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Computational Study of Ring Strain in 1,3,2-Dioxathiolane, its 2-Oxide and its 2,2-Dioxide

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The strain energies in the five-membered rings 1,3,2-dioxathiolane (**1**), its 2-oxide (**2**) and 2,2-dioxide (**3**) have been evaluated using B3LYP and QCISD(T)//MP2 calculations and the standard 6-31G* basis set. Two different models have been used, one based on an isodesmic reaction involving methane and ethane, and one applying the chair-form of cyclohexane as a strain-free reference. Thermally corrected strain energies obtained by B3LYP and with cyclohexane as a reference are 10.1, −1.3 and 5.8 kcal mol^{-1} for **1**, **2** and **3**, respectively. The corresponding values obtained by QCI calculations are 8.1, −2.1 and 4.4 kcal mol^{-1}, respectively. The negative value for **2** is interpreted in terms of absence of destabilizing interactions present in **1** and **3**.

Over recent years cyclic sulfites and cyclic sulfates have entered the mainstream of organic synthesis as important supplements to epoxides.[1] The main reason for the increased popularity is the development of catalytic asymmetric dihydroxylation of alkenes, where a wide array of alkenes are smoothly converted into the corresponding diols with good to excellent enantioselectivity.[2–9] These diols can be converted into cyclic sulfites and cyclic sulfates without any loss of enantiomeric purity. Like the epoxides, cyclic sulfites and cyclic sulfates have two carbon centres available for nucleophilic attacks. The R–O–S(O)–O– moiety in the five-membered cyclic sulfites, and the R–O–S(O)$_2$–O– moiety in the cyclic sulfates are good leaving groups, in contrast to the poor RO– leaving group of epoxides. The nucleophilic attack, proceeding without catalysts, produces a sulfate or a sulfite monoester which can easily be hydrolysed to a functionalized alcohol as with an epoxide. Several review articles on their reactivities are found in the literature.[1,10–14]

The very good leaving group ability of the R–O–S(O)$_2$–O– moiety makes five-membered cyclic sulfates very reactive. Some kind of strain effects may be involved, since the relative order of reactivity towards alkaline hydrolysis is five-membered ≫ six-membered > open-chain analogues, and the difference in enthalpy of the hydrolysis for dimethyl sulfate and ethylene sulfate is found to be 5.7 kcal mol^{-1}.[15]

According to Davis[16] the relative order of reactivity in the alkaline hydrolysis of cyclic sulfites is: five-membered > six-membered and open-chain analogues, since ethylene sulfite is 100–1000 times more reactive in base than the dimethyl sulfite, which resembles that of trimethylene sulfite. The origin of this kinetic acceleration of the cyclic sulfite esters has been the subject of much speculation, and was originally thought to arise from some kind of ring strain.[17] According to Davis[16] there is no ring strain in ethylene sulfite, since the heat of alkaline hydrolysis of this compound and the open-chain analogue, dimethyl sulfite, is essentially the same. So, the observed kinetic acceleration for sulfite esters has been attributed to differences in the entropy of activation, 'entropy strain'.[18] The argument has been as follows: the open chain and larger ring sulfites have relatively mobile forms, whereas the five-membered cyclic sulfites like ethylene sulfite have a relatively rigid structure. In the transition state for hydrolysis, these mobile-form molecules take up a more ordered structure and the molecular motions of alkyl and larger-ring sulfites are suppressed. This loss of entropy increases the free energy of activation. However, the five-membered cyclic sulfites are already constrained, and far less energy is required to reach the transitions state, which results in a much lower free energy of activation. The exchange reaction of ethylene sulfite and methanol has been investigated by Davis[16] and by Bristow and Tillett.[19] The existence of an open-chain methyl ester and its facile cyclization to the sulfite supports the argument that the five-membered cyclic sulfite ring is not strained. The reactivity of cyclic sulfites has been extensively reviewed by Tillett.[13]

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To our knowledge only a few structures of cyclic sulfites have been determined: ethylene sulfite[20] and 1,2-dimethyl-1,2-ethanediol sulfite[21] by electron diffraction, and (*R,R*)-1,2-diphenyl-1,2-ethanediol sulfite by X-ray crystallography.[10]

The main purpose of the present study is to obtain by computational methods an estimate of strain energy in the cyclic species **1**–**3** using different models for evaluation of ring strain. Our results may thus contribute to a clarification of the forces determining the reactivities of these compounds.

As shown below, the acyclic species dimethyl sulfoxylate (**4**), dimethyl sulfite (**5**) and dimethyl sulfate (**6**) which enter the isodesmic reactions may have different geometric forms. The relative energies of these forms play an important role in the interpretation of our results for the strain energies. Accordingly we also present their geometries and relative energies.

Computations

The geometries of all the species were optimized by density functional theory (DFT)[22] and by MP2 calculations.[23] In the DFT calculations we used Becke's three-parameter (B3) hybrid exchange functional[24] and the non-local correlation functional of Lee, Yang, and Parr (LYP).[25] Analytical vibrational frequencies were computed at each stationary point, using the same level of theory at which the geometries were optimized. Zero-point (ZPE) and thermal energies were evaluated from the unscaled vibrational frequencies obtained. In order to account for dynamical electron correlation QCISD(T)[26] calculations were perfomed at the MP2 optimized geometries. The 6-31G* basis set of Pople was used in all the calculations.[27] All the calculations were performed using the programs contained in Gaussian 94.[28]

Models for evaluation of strain energies

For the three cyclic species **1**, **2** and **3** two definitions of strain energy have been applied. Both make use of formal isodesmic reactions involving also the corresponding acyclic species **4**, **5** and **6**, respectively. In each of these reactions two C–H bonds, one from each methyl, is replaced by a C–C bond, and in order to obtain a balanced equation the species CH_4 and C_2H_6 have to be involved in the formal reaction:

$$(XY)S(OCH_3)_2 + C_2H_6 \rightarrow \text{cyclo-}(XY)S(OCH_2)_2 + 2\,CH_4 \quad (1)$$

where X and Y may be either a sulfur lone pair or an oxygen atom. The discrepancy from thermoneutrality in these reactions may be defined as the strain energy of the cyclic species involved in the reaction.

The second model used incorporates cyclohexane and *n*-hexane in the reaction:

$$n\text{-}C_6H_{14} + C_2H_6 \rightarrow 2\,CH_4 + \text{cyclo-}C_6H_{12} \quad (2)$$

Combination of eqns. (1) and (2) leads to the reaction:

$$(XY)S(OCH_3)_2 + \text{cyclo-}C_6H_{12} \rightarrow \text{cyclo-}(XY)S(OCH_2)_2 + n\text{-}C_6H_{14} \quad (3)$$

Deviation from thermoneutrality for eqn. (3) may be defined as a measure of the strain energy of the species **1**–**3**. If eqn. (2) were thermoneutral the numerical values of the strain energies defined by the two approaches would be equal. As discussed below, eqn. (2) is not thermoneutral, so the strain energies predicted by the two approaches will differ by a constant amount.

Results and discussion

Absolute energies as well as ZPE and thermal energies obtained by the different calculational methods are given in Table 1. In Table 2 are presented reaction energies deduced from the energy values given in Table 1, and with reference to the reactions given in the text.

Table 1. Absolute energies (in hartrees), zero-point energies (ZPE, in kcal mol^{-1}) and thermal energies (THERM, in kcal mol^{-1}) obtained by B3LYP (and QCISD(T)//MP2) calculations.

	B3LYP			MP2			QCISD(T)
Species	$-E$	ZPE	THERM	$-E$	ZPE	THERM	$-E$
1	627.175 97	40.8	43.9	625.953 89	41.6	44.1	626.015 25
2	702.412 67	43.8	47.4	701.015 64	44.8	48.2	701.076 46
3	777.610 38	47.3	51.2	776.038 84	48.3	52.1	776.098 85
4	628.395 68	53.7	58.0	627.134 96	55.0	59.3	627.203 17
5	703.614 40	56.3	61.3	702.178 54	57.6	62.5	702.246 87
6	778.820 29	60.2	65.4	777.213 02	61.6	66.7	777.280 08
CH_4	40.518 38	28.4	30.2	40.332 55	29.1	30.9	40.355 96
C_2H_6	79.830 42	47.2	49.4	79.494 74	48.4	50.6	79.534 58
c-C_6H_{12}	235.880 45	107.4	111.0	234.992 43	109.8	113.3	235.088 81
n-C_6H_{14}	237.085 50	119.3	124.6	236.157 43	122.1	127.3	236.262 03

Table 2. Reaction energies (ΔE, in kcal mol^{-1}) for reactions (1)–(3) as defined in text.

	B3LYP		MP2		QCISD(T)	
Reactions	ΔE	$\Delta E+\Delta$(THERM)	ΔE	$\Delta E+\Delta$(THERM)	ΔE	$\Delta E+\Delta$(THERM)
(1)						
X=Y=lp	+8.38	+5.78	+6.71	+2.71	+6.64	+2.64
X=lp, Y=O	−2.89	−5.79	−4.68	−7.78	−4.35	−7.45
X=Y=O	+2.24	−0.96	+2.39	−1.01	+2.44	−0.96
(2)	−0.82	−3.42	−3.36	−6.17	−2.58	−5.39
(3)						
X=Y=lp	+9.20	+9.20	+10.07	+8.88	+9.22	+8.03
X=lp, Y=O	−2.07	−2.37	−1.32	−1.61	−1.77	−2.06
X=Y=O	+3.06	+2.46	+5.75	+5.16	+5.02	+4.43

In Fig. 1 are given the geometries of the global minima obtained by complete optimization of the cyclic species. Figure 2 contains the global minima as well as other minima of the acyclic species entering the isodesmic reactions given above.

The overall impression of the results obtained is that the predicted reaction energies, as given in Table 2, are strongly influenced by the thermal energy corrections. Moreover it is found that the strain energy for the cyclic sulfite as predicted by reaction (1) is negative, irrespective of the calculational level used and independent of the thermal corrections made. For the other two sulfur-containing rings the strain energies are found to be rather small, but positive except for the sulfate, which after thermal correction obtains a slightly negative value.

For reaction (2) involving only the hexane system there are available data on gas-phase enthalpies of formation.[29] Applying these data on this reaction we find that it is exothermic by 5.1 kcal mol^{-1}. Our calculated reaction energies for this reaction show that the DFT computation underestimates its exothermicity, but that the QCISD(T) calculations corrected thermally almost reproduces the experimentally deduced value, ending up with 5.4 kcal mol^{-1}.

The absence of thermoneutrality for reaction (2) can be traced back to methane and ethane which in this context are not 'normal alkanes' like *n*-hexane. This is illustrated by the fact that the differences of enthalpies of formation of ethane and *n*-propane, between *n*-propane and *n*-butane, and higher homologs and their subsequent alkane are very nearly constant and equal to 4.9 kcal mol^{-1}. This has been referred to as the universal methylene increment.[30,31] In contrast the difference between methane and ethane is only 2.5 kcal mol^{-1}. Relatedly, the difference of the enthalpies of formation of two ethanes and one *n*-butane, of two propanes and one *n*-hexane, of two *n*-hexanes and one *n*-dodecane are all ca. 10 kcal mol^{-1}, whereas the difference of two methanes and one ethane is 15.5 kcal mol^{-1}.

It has to be emphasized that the lack of thermoneutrality for reaction (2) is of no consequence for the evaluted values as long as a single strain energy scheme is chosen in a consistent way.[32,33] We have decided to choose the definition given by eqn. (3) that makes use of the differ-

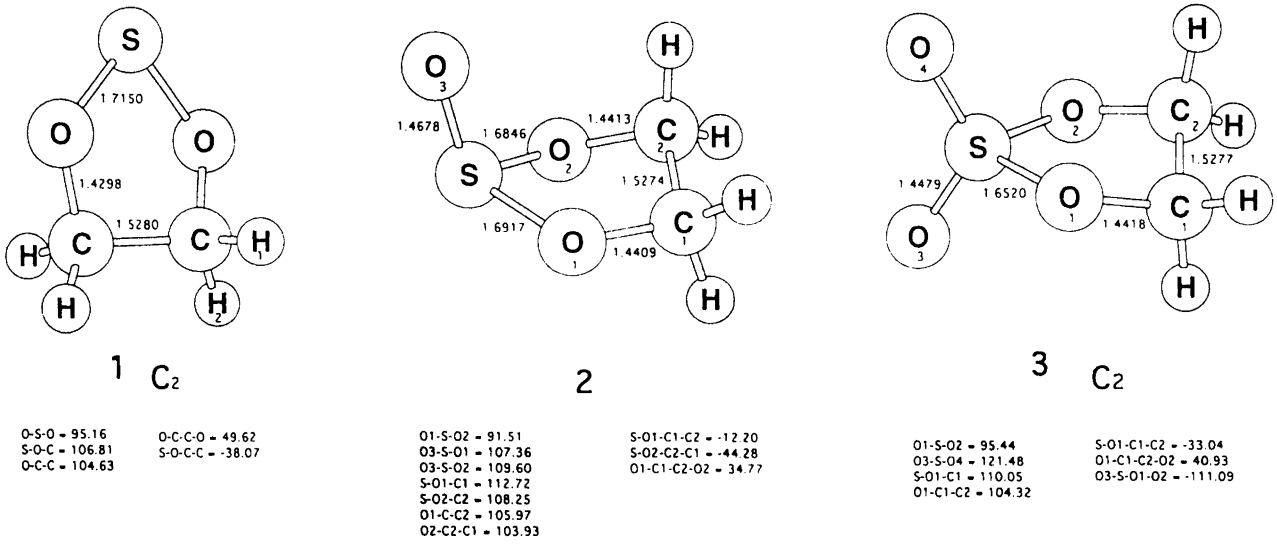

Fig. 1. Fully optimized geometries of 1,3,2-dioxathialone (**1**), its 2-oxide (**2**) and its 2,2-dioxide (**3**) using B3LYP/6-31G* calculations.

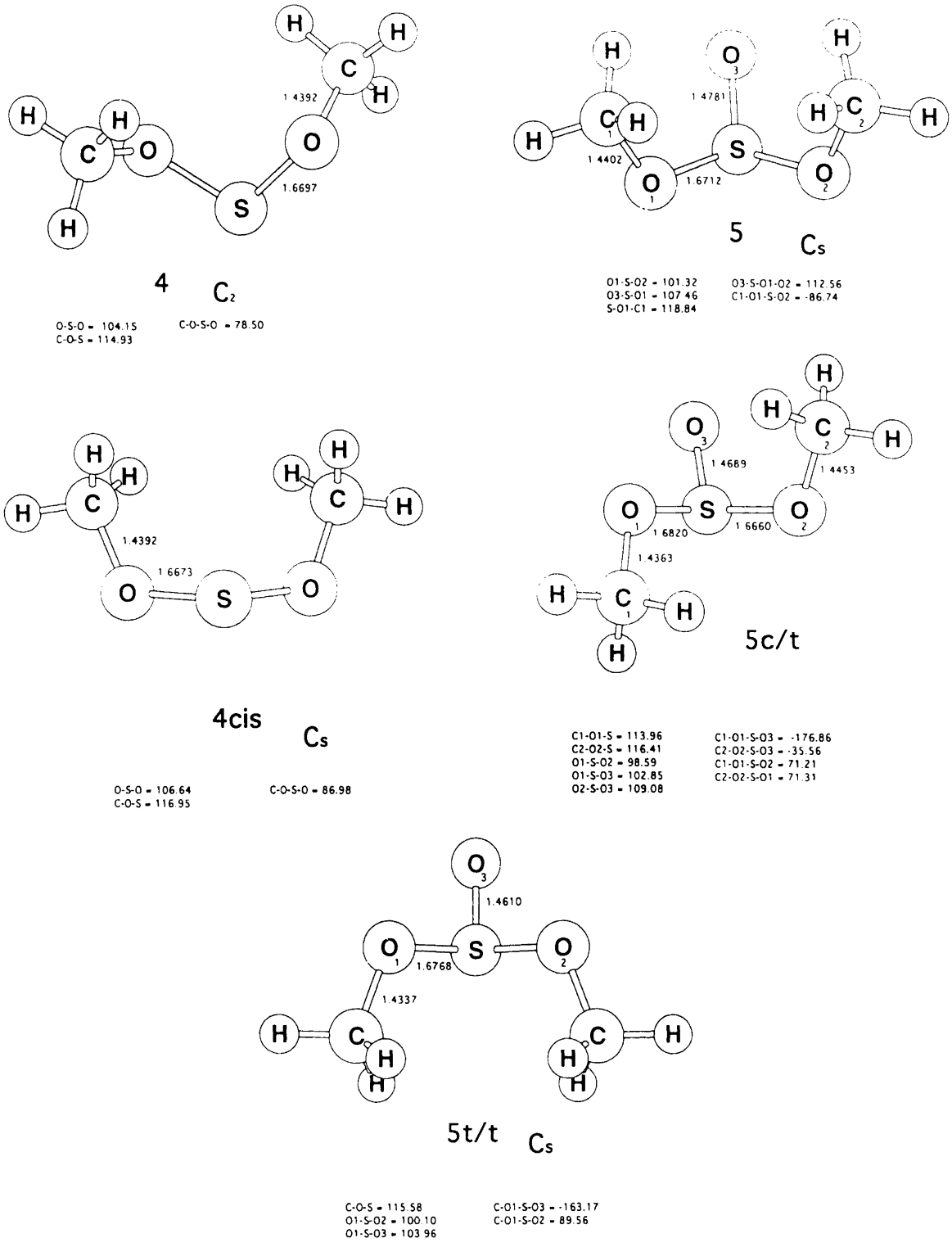

Fig. 2. Fully optimized geometries of different forms of dimethyl sulfoxylate (**4**), dimethyl sulfite (**5**) and dimethyl sulfate (**6**) using B3LYP/6-31G* calculations. The global minima are numbered **4**, **5** and **6**, respectively.

ence in the enthalpies of formation of *n*-hexane and cyclohexane. The reason for this preference is the usefulness of the universal methylene increment as an organizing principle in organic thermochemistry. As mentioned above, this increment does not apply to methyl and ethyl derivatives. An additional reason is the convenience of assuming cyclohexane is strainless. All strain energies that are discussed in the following have been evaluated using this definition. They are also found in Table 2 under the heading (3).

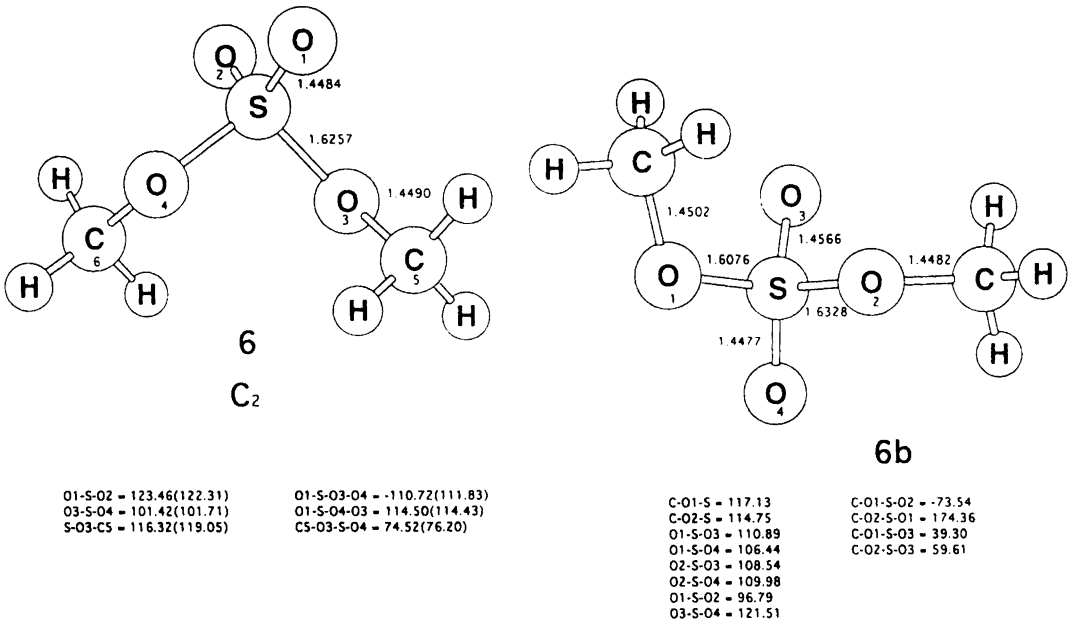

Fig. 2. (Continued.)

The results obtained by the semi-empirical B3LYP model within DFT and by QCI//MP2 calculations are seen to be nearly the same. It is particularly noteworthy that both methods predict a negative value for the strain energy in the cyclic sulfite. This makes it unlikely that the unphysical result is due to a failure of the calculational levels used.

Therefore we have to look for an interpretation of this result in terms of attractive and repulsive interactions in the dimethyl esters that enter the thermochemical equations. As expected, the C–O–S–O substructures in the most stable conformer of all three dimethyl esters are always *gauche*. However, this does not distinguish between the two methyl groups being on the same side or opposite side of the O–S–O plane. If we label these two conformers as *syn* and *anti*, respectively, we find that the *anti* conformation of dimethyl sulfoxylate is more stable than the *syn* form by 2.1 kcal mol^{-1}. This energy difference may be ascribed to a methyl–methyl repulsion. Relatedly the *anti* conformation of dimethyl sulfate is found to be more stable than the *syn* form by 3.0 kcal mol^{-1}. The attraction between the methyl group and the putatively doubly bonded oxygen in the two dimethyl sulfate conformers should be nearly equal, although in the *anti* conformation, this interaction involves the two doubly bonded oxygens, while in the *syn* conformation the same oxygen is used for both attractions. As the methyl–methyl repulsion is very nearly the same for dimethyl sulfoxylate and dimethyl sulfate we would expect it to be very nearly the same for dimethyl sulfite as well. i.e. around 2–3 kcal mol^{-1}. Equivalently, were there no methyl–oxygen attractions in the dimethyl sulfite the difference between the energies of the *anti* and *syn* conformers would be around 2.5 kcal mol^{-1}.

In the *syn* conformer of dimethyl sulfite the two methyl groups can be both *cis* or both *trans* to the doubly bonded oxygen. If we choose the former and compare it with the *anti* conformer in which one methyl group has to be *cis* and the other *trans* to the doubly bonded oxygen, we calculate an energy difference of 0.5 kcal mol^{-1} in favor of the former. The algebraic sum of the 2.5 kcal mol^{-1} mentioned above and this energy difference amounts to around 3 kcal mol^{-1}, which can be identified as the methyl–oxygen attraction energy.

If we consider the two *syn*-dimethyl sulfite conformers, we find that they have the same methyl–methyl repulsions. However, the one in which the two methyl groups are *cis* to the doubly bonded oxygen has two methyl–oxygen attractions while the other has none. Our calculations predict that the energy difference between the two conformers is around 7.5 kcal mol^{-1}. Assuming that the individual methyl–oxygen attractions may be equal to half of that difference we predict a value of around 3.8 kcal mol^{-1}. The two numbers assigned for this interaction, 3.0 and 3.8 kcal mol^{-1}, are numerically consistent.

In a conceptual process linking the two CH_3 groups together to form the three cyclic species the energy change should be the same to a first approximation. However, in the process in which the sulfur with its external oxygens try to find the optimum orientation with respect to the newly formed CH_2 groups of the ring, the ring systems will experince different energetic constraints. For the cyclic sulfoxylate there is no external oxygen so no stabilization is expected. For the cyclic sulfate there are two external oxygens and the CH_2 groups bonding more with one of them lessens the stabilization from the other. Besides, we would expect the two oxygen moieties to be the same by symmetry so

there is very little stabilization expected. On the other hand, for the cyclic sulfite there is only one external oxygen. Accordingly there would be no sacrificing of any other stabilization, and furthermore no symmetry is lost in the ring forming process. We conclude therefore that the stabilization for the cyclic sulfite will be significantly higher than for either the sulfoxylate or sulfate. This is in accordance with our findings.

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