring current of the naphthalene ring and by being axially disposed relative to H_b is anticipated as observed in sulfoxide **7** (H_e absorbs at 0.36 ppm higher field than H_f). The nonequivalence of H_c and H_d and of H_a and H_b at room temperature requires a substantial barrier to boat–boat inversion. This result is consistent with an S–S bond, which raises the barrier for such inversion. In summary, the boat conformer of **8** is the predominant conformer in solution. The boat conformer interconverts with the chair conformer; however, the formation of the S–S bond precludes either boat–boat or chair–chair interconversion.

Dissolution of monodeuterated sulfoxide **7** (X = D) (**7B** with 90% H_a replaced by deuterium) in concentrated sulfuric acid afforded dication **8A** whose ^1H NMR spectrum showed the deuterium to be 85–100% at H_b, because 85–100% of one of these protons were no longer observed and a large coupling to H_a and H_c was removed. This means that the deuterium is on the *same side* as the newly formed S–S bond. Hence, dication **8** is formed from sulfoxide **7** with *retention* of stereochemistry at sulfur. Hydrolysis of this dication regenerated monodeuterated sulfoxide **7**, which was a 1:1 mixture of deuterium α to the sulfoxide moiety and α to the sulfide moiety as described before, but also the deuterium was preferentially axial (3:1 ratio) at both positions as shown in eq 2. Although there

$$\underset{}{\mathbf{7B}\ (H_a = D)} \xrightarrow{H_2SO_4} \underset{}{\mathbf{8A}\ (H_b = D)} \xrightarrow{H_2O} \underset{32\%}{\mathbf{7B}\ (H_a = D)} + \underset{36\%}{\mathbf{7B}\ (H_e = D)} + \underset{12\%}{\mathbf{7B}\ (H_b = D)} + \underset{12\%}{\mathbf{7B}\ (H_f = D)} \quad (2)$$

was some loss of stereochemical integrity, the reaction sequence occurred predominantly with overall retention of stereochemistry. Furthermore, since the dication was formed with retention of stereochemistry, it must hydrolyze with retention of stereochemistry.

The problem at hand is to propose a mechanism for the sulfoxide–dication transformation that accounts for sulfoxide in **7** (**7B**, H_a = D), with the majority of the deuterium cis to the sulfoxide S–O bond, forming dication **8** (**8A**, H_b = D) in which the majority of the deuterium is on the same side as the S–S bond. Closure of the disulfide dication bond by backside attack of the sulfide lone pair on the protonated equatorial sulfoxide, resulting in inversion of

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(45) Block, E. In *Reaction of Organosulfur Compounds*; Academic: New York, 1978; pp 53–56. Wolfe, S. In *Organic Sulfur Chemistry*; Bernardi, F., Csizmadia, I. G., Mangini, A., Eds., Elsevier: Amsterdam, 1985, pp 133–190.
(46) Rauk, A.; Wolfe, S.; Csizmadia, I. G. *Can. J. Chem.* **1969**, *47*, 113.
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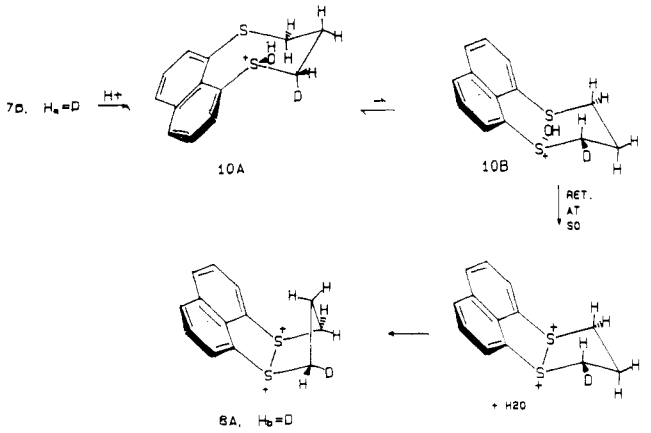
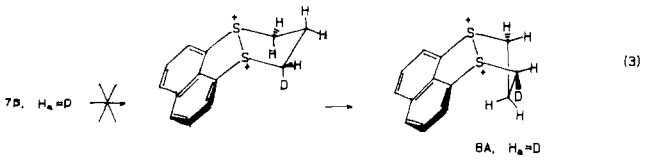
(48) Cook, M. J.; Tonge, A. P. *J. Chem. Soc., Perkin Trans. 2* **1974**, 767. Van Acker, L.; Anteunis, M. *Tetrahedron Lett.* **1974**, 225. Khan, S. A.; Lambert, J. B.; Hernandez, O.; Carey, F. A. *J. Am. Chem. Soc.* **1975**, *97*, 1468.
(49) Folli, U.; Iarossi, D.; Taddei, F. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1658.

Scheme I



stereochemistry at the sulfoxide sulfur atom, would give **8A** (H_a = D) as is shown in eq 3. This pathway *cannot*

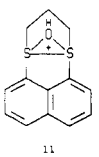


(3)

account for the majority of intermediate **8A** (H_b = D). This reemphasizes that the major pathway for formation of the disulfide dication **8** is *not* by *inversion* of stereochemistry at the sulfoxide center, rather dication **8** is formed with *retention* of stereochemistry at the sulfoxide center.

Retention of stereochemistry in the formation of dication **8** from sulfoxide **7** is a very surprising result for two reasons. Nucleophilic displacement reactions at sulfonium centers typically occur with inversion of configuration at sulfur,[50] e.g., nucleophilic displacement by hydroxide ion on alkoxysulfonium salts.[51] Furthermore, the geometry at the sulfoxide sulfur in **7** is approaching a trigonal bipyramid with the oxygen and transannular sulfur atom occupying apical positions. Double protonation at oxygen with apical displacement by the transannular sulfur atom of the apical water would result in inversion of configuration.

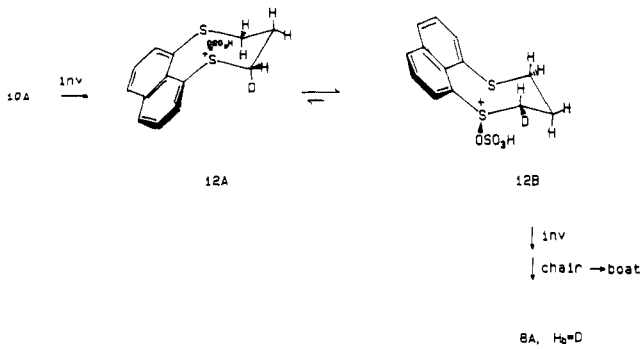
Two pathways resulting in retention of configuration can be envisioned for this reaction. Several examples of nucleophilic displacement reactions at sulfinyl sulfur occurring with retention of configuration are postulated to involve a four-membered ring sulfurane[50] in which the ring ensures that the entering and leaving groups are on the same side. A comparable sequence with **7** would involve protonation, chair–chair inversion to **10B**, and formation of bridged intermediate **11**. However, ab initio calcula-



11

tions on a model for **11**[34] suggest that it would be an unlikely intermediate owing to its high energy. Retention

Scheme II



of configuration has also been reported in cases in which bridge intermediates are not involved.[52] The stereochemical result is ascribed to involvement of trigonal-bipyramidal intermediates in which there is apical attack by the nucleophile and equatorial departure of the leaving group[50] or pseudorotational processes[53] with apical attack and apical departure. Such mechanistic possibilities for transforming **7** into **8A** are limited by the unique geometrical constraints of the ring system, which require unusual features in these mechanisms.[54] In any case, as is shown in Scheme I, closure of the S–S bond with retention of configuration at the sulfoxide center results in **8A** with H_b = D.

Alternatively, protonation of **10A** and nucleophilic displacement by sulfuric acid or bisulfate with inversion of configuration generates **12A**. Ring inversion of **12A** forms **12B**, which on displacement of bisulfate by the transannular sulfur atom with inversion of configuration yields dication **8A** with overall retention of configuration. The strong interaction observed in the crystal structure of 1,5-dithiocane dication bis(trifluoromethanesulfonate)[18] between the sulfur atoms of the dication and the oxygen atoms of the trifluoromethanesulfonate anion, which is less nucleophilic than bisulfate anion, the observed involvement of buffers prior to neighboring group participation in the iodine oxidation of thioethers[55] and the observed oxygen exchange between diphenyl sulfoxide and sulfuric acid[24] support the feasibility of this mechanism. As is shown in Scheme II, this double inversion mechanism also gives **8A** with H_b = D.

Since the overall stereochemistry of the reaction sequence (formation and hydrolysis of dication) occurs predominantly with retention of stereochemistry, the hydrolysis (microscopic reverse of the formation) must occur predominantly with retention of configuration.

Loss of stereochemical integrity may be due to sulfide sulfur lone-pair attack on the sulfoxide moiety with inversion of stereochemistry and/or hydrolysis of the dica-

(50) Mikolajczyk, M. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. M., Eds.; Wiley: New York, 1982, Vol. 13, pp 333–468.

(51) Johnson, C. R. *J. Am. Chem. Soc.* **1963**, *85*, 1020. Johnson, C. R.; McCants, D., Jr. *Ibid.* **1965**, *87*, 5404. Tang, R.; Mislow, K. *Ibid.* **1969**, *91*, 5644. Glass, R. S.; Hojjatie, M.; Setzer, W. N.; Wilson, G. S. *J. Org. Chem.* **1986**, *51*, 1815.

(52) Mikolajczyk, M.; Drabowicz, J.; Bujnicki, B. *Tetrahedron Lett.* **1985**, *26*, 5699. Colonna, S.; Germinario, G.; Stirling, C. J. M. *Gazz. Chim. Ital.* **1987**, *117*, 67. Colonna, S.; Germinario, G.; Manfredi, A.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1695.

(53) Mikolajczyk, M. In *Perspectives in the Organic Chemistry of Sulfur*; Zwanenburg, B., Klunder, A. J. H., Eds., Elsevier: Amsterdam, 1986; pp 23–40.

(54) For example, protonation of **7** followed by chair–chair inversion to give **10B** and then apical attack by the transannular sulfur atom and equatorial departure of water after a second protonation accounts for the observed stereochemistry. However, apical attack by the transannular sulfur atom with an equatorial OH group would require the other apical position to be occupied by an unshared pair of electrons that strongly prefers the equatorial position. Equatorial attack by the transannular sulfur atom in **10B** followed by equatorial or apical departure of water also results in retention of stereochemistry but apical attack and departure is energetically preferred.

(55) Hirschon, A. S.; Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* **1982**, *104*, 725 and references therein.

tion with inversion of stereochemistry at the sulfur center. These pathways, however, are minor as already discussed.

Experimental Section

Melting points were measured in open glass capillary tubes on a Thomas-Hoover melting point apparatus and are uncorrected. A Perkin-Elmer Model PE983 spectrometer was used for recording IR spectra. A Bruker WM-250 NMR spectrometer operating at 250 MHz for ^1H and 62.9 MHz for ^{13}C was used for determining spectra with tetramethylsilane as the internal standard. High resolution MS were obtained from the Midwest Center for Mass Spectroscopy at the University of Nebraska—Lincoln. UV spectra were measured on an IBM 9420 UV-vis spectrophotometer. All reagents were obtained from the Aldrich Chemical Co., Milwaukee, WI, and were used as delivered unless specified otherwise.

Synthesis of Naphtho[1,8-*bc*]-1,5-dithiocin 1-Oxide (7, X = H). A solution of sodium metaperiodate (221 mg, 1.03 mmol) dissolved in water (2.5 mL) and methanol (2.5 mL) was added dropwise with ice-bath cooling to a solution of naphtho[1,8-*bc*]-1,5-dithiocin (120 mg, 0.52 mmol) dissolved in methanol (5 mL). After completion of the addition, the solution was allowed to warm to room temperature and stirred for 15 min. Analysis of this solution, which turned from yellow to colorless with the formation of a white precipitate, by TLC showed the reaction to be complete. The methanol was removed by using a rotary evaporator. Additional water (20 mL) was added and the mixture extracted with dichloromethane (3 × 50 mL). The extracts were combined, dried (anhydrous $MgSO_4$), filtered, and evaporated to a white solid, which was purified by preparative TLC on silica gel, eluting with ethyl acetate to give naphtho[1,8-*bc*]-1,5-dithiocin 1-oxide (7, X = H) (120 mg, 92% yield): mp 134–135 °C; IR (KBr) 2946, 1024, 1007, 977, 826, 766 cm^{-1}; ^1H NMR (CD_2Cl_2) δ 1.51 (1 H, ddddd, J = 3.7*, 3.9, 13.3*, 13.1*, 15.5 Hz, H_d), 2.21 (1 H, ddddd, J = 2.2, 3.4, 3.7*, 4.1, 15.5 Hz, H_c), 2.49 (1 H, ddd, J = 4.1, 4.1, 13.3* Hz, H_b), 2.64 (1 H, ddd, J = 4.1, 13.1, 13.3* Hz, H_e), 3.00 (1 H, dddd, J = 1.5, 2.2, 3.9, 13.1 Hz, H_f), 3.71 (1 H, ddd, J = 3.4, 12.8, 13.1* Hz, H_a), 7.49 (1 H, dd, J = 7.5*, 7.5* Hz), 7.72 (1 H, dd, J = 7.7*, 7.7* Hz), 7.87 (1 H, dd, J = 1.0, 7.0 Hz), 7.93 (1 H, dd, J = 1.0, 7.3 Hz), 7.95 (1 H, dd, J = 1.0, 8.3 Hz), 8.46 (1 H, dd, J = 1.0, 7.4 Hz) [* denotes an average of the coupling constants J_{mn} and J_{nm}]; ^{13}C NMR ($CDCl_3$) δ 26.6, 37.8, 62.1, 125.4, 126.3, 126.4, 127.8, 130.8, 131.2, 134.6, 138.0, 142.0; UV (EtOH) 226 (51 000), 284 (8500), 317 (61 000) nm; exact mass calcd for $C_{13}H_{12}S_2O$ m/e 248.0329, found 248.0320; MS m/e 248.0320 (56), 232.0356 (13), 205.9848 (15), 203.0024 (11), 189.9911 (100), 176.9840 (11), 174.0063 (35), 171.0277 (23). Aromatic solvent and europium-induced ^1H NMR spectroscopic data are given in Table I.

X-ray Single-Crystal Structure Study of Sulfoxide 7 (X = H). Crystals suitable for X-ray crystallographic analysis were grown by vapor diffusion of a solution of the compound in 1,2-dichloroethane with pentane. A colorless, irregular crystal (0.58 × 0.50 × 0.30 mm) was sealed to a glass capillary and mounted on a Syntex $P2_1$ autodiffractometer. Mo Kα radiation (λ = 0.71073 Å) was used with graphite as monochromator. Cell constants and a orientation matrix for data collection were obtained from least-squares refinement using 25 reflections. The cell constants for the triclinic cell and other parameters are given in Table II. The $\theta/2\theta$ scan technique was used and data were collected to a maximum 2θ of 55.0°. The data with $F \geq 3\sigma(F)$ were used in the calculations. The data were reduced to F_o and $\sigma(F_o)$. Lorentz and polarization corrections were applied to the data. Three representative reflections were measured every 46 reflections and indicated no decay.

The structure was solved by direct methods using the SDP-PLUS program package.[56] A total of 18 atoms were found by using default parameters. The remaining atoms were located in succeeding difference maps. The hydrogen atoms were added at idealized positions and in all subsequent refinements all hydrogen atoms were restricted to fixed isotropic thermal parameters and restrained to ride on the atom to which they are bonded (refinement with refined hydrogen locations gave the same results and equal agreement factors as those with fixed, idealized hydrogen). The structure was refined by full-matrix least-squares techniques[56] by using neutral scattering factors[57] with anomalous dispersion terms included.[58] The final cycle of refinement included 289 variable parameters and converged with unweighted (R) and weighted (R_w) agreement factors of 0.040 and 0.053, respectively. The standard deviation of an observation of unit weight was 1.74. The highest peak in the final difference Fourier had a height of 0.57 $e^-/Å^3$ with an estimated error based on $\sigma(F)$ of 0.14.[59]

Table II. Crystal Data[a] for Sulfoxide 7 (X = H)

mol formula	$C_{13}H_{12}OS_2$
mol wt	248.37
space group	$P\bar{1}$ (no. 2)
a, Å	8.959 (2)
b, Å	11.313 (3)
c, Å	12.975 (3)
α, deg	64.98 (2)
β, deg	81.18 (2)
γ, deg	78.67 (2)
Z	4
d_{obsd}, g cm^{-1}	1.40[b]
d_{calcd}, g cm^{-3}	1.42
cryst color, shape	colorless, irregular
cryst dimens, mm	0.58 × 0.50 × 0.30
no. unique data	5360
no. obsd data	3780
abs coeff [$\mu(\lambda)$], cm^{-1}	4.1

[a] Standard deviation of the least significant figure is given in parentheses. [b] Density was determined by the flotation method using aqueous sodium iodide solution.

Formation of Dication 8. A sample of monosulfoxide 7 (X = H) (9.7 mg, 0.039 mmol) was dissolved in ice-cold D_2SO_4 (95–97%, 2.0 mL). This red-brown solution was characterized by NMR and UV spectroscopy: ^1H NMR (D_2SO_4) δ 2.22 (1 H, m, $w_{1/2}$ = 0.14 ppm, H_c) , 3.59 (1 H, br d, J = 14.8 Hz, H_d), 4.42 (2 H, br dd, J = 11.3, 11.3 Hz, H_b), 4.58 (2 H, br d, J = 11.3 Hz, H_a), 8.06 (2 H, dd, J = 8.0, 8.0 Hz, H_{meta}), 8.47 (4 H, d, J = 8.0 Hz, H_{ortho}, H_{para}); ^{13}C NMR (D_2SO_4) δ 36.8, 64.3, 122.8, 134.3, 134.7, 138.2, 138.4, 138.6; UV (D_2SO_4) 225 (35 900), 278 (7100), 300 (7950), 313 (5750), 400 (273) nm.

Hydrolysis of Dication 8. After being allowed to stand for 30 min, the above solution of dication 8 was poured into a vigorously stirred solution of ice-cold anhydrous ether, resulting in a pale yellow solution. Ice-cold water (15 mL) was added cautiously followed by sufficient ice-cold 4 M aqueous potassium hydroxide solution to make the aqueous solution basic. The mixture was extracted with dichloromethane (3 × 50 mL). The combined extracts were dried, evaporated to dryness, and purified by preparative TLC, eluting with ethyl acetate, to afford sulfoxide 7 (X = H) (7.0 mg, 72% yield), identical with authentic material (mp, mmp, IR, and ^1H NMR). A small amount of disulfoxide (0.5 mg, 5% yield) was also obtained.

Deuteration of Sulfoxide 7 (X = H). To a sample of sulfoxide 7 (X = H) (19 mg, 0.076 mmol) dissolved in anhydrous tetrahydrofuran (3 mL) cooled in a dry ice/acetone bath and under an argon atmosphere was added a solution of methyllithium in ethyl ether (1.4 M, 140 μL, 0.20 mmol). The solution immediately turned red-brown in color. The solution was removed from the dry ice/acetone bath and allowed to warm to room temperature. During this warming period, a precipitate formed and the color became green and then deep blue. After being stirred for 1 h at room temperature, the blue solution was placed in a dry ice/acetone bath and deuterium oxide (99% D, 2.0 mL) was added dropwise. The reaction mixture immediately turned pale orange in color. After removal of the organic solvents on a rotary evaporator, the residual aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined extracts were dried

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with anhydrous magnesium sulfate, concentrated on a rotary evaporator, and purified by preparative TLC, eluting with ethyl acetate to give monodeuterated sulfoxide 7 (X = D) (90% D as determined by ^{1}H NMR spectroscopic analysis, 10, mg 52% yield): IR (KBr) 2170, 2042 (C-D) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.51 (1 H, br dd, J = 13.5, 13.5 Hz, H_d), 2.21 (1 H, br d, J = 15.5 Hz, H_c) 2.49 (0.96 H, m, H_b), 2.64 (1 H, ddd, J = 4.1, 13.5, 13.5 Hz, H_e), 3.00 (1 H, br d, J = 13.1 Hz, H_f), 3.71 (0.13 H, ddd, J = 3.0, 12.9, 12.9 Hz, H_g), 7.49 (1 H, dd, J = 7.5, 7.5 Hz, H_k), 7.72 (1 H, dd, J = 7.7, 7.7 Hz, H_h), 7.87 (1 H, dd, J = 1.0, 7.0 Hz, H_l), 7.93 (1 H, dd, J = 7.7, 7.7 Hz, H_j), 7.95 (1 H, dd, J = 1.0, 8.3 Hz, H_i), 8.46 (1 H, dd, J = 1.0, 7.4 Hz, H_g).

Formation of Deuterated Dication 8 from Deuterated Sulfoxide 7 (X = D). A sample of monodeuterated sulfoxide 7 (X = D) (9.0 mg, 0.036 mmol) prepared as above was dissolved in ice-cold D_2SO_4 (95–97%, 1.5 mL). This red-brown solution was characterized as follows: ^{1}H NMR (D_2SO_4) δ 2.21 (1 H, m, $w_{1/2}$ = 0.14 ppm, H_c), 3.59 (1 H, br d, J = 14 Hz, H_d), 4.41 (1 H, br dd, J = 11.3, 11.3 Hz, H_b), 4.56 (2 H, br s, H_g), 8.06 (2 H, dd, J = 7.2, 7.2 Hz, H_{meta}), 8.47 (4 H, d, J = 7.6 Hz, H_{ortho}, H_{para}).

Hydrolysis of Deuterated Dication 8. After being allowed to stand at 0 °C for 15 min, the solution of deuterated dication 8 prepared as above was hydrolyzed in the same way as the undeuterated material to produce purified monodeuterated sulfoxide 7 (6.2 mg, 68% yield): ^{1}H NMR ($CDCl_3$) δ 1.58 (1 H, br dd, J = 15.5, 12.4 Hz, H_d), 2.23 (1 H, br dd, J = 15.5, 2.5 Hz, H_c), 2.54 (0.88 H, br d, J = 12.9 Hz, H_b), 2.61 (0.64 H, ddd, J = 12.4, 12.3, 4.1 Hz, H_e), 3.00 (0.88 H, br d, J = 12.3 Hz, H_f), 3.71 (0.68 H, ddd, J = 12.9, 12.4, 3.3 Hz, H_g), 7.47 (1 H, dd, J = 8.1, 7.1 Hz, H_k), 7.71 (1 H, dd, J = 8.1, 7.4 Hz, H_h), 7.86 (1 H, dd, J = 7.1, 1.2 Hz, H_l), 7.94 (1 H, dd, J = 8.1, 1.2 Hz, H_j), 7.95 (1 H, dd, J = 8.1, 1.2 Hz, H_i), 8.51 (1 H, dd, J = 7.4, 1.2 Hz, H_g).

Preparation of ^{18}O-Labeled Sulfoxide 7 (X = H). To a sample of naphtho[1,8-*bc*]-1,5-dithiocin (30.7 mg, 0.132 mmol) dissolved in glacial acetic acid (4 mL) was added ^{18}O-labeled water (97% ^{18}O, 150 μL) followed by the bromine complex of 1,4-diazabicyclo[2.2.2]octane[23] (50 mg, 0.12 mmol). After the reaction mixture was stirred at room temperature for 2 h, the solvent was removed under vacuum and dichloromethane (20 mL) was added. The mixture was filtered and the filtrate evaporated to a yellow oil on a rotary evaporator and purified by preparative TLC, eluting with ethyl acetate, to yield ^{18}O-labeled sulfoxide 7 (X = H) (22 mg, 77% yield): IR (KBr) 991, 968 (S-^{18}O) cm^{-1}; MS m/e $^{12}C_{13}{}^{32}S_2{}^{16}O$:$^{12}C_{13}{}^{32}S_2{}^{18}O$ ratio, 0.16:99.90.

Formation and Hydrolysis of Dication 8 from ^{18}O-Labeled Sulfoxide 7 (X = H). A sample of ^{18}O-labeled sulfoxide 7 (X = H) (11.4 mg, 0.046 mmol) was dissolved in ice-cold concentrated sulfuric acid (95–98%, 1.5 mL). The resulting red-brown solution was allowed to stand in an ice-water bath for 15 min and then it was added dropwise to a vigorously stirring ice-cold saturated aqueous solution of sodium bicarbonate (75 mL). The colorless aqueous solution was extracted with dichloromethane (3 × 100 mL). The extracts were combined, dried ($MgSO_4$), concentrated on a rotary evaporator, and purified by preparative TLC, eluting with ethyl acetate, to produce sulfoxide 7 (X = H) (8.7 mg, 77% yield): IR (KBr) 1024, 1007 (S-^{16}O) cm^{-1}; MS m/e $^{12}C_{13}{}^{32}S_2{}^{16}O$:$^{12}C_{13}{}^{32}S_2{}^{18}O$ ratio, 100:1.14.

Reaction of Sulfoxide 7 (X = H) with ^{18}O-Enriched Sulfuric Acid Followed by Hydrolysis. ^{18}O-Enriched sulfuric acid was prepared by slowly adding ^{18}O-labeled water (97% ^{18}O, 167 mg) to fuming sulfuric acid (18–24% SO_3, 1.748 g) with ice-water cooling. This material is 95–97% sulfuric acid with 10.6% ^{18}O enrichment. A sample of sulfoxide 7 (X = H) (13.6 mg, 0.055 mmol) was dissolved in the ^{18}O-enriched sulfuric acid (1.91 g) prepared as above with ice-water cooling. After allowing the red-brown mixture to stand at 0 °C for 15 min, it was added dropwise to a vigorously stirring ice-cold saturated aqueous solution of sodium bicarbonate (100 mL). The mixture was worked up as before to afford sulfoxide 7 (X = H) (9.4 mg, 70% yield) after purification: IR (KBr) 1024, 1007 (S-^{16}O) cm^{-1}; MS m/e $^{12}C_{13}{}^{32}S_2{}^{16}O$:$^{12}C_{13}{}^{32}S_2{}^{18}O$ ratio, 100:0.13.

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Supplementary Material Available: Stereoscopic view of sulfoxide 7 (X = H) and the packing of the molecules in the unit cell and tables of final atomic positional and thermal parameters, bond lengths, bond angles, and selected torsion angle data (8 pages) (a listing of structure factor amplitudes is available from the authors). Ordering information is given on any current masthead page.

Cubanourea: A Cubane-Propellane

Philip E. Eaton* and Kakumanu Pramod

Department of Chemistry, The University of Chicago, Chicago, Illinois 60637

Richard Gilardi

Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, DC 20375

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Reaction of 1,2-diisocyanatocubane with limited amounts of water gives a propellane (2) in which a urea is fused to an edge of cubane. A suggestion for the unexpectedly ready formation of this new, strained ring system is given along with some of its chemistry. The structure of 2, determined by X-ray crystallography, is discussed in comparison of those of other ureas. Nitration of 2 gives the high-energy bisnitramine derivative, whose detailed structure is established by X-ray analysis.

Excellent methodology has been developed for the preparation of variously substituted cubanes.[1] This allows us to start with the cubane system, already an extraordinary structure, and move further in our continuing exploration of highly strained systems.[2] We report now on the synthesis and structure of a cubane derivative wherein

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