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CONFORMATIONAL ANALYSIS OF NAPHTHO[1,8-b,c]-1,5-DITHIOCIN AND ITS S-OXIDES IN SOLUTION

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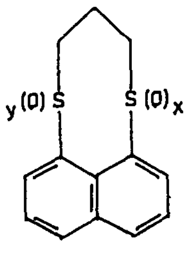
Abstract - The conformation and conformational barriers in dithioether 1: naphtho[1,8-*b*,*c*]-1,5-dithiocin were determined in solution by ^{1}H and ^{13}C NMR spectroscopic analysis and AM1 semiempirical computations. In solution the chair conformer of dithioether 1 is 0.6 kcal/mol lower in energy than the boat conformer. The barriers for chair-to-chair ring inversion and chair-to-boat conversion in this compound are 8.9 kcal/mol and 7.9 kcal/mol, respectively. Monosulfone 3, disulfoxide 4, and sulfoxide-sulfone 5, adopt the chair conformation in solution in contrast to their boat conformation in the solid state. In solution the chair conformation for 3-5 with equatorial sulfoxides is more stable than either the chair conformation with axial sulfoxides or the boat conformers by at least 1 kcal/mol. The barrier for chair-to-chair ring inversion for monosulfone 3 has been determined to be 10.8 kcal/mol. In solution, disulfone 6 appears to adopt either a boat or chair conformation in contrast to the twist conformation in the solid state. The maximum barrier for ring inversion of 6 is 7 kcal/mol. New evidence for the geometry of the transition state for the ring inversion is presented.

The effects of heteroatom substitution on the conformation of medium-sized rings has long been of interest in the study of transannular interactions between heteroatoms in the ring.[1] Conformational analysis of the parent hydrocarbon and some of its derivatives has been reported.[2-7] In the preceding paper, the effects of 1,5-heteroatom substitution and substituents attached to the heteroatom on the conformational behavior of an eight-membered ring *peri*-fused to a naphthalene ring have been explored in the solid state;[8] monosulfone 3, disulfoxide 4, sulfoxide-sulfone 5, and disulfone 6 were found to adopt a distorted boat, a boat with diequatorial sulfoxides, a boat with equatorial sulfoxide and a twist conformer, respectively. In the solid state dithioether 1 preferentially adopts a chair conformation as previously reported.[9]



1, x=y=0 4, x=y=1
2, x=1, y=0 5, x=2, y=1
3, x=2, y=0 6, x=y=2

In this paper, conformational analysis of dithioether 1, monosulfone 3, disulfoxide 4, sulfoxide-sulfone 5, and disulfone 6 in solution are reported. Variable temperature NMR studies provided insight into the barriers for ring inversion, the relative energies of conformers and the barrier for interconversion of the chair and boat forms of dithioether 1, data which was unavailable from the previous solid-state studies. In contrast to the usual correspondence between solid-state structure and predominant conformation in solution, the lowest energy conformer of monosulfone 3, disulfoxide 4, sulfoxide-sulfone 5 and disulfone 6 in solution is not that found in the solid-state. This phenomenon was reported before for monosulfoxide 2[10] and 1,6-dithiacyclodecane.[11]

RESULTS AND DISCUSSION

A. Dithioether 1

The conformation of dithioether 1 in solution was determined by dynamic ^1H and ^{13}C NMR spectroscopy. At room temperature the ^1H NMR spectrum of 1 showed only two unique protons. Chair conformation 1A has four nonequivalent hydrogen atoms as seen in Figure 1. However, ring inversion of 1A affords chair conformation 1A' in which H_a and H_b are interchanged as well as H_c and H_d. Thus, if ring inversion is rapid between chair conformation 1A and 1A' only two unique protons will be observed Similarly boat conformation 1B has four nonequivalent hydrogen atoms. But, if ring inversion to 1B' is fast on the NMR time scale, only two unique hydrogen

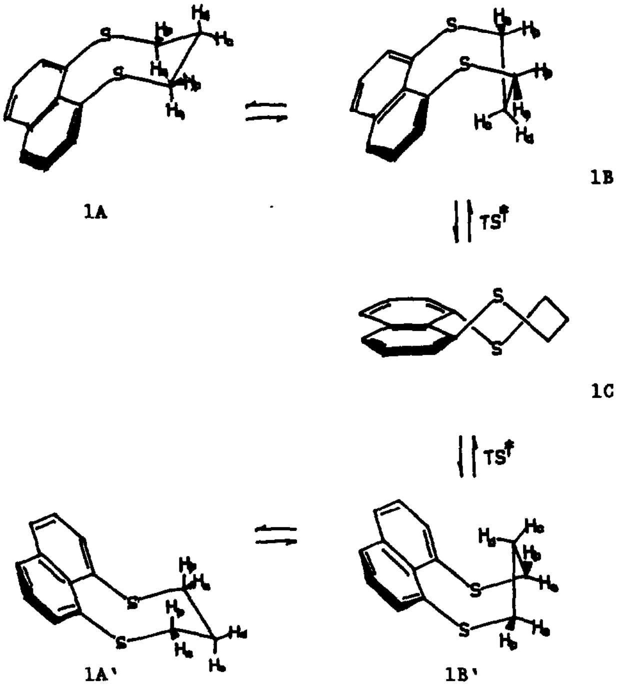
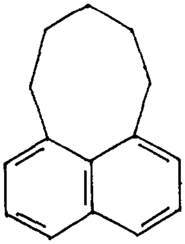


Figure 1.

atoms will be observed. The mechanism for ring inversion and the conformational minima shown in Figure 1 are based on the analysis of Kamada *et al.*[3-8] who studied 8,9,10,11-tetrahydro-7H-



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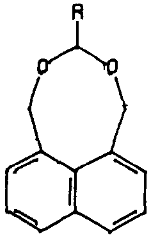
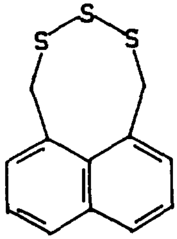


8a, R=H
b, R=tBu



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cyclooctane[*d*,*e*]naphthalene 7 and its derivatives.[3-6] For these compounds the boat conformation predominates in solution. The higher energy of the chair conformer compared with the boat was attributed to the additional eclipsing interactions between the hydrogen atoms on the "peri" carbon atoms and the hydrogen atoms of the adjacent CH_2 units. Note that the eclipsing interactions in the chair form which are absent in the boat form in which these hydrogen atoms are staggered is just the opposite of the situation for chair and boat conformations of cyclohexane. These eclipsing interactions are eliminated in 1, 8, and 9 with the consequence of stabilizing the chair conformer relative to boat as observed. Thus both conformers are observed in solution for 8 and 9,[12-14] and in the solid state, the chair conformer was found for 1[9] and 8b. Dynamic ^1H NMR spectroscopic studies on 7 and its derivatives revealed that ring inversion is rapid.[6-8,14] The energy barriers for ring inversion and boat-chair interconversion of dithioether 1 were determined by variable temperature ^1H and ^{13}C NMR spectroscopic studies. The results are summarized in Table I.

The coalescence in the ^1H NMR spectrum at 190 K ($\Delta G^\ddagger$ = 8.9 kcal/mol) is due to boat to boat or chair to chair ring inversion (1B ⇌ 1B' or 1A ⇌ 1A') because the free energy difference between the equilibrating species is zero and the ^{13}C NMR spectrum shows no coalescence at or above this temperature. The latter point is important because coalescence of the boat to boat or chair to chair ring inversion should not be detected by ^{13}C NMR spectroscopy since the C(6), C(7), and C(8) carbons in 1B or 1A are equivalent to the C(6), C(7), and C(8) carbons in 1B' or 1A', respectively. The ^1H NMR spectrum below the 190 K coalescence temperature showed four unique aliphatic protons. This eliminates the twist conformer as the lowest energy conformation because there would be only three unique aliphatic protons in this conformer owing to its C_2 symmetry. The assignments of these protons are given in the Experimental Section. The photoelectron spectrum of dithioether 1A showed a 1.6-2.0 eV splitting between the sulfur lone pairs. This is also in accord with the boat or the chair conformers being the lowest energy conformations, and consistent with the twist conformation having no significant population because the sulfur lone pairs would not overlap enough in the twist conformation to give such a large splitting.

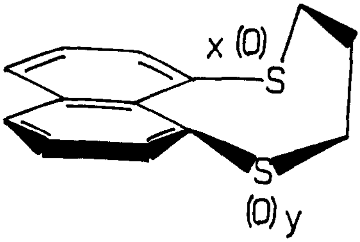
Table I. Results of Variable Temperature ^1H and ^{13}C NMR Spectroscopy.

Cmpd	*Solvent*	T_c(K)[a]	$\Delta G^‡$(kcal/mol)[b,c]	ΔG(kcal/mol)[d]
1[e]	CD_2Cl_2/ vinyl chloride	190	8.9	0
1[f]	CD_2Cl_2/ vinyl chloride	175	7.9	0.6
3[e]	CD_2Cl_2	227	10.8	0

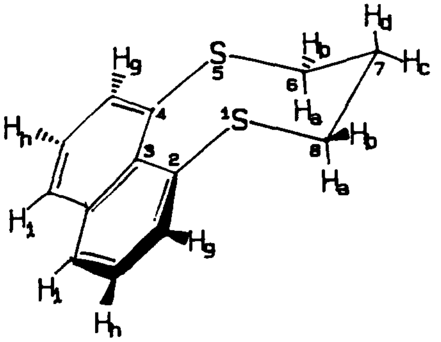
[a] T_c = coalescence temperature
[b] $\Delta G^‡$ = transition state energy barrier
[c] The energy barriers were calculated using the equation below:[15]
$\Delta G^‡/RT_c = 22.96 + \ln[T_c/\Delta\nu]$
$\Delta\nu$ = separation of peaks in Hz.
The reported $\Delta G^‡$'s and T_c's are averages of the two coalescences, [(H_a, H_b) and (H_c, H_d)] for compound 1, and averages of the three coalescence temperatures for compound 3 [(H_a, H_b), (H_c, H_d), (H_e, H_f)]
[d] ΔG = free energy difference between coalescing species
[e] Results from variable temperature ^1H NMR spectroscopic studies
[f] Results from variable temperature ^{13}C NMR spectroscopic studies

The coalescence at 175 K ($\Delta G^‡$ = 7.9 kcal/mol) in the ^{13}C NMR spectrum can be assigned to an equilibrium between the chair and boat conformers, **1A** and **1B**. Coalescence of this equilibrium was not seen in the ^1H NMR low temperature spectrum presumably because of the lower temperature needed to observe coalescence in ^1H as compared to ^{13}C NMR spectroscopy,[15] and because temperatures lower than about 160 K are difficult to obtain with the spectrometer used. Integration of the peaks corresponding to the boat and chair conformers in the ^{13}C NMR spectrum below 175 K showed that one conformer was 0.6 kcal/mol lower in energy than the other conformer, but no data were obtained that could unambiguously assign the lowest energy conformer to either a boat or a chair conformation. Consequently, AM1 (Austin Model 1) semiempirical molecular orbital calculations[9,16] with an updated version of sulfur parameters[17] were used to determine the conformational potential energy surface of dithioether **1** in the gas phase. The results of the AM1 calculations are that the relative energies of chair conformer **1A**, boat conformer **1B**, and twist conformer **1C** are 0.0, 0.5, 6.7 kcal/mol, respectively. In addition the energies of activation ($\Delta G^{\neq}$) for converting chair **1A** to boat **1B**, chair **1A** to twist **1C**, and boat **1B** to twist **1C** are 8.5, 10.4, and 9.9 kcal/mol respectively; for chair ring inversion (**1A** → **1A'**) and boat ring inversion (**1B** → **1B'**) 10.4 and 9.9 kcal/mol, respectively.

The AM1 calculations and the variable temperature NMR spectroscopic data give very similar potential surfaces for dithioether **1A**. AM1 predicts the chair conformation to be more stable than the boat conformer by 0.5 kcal/mol and to be more stable than the twist conformer by 6 7 kcal/mol. This is consistent with the NMR spectroscopic data which show a 0.6 kcal/mol difference between the boat and chair conformers and do not give any evidence for the twist conformer. The computational and experimental energies of activation are also in agreement since AM1 predicts 8.5 kcal/mol and 10.4 kcal/mol for the chair to boat conversion and the chair to chair ring inversion processes, respectively, while the NMR spectral data show 7.9 and 8.9 kcal/mol for these activation energies respectively. The transition state for the ring inversion **10a**, as calculated by AM1, is very close in structure to the accepted transition state[6-8,14] for inversion of 7 and its derivatives. It should be noted that this "transition state" was found by rotating the C(2)-S(1)-C(8)-C(7) and S(1)-C(8)-C(7)-C(6) torsional angles by 5-10° intervals and allowing the other parameters in the eight-membered ring to relax. No attempt was made to find the formal transition state with fully optimized parameters and one negative eigenvalue. The calculations showed that there is a direct pathway from boat conformer 1B to 1B' via transition state **10a**. The potential energy surface was downhill from **10a** to either the twist conformer 1C or to the other boat conformer 1B'. Thus the AM1 results show that boat 1B can invert to boat 1B' directly, or through twist conformer 1C, and both pathways have comparable energy barriers.



10a, x=y=0
b, x=2, y=0
c, x=0, y=2

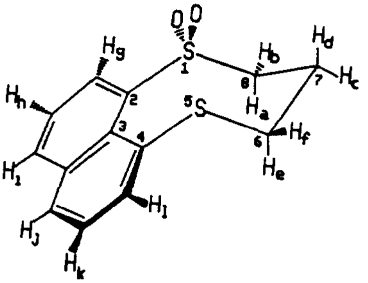


In summary, substitution of the methylene groups at the peri positions for sulfur atoms stabilizes the chair conformation relative to the boat conformation, as compared to the hydrocarbon analogues, such that both conformers are significantly populated in solution and in the gas phase as determined by dynamic ^1H and ^{13}C NMR spectroscopy, and AM1 calculations.

B. Monosulfone 3

The conformation of monosulfone 3 in solution was analyzed by ^1H and ^{13}C NMR spectroscopy. At room temperature the ^1H NMR spectrum showed only three unique aliphatic proton resonances. This result can be accounted for in the same way as in the case of dithioether 1, that is, the chair or two boat conformers rapidly interconvert by ring inversion. Since the hydrogen atoms α to the thioether sulfur are not equivalent to the hydrogen atoms α to the sulfone sulfur in 3 there are three unique aliphatic proton resonances in monosulfone 3 but only two such absorbances in dithioether 1. By variable temperature ^1H NMR spectroscopy the barrier for ring inversion was determined to be 10.8 kcal/mol as reported in Table I. This barrier can be assigned to the chair to chair or boat to boat ring inversion since there is zero free energy difference between the equilibrating species and since there is a lack of coalescence in the ^{13}C NMR spectrum of monosulfone 3 at or above 227 K which is the coalescence temperature observed in the ^1H NMR spectrum of this compound. The barrier for ring inversion in monosulfone 3 is 1.9 kcal/mol higher than that in dithioether 1. This is consistent with increased steric strain in the transition state 10b for ring inversion in 3 due to the close proximity of the endodentate oxygen and endodentate hydrogen atom α to the thioether sulfur atom, or in transition state 10c due to the close proximity of the endodentate oxygen and endodentate hydrogen atom on C(7). Thus S-O...C-H interactions increase the energy of the transition state of 3 (10b,c) more than the ground state of 3 causing the increased barrier in 3 relative to 1.

The ^1H NMR spectrum of monosulfone 3 below 227° K showed six unique aliphatic protons and the assignments are given in the Experimental Section and Supplementary Material. The twist conformation for monosulfone 3 is eliminated as the lowest energy conformer based on the following observation. One of the β protons of this low temperature spectrum has three large coupling constants (H_d in 3A) while the other β proton has only one large coupling constant (H_c in 3A). This is consistent only with a boat or a chair conformation since in the twist conformation each β proton would have two large coupling constants. The conformation of monosulfone 3 was determined to be the chair conformer 3A from the results of an aromatic induced shift experiment in toluene-d_8 listed in Table II in the Experimental Section. A collision complex is envisioned as being formed between the electron rich face of toluene and the electron deficient concave side of the sulfone molecule (side opposite protruding S-O bonds). This results in greater shielding of the β equatorial proton (H_c in 3A)[18] over the β axial proton (H_d in 3A), and about equal shielding of the α protons and the γ protons. These shieldings are consistent with those expected for the chair conformer, whereas the boat conformer would give the exact opposite results for the equatorial and axial hydrogens. That is, there would be a greater shielding of the α-equatorial over α-axial protons and a greater shielding of β-axial over the β-equatorial protons in a collision complex with the boat conformers. Further support for the chair conformation 3A is provided by the relatively small difference in chemical shift of 0.42 ppm between H_c and H_d in CD_2Cl_2.[19] The chair conformer 3A is at least 1.0 kcal/mol lower in energy than the boat conformer 3B since no averaging of the magnitude of the coupling constants is observed in protons H_a and H_b, H_c and H_d, or H_e and H_f. Variable temperature ^{13}C NMR spectroscopy from 253 to 153 K showed no coalescenece of peaks in the carbon spectrum which further supports the conclusion that the chair conformer predominates by at least 1 kcal/mol.

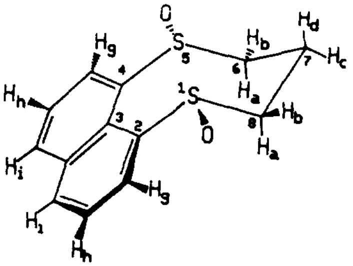


3A

The ^{1} NMR spectrum of monosulfone 3 also shows that the conformation is not a perfect chair. The sulfone inner oxygen is twisted away from the sulfide sulfur lone pair to the extent that the proton pairs (H_b, H_d), (H_a, H_c) and (H_c, H_f), as assigned in the chair conformer **3A**, have torsional angles of about 90° (deduced from the Karplus equation).[15] This is evident from the ^{1}H NMR spectrum because these pairs of protons are not coupled to each other even though they are attached to adjacent carbons. Thus in solution, as in the solid state, monosulfone 3 twists its conformation to avoid the steric interaction of the sulfur moieties.

C. Disulfoxide 4

The conformation of disulfoxide 4 in solution was determined to be chair by ^{1}H and ^{13}C NMR spectroscopy. At room temperature the ^{1}H NMR spectrum of 4 showed four unique protons. Thus there is only one conformer in solution. The spectroscopic assignments are given in the Experimental Section and Supplementary Material. The evidence that the conformation of 4 in solution is chair conformer **4A** is similar to that obtained for the chair conformer of sulfoxide 2 in solution presented in detail elsewhere[10] and is delineated in the Supplementary Material.

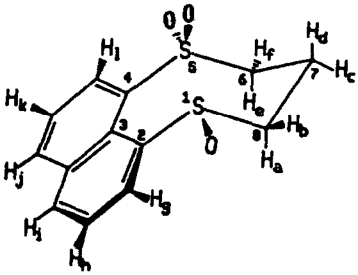


4A

The ^{1}H NMR spectrum of disulfoxide 4 was essentially unchanged from 153-393K. Proton pairs (H_a, H_b), (H_c, H_d) show no magnetic equivalence as they did for dithioether 1. This nonequivalency occurs because ring inversion (see Fig. 1) does not produce equivalent chair conformers. Ring inversion converts the more stable equatorial sulfoxides to the less stable axial sulfoxides. This is in contrast to the relative energy of the chair conformers of the six-membered ring sulfoxide, thiane-1-oxide. In this case the axial sulfoxide conformer is more stable than the equatorial[20,21] owing to attractive interaction between the axial oxygen atom and syn-axial hydrogen atoms. However, the axial oxygen atoms in 4 are endodentate and repel each other (sterically and electrostatically). The energy barrier for the ring inversion in 4 should be about 11 kcal/mol, since the barrier of this process for monosulfone 3 is 10.8 kcal/mol. The absence of coalescence in 4 from 153-393 K is evidence that the chair conformer **4A** with equatorial oxygens is more than 3 kcal/mol lower in energy than the chair conformer with axial sulfoxide oxygens. This is consistent with ab initio calculations on model compounds which showed the axial sulfoxide to be about 8 kcal/mol higher in energy than the equatorial sulfoxide.[22] The chair conformer **4A** is at least 1 kcal/mol lower in energy than the boat conformer **4B** since no averaging of the magnitude of the coupling constants is observed in protons H_a and H_b or H_c and H_d. The observation of a single species over the temperature range of 153-393 K further supports the predominance of 4A over 4B.

D. Sulfoxide-Sulfone 5

The conformation of sulfoxide-sulfone 5 in solution was determined by ^1H and ^{13}C NMR spectroscopic analysis. At room temperature the ^1H NMR spectrum of this compound showed absorption due to six unique protons. Thus there is only one conformer in solution. The assignments of these signals are given in the Experimental Section and Supplementary Material. The evidence that the conformation of 5 in solution is chair conformer 5A is analogous to that presented for the chair conformer of disulfoxide 4 and is delineated in the Supplementary Material.



5A

The ^1H NMR spectrum of sulfoxide-sulfone 5 was essentially unchanged from 153-393K. Proton pairs (H_a, H_b), (H_c, H_d) and (H_e, H_f) show no magnetic equivalence as they did for dithioether 1. This nonequivalence occurs because ring inversion (see Fig. 1) does not produce equivalent chair conformers. Rather ring inversion converts the more stable equatorial sulfoxide to the less stable axial sulfoxide analogous to the situation with disulfoxide 4. Since only one species can be detected in the NMR spectra of compound 5 over the full temperature range (153-393°K) the equatorial sulfoxide must be populated to the exclusion of the axial sulfoxide, requiring an energy difference of at least 3 kcal/mol. In addition chair conformer 5A must be more stable than the corresponding boat conformer by more than 1 kcal/mol in solution, because of the large difference in the magnitude of the coupling constants in protons H_a and H_b, H_c and H_d, and H_e and H_f.

That monosulfoxide 2,[10] disulfoxide 4, and sulfoxide-sulfone 5 exist in the boat conformation in the solid state and in the chair conformation in solution is evidence that the boat and chair conformers of these compounds are close in energy, as they are for dithioether 1. This is expected when comparing these compounds to 7 and its derivatives, 8 and 9 because some of the eclipsing interactions in the hydrocarbon analogues are absent in monosulfoxide 2, disulfoxide 4, and sulfoxide-sulfone 5 and other eclipsing interactions are ameliorated by the longer C-S bonds as compared to the C-C bonds in 7 and its derivatives. The boat conformation is favored in the crystalline state presumably because of packing forces. The crystals pack more efficiently with the boat conformation. The boat conformer allows two naphthalene rings to stack on top of each other, with the saturated three carbon bridges (C(6)-C(7)-C(8)) on each molecule pointing away from each other. In the chair conformation the three carbon bridges would have close steric interference with each other.

This can be seen by comparing the packing of the unit cell of monosulfoxide 2 which adopts the boat conformation[10] with the unit cell of dithioether 1 which adopts the chair conformation.[9]

The conformational assignment for disulfoxide 4 and sulfoxide-sulfone 5 in solution are based in part on the lanthanide-induced shift changes. This engenders the concern that the lanthanide affects the boat-chair equilibrium.[23] However, it is deemed unlikely that the boat conformation predominates in the absence of the lanthanide shift reagent because the NMR spectroscopic results in the absence of the reagent and also the shifts induced by benzene all suggest a predominance of the chair conformation as discussed above.

E. Disulfone 6

The conformation of disulfone 6 in solution was determined by ^1H and ^{13}C NMR spectroscopy. At room temperature the ^1H NMR spectrum showed only two unique aliphatic protons. This result requires ring inversion and this process was investigated by variable temperature NMR spectroscopy. On cooling, the absorption due to the aliphatic protons in the ^1H NMR spectrum of 6 broadened beginning at 198K, but coalescence was not achieved on cooling to 153K which was the lowest temperature obtainable in this study. The ^{13}C NMR spectrum for 6 showed no coalescence at or above 153K. The predominant conformer in solution for 6 is tentatively assigned as either the boat or chair conformer. The ^1H NMR spectrum of 6 suggests that the twist conformer can be eliminated because all of the aliphatic protons broaden in the 198-153K temperature range. The β-hydrogen atoms are equivalent in the twist conformer which has C_2 symmetry so that there should not be any broadening or coalescence of these protons if the predominant conformation of 6 in solution is the twist conformer. The maximum barrier for ring inversion in 6 is 7 kcal/mol which is more than 1.9 kcal/mol lower than that in dithioether 1. This may be due to the considerable steric and electrostatic strain in the ground state of disulfone 6 from destabilizing S-O...S-O interactions which are ameliorated in the transition state structure for ring flipping of 6. The ground state of disulfone 6 would be considerably destabilized relative to dithioether 1 (note the considerably greater nonbonded S...S distance in disulfone 6 than in dithioether 1), but the energies of the transition state geometries for 1 and 6 would be closer in energy relative to these ground state energies because of the relief of the S-O...S-O strain in the transition state of 6. Thus the inversion barrier for disulfone 6 would be lower than this barrier for 1.

CONCLUSIONS

Dithioether 1 has the same chair conformation in solution and in the solid state. Monosulfone 3, disulfoxide 4, and sulfoxide-sulfone 5, however, adopt the chair conformation in solution even though all are in the boat conformation in the solid state. Disulfone 6, appears to prefer either the boat or chair conformation in solution but adopts the twist conformation in the solid state. This emphasizes the danger in inferring conformations in solution based on x-ray crystallographic data.

The barrier to ring flipping in solution for compounds 1, 3, and 6 is 8.9, 10.8 and <7 kcal/mol respectively. The transition state geometry 10a-c for the ring flipping is consistent with the magnitude of these barriers as S-O...C-H interactions will destabilize the transition state of 3 (10b,c) increasing the barrier relative to 1, and as repulsive S-O...S-O interactions in the ground state of 6 lower this barrier relative to 1. AM1 calculations further support 10a-c as the transition state geometry for this barrier.

EXPERIMENTAL SECTION

Dithioether 1,[9] monosulfone 3,[2] disulfoxide 4,[2] sulfoxide-sulfone 5,[2] and disulfone 6[2] were prepared as previously reported. ^{1}H NMR spectra at 250 MHz and ^{13}C NMR spectra at 62.9 MHz were recorded on a Bruker WM-250 FT NMR Spectrometer with 0.368 Hz/Pt digital resolution using a 5 mm tube and tetramethylsilane as the internal reference. The deuterated solvent shown for each compound was used to lock the instrument. All spectra were recorded at ambient temperature unless specified otherwise. The Austin Model 1 (AM1) molecular orbital method was used for the semiempirical calculations (AMPAC program; QCPE-506). All deuterated solvents and lanthanide shift reagent were obtained from Aldrich Chemical Company, Milwaukee, WI and were used as delivered. The shift reagent was kept and used under anhydrous conditions. Assignments of the protons for the ^{1}H NMR spectra of compounds 1, 3-5 are described in the Supplementary Material.

Dithioether 1: ^{1}H NMR ($CDCl_3$) δ 1.85 (2H, pentuplet, *J*=6 Hz, H_c and H_d), 3.02 (4H, t, *J*=6 Hz, H_a and H_b), 7.38 (2H, dd, *J*=8, 8 Hz, H_h), 7.75 (2H, dd, *J*=1, 8 Hz, H_g), 7.97 (2H, dd, *J*=1, 8 Hz, H_i); low temperature ^{1}H NMR at 153°K (CD_2Cl_2/vinyl chloride) δ 1.20 (1H, ddd, *J*=13, 13, 13 Hz, H_d), 1.84 (1H, d *J*=13 Hz, H_c), 2.78 (2H, dd, *J*=13, 13, Hz, H_a), 3.18 (2H, d, J=13 Hz, H_b), 7.37 (2H, m, H_h), 7.90 (4H, m, H_g and H_i); low temperature ^{13}C NMR at 150°K (CD_2Cl_2) δ139.6, 131.6, 125.8, 37.0, 24.4; low temperature ^{13}C NMR (CD_2Cl_2) δ (aliphatic carbons) 38.0 (0.28 carbons), 35.5 (1.72 carbons), 26.6 (0.16 carbons), 22.2 (0.84 carbons).

Table II. Aromatic Solvent[a] Data for Monosulfone 3

proton	$\delta(C_7D_8)$	$\delta(CDCl_3)$	$\Delta\delta$
H_a	3.44	3.99	-0.55
H_b	3.15	3 73	-0.58
H_c	1.09	2.34	-1.25
H_d	1.09	1.92	-0.83
H_e	1.84	2.75	-0.91
H_f	2.15	3.01	-0.86
H_g	8.65	8.60	+0.05
H_h	7.10	7.60	-0.50
H_i	7.51	8.12	-0.61
H_j	7.83	8.09	-0.26
H_k	7.04	7.52	-0.48
H_l	7.44	8.00	-0.56

[a]Toluene-d_8 was used as solvent

Monosulfone 3: ^{1}H NMR ($CDCl_3$) δ 2.22 (2H, pentuplet, *J*=6 Hz, H_c and H_d), 2.93 (2H, t, *J*=6 Hz, H_e and H_f), 3.87 (2H, t, *J*=6 Hz, H_a and H_b), 7.50 (1H, dd, *J*=8, 8 Hz, H_k), 7.59 (1H, dd, *J*=8, 8 Hz, H_h), 7.96 (1H, dd, *J*=1, 8 Hz, H_l), 8.09 (1H, dd, *J*=1, 8 Hz, H_j), 8.12 (1H, dd, *J*=1, 8 Hz, H_i), 8.73 (1H, dd, *J*=1, 8 Hz, H_g); low temperature ^{1}H NMR at 193° K (CD_2Cl_2) δ 1.92 (1H, dddd, *J*=15, 13, 13, 5 Hz, H_d), 2.34 (1H, ddd, *J*=15, 6, 6 Hz, H_c), 2.75 (1H, ddd, *J*=13, 13, 6 Hz, H_e), 3.01 (1H, dd, *J*=13, 5 Hz, H_f), 3.73 (1H, dd, *J*=13, 5 Hz, H_b), 3.99 (1H, dd, *J*=13, 13 Hz, H_a), 7.52 (1H, dd, *J*=8, 8 Hz, H_k), 7.61 (1H, dd, *J*=8, 8 Hz, H_h), 8.00 (1H, dd, *J*=1, 8 Hz, H_l), 8.09 (1H, dd, *J*=1, 8 Hz, H_j), 8.12 (1H, dd, *J*=1, 8 Hz, H_i), 8.60 (1H, dd, *J*=1, 8 Hz, H_g).

Disulfoxide 4: ^{1}H NMR ($CDCl_3$) δ 1.26 (1H, ddddd, *J*=15, 13, 13, 4, 4 Hz, H_d), 2.05 (1H, ddddd, *J*=15, 4, 4, 4, 4 Hz, H_c), 2.58 (2H, ddd, *J*=13, 4, 4 Hz, H_b), 3.72 (2H, ddd, *J*=13, 13, 4 Hz, H_a), 7.74 (2H, dd, *J*=8, 8 Hz, H_h), 8.04 (2H, dd, *J*=1, 8 Hz, H_i), 8.34 (2H, dd, J=1, 8 Hz, H_g).

Table III. **Aromatic Solvent[a] and Europium Induced Shift Data for Disulfoxide 4.**

proton	$\delta(CDCl_3)$	$\delta(C_6D_6)$	$\Delta\delta$	δ + 0.16 equiv of Eu(fod)$_3$ (CDCl$_3$)	Eu(fod)$_3$ induced relative upfield shift,$\Delta\delta$
H_a	3.72	2.75	-0.97	4.45	0.73
H_b	2.58	1.87	-0.71	3.98	1.40
H_c	2.05	0.56	-1.49	2.41	0.36
H_d	1.26	0.38	-0.88	2.11	0.85
H_g	8.34	8.51	+0.17	9.80	1.46
H_h	7.74	7.18	-0.56	7.97	0.23
H_i	8.04	7.38	-0.66	8.31	0.27

[a]Benzene-d_6 was used as solvent

Table IV. Aromatic Solvent[a] and Europium Induced Shift Data for Sulfoxide-sulfone 5.

proton	$\delta(CDCl_3)$	$\delta(C_6D_6)$	$\Delta\delta$	δ + 0.12 equiv of Eu(fod)$_3$ (CDCl$_3$)	Eu(fod)$_3$ induced relative upfield shift, $\Delta\delta$
H_a	3.89	3.20	-0.69	4.82	0.93
H_b	2.64	2.10	-0.54	4.27	1.63
H_c	2.35	0.88	-1.47	2.64	0.29
H_d	2.07	1.09	-0.98	2.64	0.57
H_e	3.61	2.63	-0.98	3.80	0.19
H_f	3.33	2.25	-1.08	3.58	0.25
H_g	8.65	8.63	-0.12	10.84	2.19
H_h	7.87	7.21	-0.66	8.07	0.20
H_i	8.16	7.30	-0.86	8.34	0.18
H_j	8.33	7.39	-0.94	8.47	0.14
H_k	7.73	6.88	-0.85	7.88	0.15
H_l	8.63	8.98	+0.35	8.84	0.21

[a]Benzene-d_6 was used as solvent

Sulfoxide-sulfone 5: ^{1}H NMR (CDCl$_3$) δ 2.07 (1H, ddd, J=16, 13, 13 Hz, H_d), 2.35 (1H, d, *J*=16 Hz, H_c), 2.64 (1H, d, *J*=13 Hz, H_b), 3.33 (1H, m, *J*=13 Hz, H_f), 3.61 (1H, ddd, *J*=13, 13, 4 Hz, H_e), 3.89 (1H, ddd, *J*=13, 13, 3 Hz, H_a), 7.87 (1H, dd, *J*=8, 8 Hz, H_h), 7.73 (1H, dd, *J*=8, 8 Hz, H_k), 8.33 (1H, dd, *J*=1, 8 Hz, H_j), 8.16 (1H, dd, *J*=1, 8 Hz, H_i), 8.63 (1H, dd, *J*=1, 8 Hz, H_l), 8.65 (1H, dd, *J*=1, 8 Hz, H_g).

Disulfone 6: ^{1}H NMR (CDCl$_3$) δ 2.72 (2H, pentuplet, *J*=7 Hz, H_c and H_d), 4.33 (4H, t, *J*=7 Hz, H_a and H_b), 7.68 (2H, dd, *J*=8, 8 Hz, H_h), 8.12 (2H, dd, *J*=1, 8 Hz, H_i), 8.60 (2H, dd, *J*=1, 8 Hz, H_g).

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Supplementary Material Available: A detailed analysis of the NMR spectroscopic assignments for 1,3-5 and conformational analysis of 4 and 5 is available from the authors

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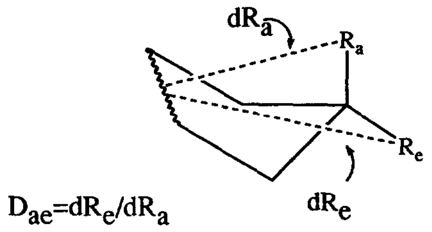
18. Anet, F.A.L., *Tetrahedron Lett.*, **1990**, in press. Recently Anet has proposed general definitions for substituent positions for tetracoordinated atoms in cyclic compounds. In this definition one considers a five-atom chain in the ring with the substituents in question on the central carbon. The 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 1-6 the ratio D_{ae} is between 1.3-1.4 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 in **2**, **4**, and **5** and oxygen pairs of the sulfone moieties in **3** and **6**. Thus according to the above definition, the aliphatic protons and sulfoxide oxygen or sulfone oxygens can be unambiguously assigned as axial or equatorial.

19. In boat conformations, e.g. **1B**, the distance between the axial hydrogen, H_c, and C(9) on the naphthalene ring is 2.6Å, while the distance between equatorial H_d and C(9) is 4.5Å, (using molecular models). Using the analysis developed by Kamada *et al.*[3] 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, e.g. **1A**, the distance between H_c and H_d and C(9) is about 5Å. 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 than boat conformers.
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