Calorimetric and computational study of sulfur-containing six-membered rings

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Thermochemical data, and in particular the enthalpies of formation of oxygen- and sulfur-containing six-membered heterocycles provide essential information on the factors responsible for the contrasting behavior (structural, conformational and reactivity) between these types of compounds. A proper understanding of the experimental observations requires theoretical modeling in order to confirm the relative importance of the steric, electronic, electrostatic and stereoelectronic interactions that are responsible of the enthalpies of formation for the heterocyclic compounds of interest.

1. Introduction

Oxygen- and sulfur-containing six-membered heterocycles occupy a fundamental position in chemistry.[1] Nevertheless, whereas the chemistry of pyrans (oxanes) constitutes a very large body of knowledge, that of thiopyrans (thianes) has been less extensively investigated. In this regard, the difference in size, electronegativity, and bond polarities associated with oxygen and sulfur, as well as the availability of 3d orbitals in sulfur, are reflected in contrasting structural,[2] conformational,[3,4] and reactivity behavior[5] of the corresponding heterocycles.

Regarding conformational behavior, O–C–C–O segments exhibit a preference for *gauche* arrangements (Scheme 1a),[6] whereas S–C–C–S segments generally adopt *anti* conformations, as a consequence of repulsive *gauche* interactions. (Scheme 1b).[6] Furthermore, the anomeric effect[7] tends to be stronger in O–C–O relative to S–C–S segments.

Thermodynamic data such as the enthalpy of formation, symbolized $\Delta_f H^\circ_m$, offer a powerful procedure for the

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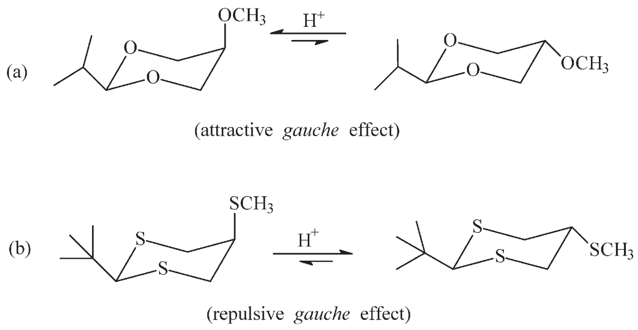


Scheme 1

understanding of the contrasting structural, conformational, and reactivity trends exhibited by oxygen- and sulfur-containing six-membered compounds. For example, relative to cyclohexane, **1**, the enthalpy of formation of oxane, **2**, is much more negative, -123.3 and -223.4 kJ mol^{-1}, respectively (Fig. 1). By contrast, the enthalpy of formation of thiane, **3**, is significantly less negative than that for cyclohexane, -63.5 kJ mol^{-1} (Fig. 1).[8] These enthalpies of formation are all relative to the elements in their standard states; that is, 5 C, 5 H_2 and ½ O_2 for oxane **2** and 5 C, 5 H_2 and $^1/_8$ S_8 for thiane **3**. Thus, the large negative enthalpy of formation for the former heterocycle indicates that formation of two C–O bonds more than compensates for the broken O–O bond. By contrast, the energy gained from two C–S bonds being formed in the latter heterocycle is less sizable, in principle as a consequence of the higher energy cost involved in the dissociation of the S_8 molecule. Alternatively, these thermochemical data give evidence of the relative strength of the C–O and C–S bonds: the lower electronegativity of sulfur relative to oxygen results in diminished Coulombic attraction between the heteroatom and bonded carbon atoms, and thus weaker C–S bonds.

In this regard, comparison of the enthalpies of formation for isomeric compounds is particularly useful since it shows their relative stability, and provides relevant evidence on the steric, electrostatic, and stereoelectronic interactions that are responsible for the enthalpy of formation of each isomer. For example, Fig. 2 depicts graphically the enthalpies of formation of butane ($\Delta_f H^\circ_m = -127.5$ kJ mol^{-1}) and that of 2-methylpropane ($\Delta_f H^\circ_m = -136.1$ kJ mol^{-1}) from their elements in their standard state.[9]

Fig. 2 shows that butane and 2-methylpropane are both more stable (have lower enthalpy) than four carbon atoms and five hydrogen molecules in their standard states. Nevertheless, the enthalpies of formation of the butane isomers reveal that 2-methylpropane (the more branched hydrocarbon) is more stable than butane by 8.6 kJ mol^{-1}.

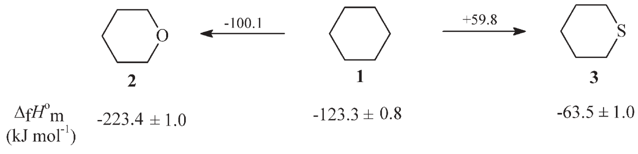


Fig. 1 Comparison of the experimental gas-phase enthalpies of formation of cyclohexane, oxane, and thiane.[7]

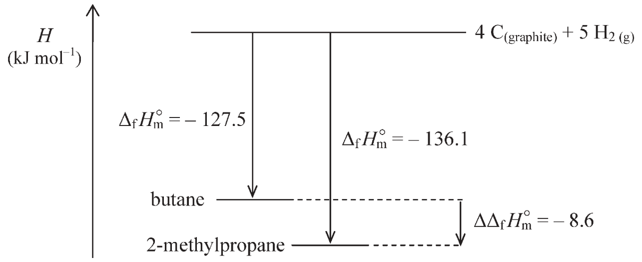


Fig. 2 The enthalpies of formation of butane and 1-methylpropane, illustrating the use of $\Delta_f H^\circ_m$ values to determine the relative stability of isomeric compounds.[9]

The development of faster computers coupled with the advances in theoretical methodologies during the past 10–15 years has resulted in tremendous progress in computational capabilities for the calculation of accurate thermochemical data.[10] Furthermore, molecular modeling is essential to the proper interpretation of most experimental observations and measurements.[11] Indeed, the following account will provide several examples where the synergy between experiment and theory made possible the comprehension of various fundamental interactions in oxygen- and sulfur-containing six-membered heterocycles.

2. 1,3-Dioxane and 1,4-dioxane

Comparison of the enthalpies of formation for oxane, **2**, and 1,3-dioxane, **4**, shows that introduction of the second heteroatom is significantly more exothermic than conversion of cyclohexane to oxane. Indeed, $\Delta_f H^\circ_m(\mathbf{2})$ is 100.1 kJ mol^{-1} more negative than $\Delta_f H^\circ_m(\mathbf{1})$ (Fig. 1), whereas $\Delta_f H^\circ_m(\mathbf{4})$ is 117.2 kJ mol^{-1} more negative than $\Delta_f H^\circ_m(\mathbf{2})$.[8,12] Thus, the second substitution of –CH_2– for –O– (in **2** → **4**) results in 17.1 kJ mol^{-1} further stabilization. (Fig. 3).

The additional stabilization of 17.1 kJ mol^{-1} is not observed when the oxygen atoms are not geminal, as evidenced from examination of $\Delta_f H^\circ_m(\mathbf{5}) = -315.3$ kJ mol^{-1}, which is only 91.9 kJ mol^{-1} more negative than the enthalpy of formation of oxane **2**. (Fig. 3). These results can be explained in terms of $n_O \rightarrow \sigma^*_{C\text{–}O}$ hyperconjugation,[7] which provides "double bond–no bond" stereoelectronic stabilization to 1,3-dioxane **4**. (Scheme 2).

Dioxanes **4** and **5** are isomeric and therefore comparison of their enthalpies of formation provides direct quantitative information on their relative stability. Although oxane **2** is not an isomer of dioxanes **4** and **5**, examination of the **2** → **4** and **2** → **5** enthalpy changes is reasonable as evidenced by means of isodesmic reactions. Indeed, the hypothetical reaction of oxane **2** with ethylene oxide to give 1,3-dioxane **4**

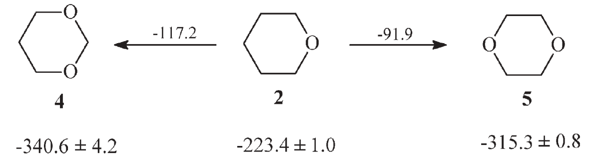
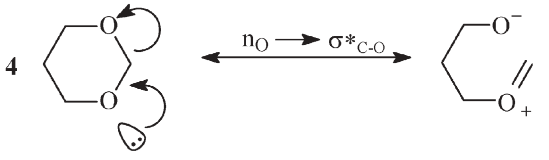


Fig. 3 Experimental gas-phase enthalpies of formation in kJ mol^{-1} for several oxygen-containing heterocycles.



Scheme 2

and cyclopropane, $\Delta\Delta_fH^\circ_m$ = (−223.4 − 52.7) − (340.6 + 53.1) = −11.4 kJ mol^{-1}, is 25.3 kJ mol^{-1} more exothermic than conversion of oxane **2** and ethylene oxide to 1,4-dioxane **5** and cyclopropane, $\Delta\Delta_fH^\circ_m$ = (−223.4 − 52.7) − (315.3 + 53.1) = +13.9 kJ mol^{-1}, in line with the experimental measurements.

3. 1,3-Dithiane and 1,4-dithiane

As illustrated in Fig. 4, the enthalpy of formation of 1,3-dithiane, **6**, was determined from its enthalpy of combustion, $\Delta_cH^\circ_m$.[13] Furthermore, in order to obtain $\Delta_fH^\circ_m$(**6**) in the gas phase, the corresponding enthalpy of sublimation, $\Delta_sH^\circ_m$, for the crystalline heterocycle was determined and taken into account.[13] (Fig. 4).

The experimental value for the enthalpy of formation of 1,3-dithiane, $\Delta_fH^\circ_m$ = −2.7 kJ mol^{-1} (Fig. 4) shows that introduction of a second heteroatom has quite contrasting consequences in the oxygen and sulfur heterocycles. Thus, conversion of oxane **2** into 1,3-dioxane **4** is a highly exothermic process, $\Delta\Delta_fH^\circ_m$ = −117.2 kJ mol^{-1} (Section 2), whereas conversion of thiane **3** into 1,3-dithiane **6**, is strongly endothermic, $\Delta\Delta_fH^\circ_m$ = +60.8 kJ mol^{-1}.[13] The lack of stabilization in the geminal S–C–S segment present in 1,3-dithiane **6** suggests that the "double bond–no bond" stereoelectronic interaction operative in the oxygen analogue 1,3-dioxane **4** (Scheme 2) is not effective here; *i.e.*, the nonbonding orbitals at sulfur are less efficient in $n_S \rightarrow \sigma^*_{C-S}$ hyperconjugation.[7,14]

Examination of the experimental enthalpies of formation for the 1,4-diheterocyclohexanes provides support for the previous interpretation in terms of the *gem* effect ($n_X \rightarrow \sigma^*_{C-X}$ hyperconjugation). Indeed, loss of this stabilizing interaction during 1,3-dioxane **4** to 1,4-dioxane **5** isomerization is shown to be substantially endothermic ($\Delta\Delta_fH^\circ_m$ = + 25.3 kJ mol^{-1}, Fig. 3). In contrast, conversion of 1,3-dithiane **6**, where no *gem* effect is apparent, to its 1,4-analogue **7** is actually slightly exothermic by $\Delta\Delta_fH^\circ_m$ = −4.2 kJ mol^{-1}; that is, 1,4-dithiane **7** is *ca.* 4 kJ mol^{-1} more stable than its 1,3-isomer.[15] (Fig. 5).

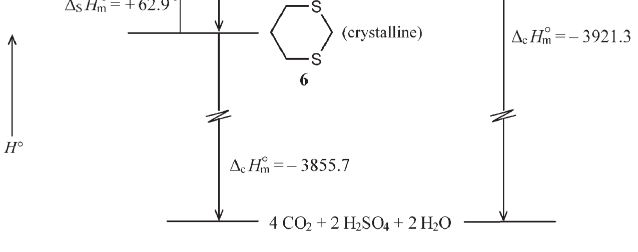


Fig. 4 The relationship between the enthalpies of formation, combustion and sublimation of 1,3-dithiane, **6**.[13]

To confirm the reliability of the measured enthalpies of formation of 1,3- and 1,4-dithiane, theoretical values at the G2(MP2) and G3 levels of theory[16] were then computed. G3 theory clearly afforded better results, especially when the bond separation isodesmic reaction scheme[17] was used. In this fashion, excellent agreement between calculated and experimental enthalpies of formation was achieved[15] (Fig. 6).

4. 1,3,5-Trithiane and 1,3,5-trioxane

The more negative enthalpy of formation (increased stability) of 1,4-dithiane **7** relative to 1,3-dithiane **6** supported the existence of a repulsive interaction between sulfurs in a 1,3 arrangement.[18] Such effect should be more apparent in 1,3,5-trithiane **8**, so we proceeded to determine the enthalpies of combustion, sublimation, and formation in this heterocycle[19] (Fig. 7).

The experimentally observed gas-phase enthalpy of formation of 1,3,5-trithiane **8**, $\Delta_fH^\circ_m$ = +84.6 ± 2.6 kJ mol^{-1}, is 87.3 kJ mol^{-1} more endothermic than the enthalpy of formation of 1,3-dithiane **6**, $\Delta_fH^\circ_m$ = −2.7 ± 2.3 kJ mol^{-1}.[19] Thus, substitution of a meta methylene group in the **6** to **8** conversion is 26.5 kJ mol^{-1} more energetically unfavorable than a similar $CH_2 \rightarrow S$ substitution in the thiane **3** to 1,3-dithiane **6** transformation, $\Delta_fH^\circ_m$(**6**) − $\Delta_fH^\circ_m$(**3**) = −2.7 − (−63.5) = 60.8 kJ mol^{-1}. This observation is in line with the suggested repulsion between sulfurs in a 1,3 arrangement. Indeed, there is spectroscopic evidence for the existence of through-space lone pair-lone pair repulsive orbital interactions in 1,3-dithiane and 1,3,5-trithiane.[18]

The theoretical studies undertaken to understand the thermochemical results supported the relevance of the lone pair-lone pair electronic repulsion advanced above for 1,3-dithiane **6** and 1,3,5-trithiane **8**. On one hand, the electrostatic potential distribution for these compounds allow the assignment of the lone electron pairs on sulfur, and it was clearly appreciated that through-space repulsion causes drastic

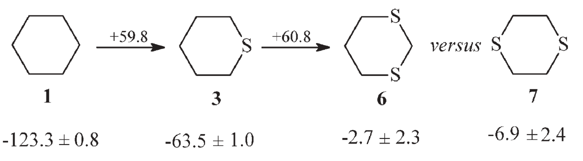


Fig. 5 Enthalpies of formation (in kJ mol^{-1}) for thiane **3**, 1,3-dithiane **6**, and 1,4-dithiane **7**.

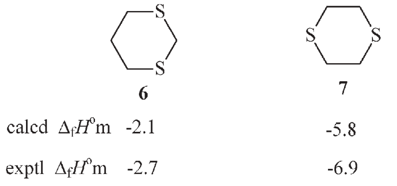


Fig. 6 Calculated (G3, bond separation isodesmic reactions) and experimental enthalpies of formation for 1,3- and 1,4-dithiane.[13,15]

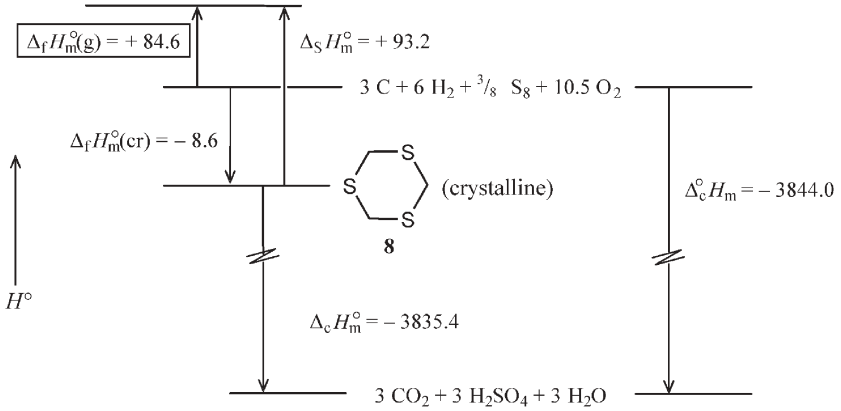


Fig. 7 The relationship between the enthalpies of formation, combustion, and sublimation of 1,3,5-trithiane **8**.

displacement of the lone pairs away from the nuclear framework, to minimize lone pair-lone pair through-space overlap.[19]

On the other hand, the charge distribution in the compounds of interest was analyzed by means of the natural bond orbital (NBO) method.[20] Fig. 8 collects the natural atomic charges at the heavy atoms for thiane **3**, 1,3-dithiane **6** and 1,3,5-trithiane **8**, as well as for the oxane analogues **2**, **4** and **9**.

The results in Fig. 8 exhibit the different behavior of sulfur and oxygen in the homologous series of compounds. As a consequence of the higher electronegativity of oxygen relative to that of sulfur, the positive charge in thianes is located at the sulfur atoms, whereas the negative charge in oxanes is located at the oxygen atoms. More interesting, the positive charge at sulfur increases in the series **3** < **6** < **8**, while the negative charge at the adjacent carbons increases simultaneously. This trend is in line with a mechanism in which electron density concentrates on carbon in order to minimize lone pair-lone pair repulsion in the S–C–S segments. By contrast, the negative charge at oxygen in the oxygen analogues remains constant in the series **2** → **4** → **9**, suggesting that through-space lone pair-lone pair repulsion is not significant with the less diffuse oxygen lone pair orbitals.

The experimental enthalpy of formation of 1,3,5-trioxane **9**, $\Delta_f H^\circ_m$ = −465.9 kJ mol^{-1}, is 125.3 kJ mol^{-1} more negative (exothermic) than $\Delta_f H^\circ_m$ for 1,3-dioxane **4**. In strong contrast, the experimental enthalpy of formation of 1,3,5-trithiane **8**, $\Delta_f H^\circ_m$ = +84.6 kJ mol^{-1}, is 87.3 kJ mol^{-1} more *endothermic* than $\Delta_f H^\circ_m$ for 1,3-dithiane **6** (Fig. 9). These results are in line with the "anomeric" stabilization operative in the three O–C–O segments present in **9**, to be contrasted with through-space lone pair-lone pair repulsion in 1,3,5-trithiane **8**.

5. Thiane sulfoxide and thiane sulfone

Over the past three of four decades the use of sulfoxides and sulfones in organic synthesis has increased enormously.[21,22] Nevertheless, the nature of the S–O bond is still a matter of controversy,[23] as well as the interpretation of the conformational behavior of thiane oxide and derivatives.[24]

The optimized geometries of thiane sulfoxide **10** and thiane sulfone **11** were calculated at the MP2(FULL)/6–31G(3df,2p) level of theory.[25] In both compounds, the most stable form is the chair conformation. In thiane sulfoxide **10**, the oxygen atom can be in the axial or equatorial position. Calculations show that the axial conformer is preferred by 7.4 kJ mol^{-1}, in good agreement with previous experimental and theoretical studies[24] (Scheme 3). The accepted interpretation attributes the axial preference of the sulfoxide oxygen to an attractive interaction between the oxygen and the *syn*-axial hydrogens.

The experimental enthalpy of formation (in the gas phase) for thiane sulfone **11** is a very exothermic $\Delta_f H^\circ_m$(**11**) = −394.8 ± 1.4 kJ mol^{-1}, which is a manifestation

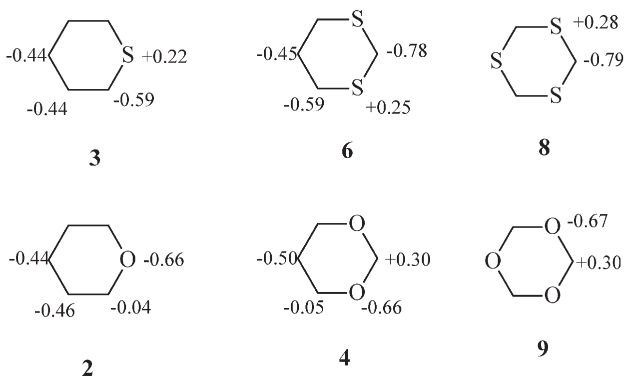


Fig. 8 NBO charges [MP2(FULL)/6–31(d) Level] at the heavy atoms in thianes and oxanes.[19]

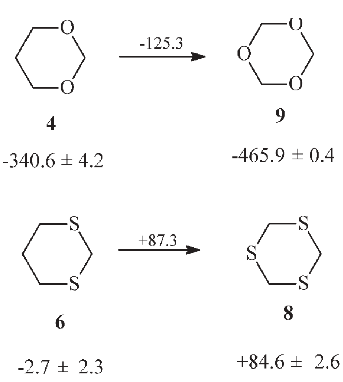
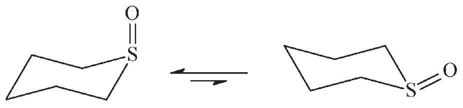


Fig. 9 Experimental gas-phase enthalpies of formation in kJ mol^{-1} for 1,3-dioxane **4**, 1,3,5-trioxane **9**, and their sulfur analogues.[19]



10-axial **10**-equatorial

ΔE = +7.4 kJ mol^{-1} [MP2(FULL)/6-31G(d)]

Scheme 3

of the remarkable strength of the S=O bonds, as well as the significantly strong C–SO$_2$ bonds.

With the value of the enthalpy of formation of **11** at hand, and given the known enthalpy of formation of atomic oxygen in the gas phase, $\Delta_f H^\circ_m$(O,g) = +249.18 kJ mol^{-1},[26] as well as the reported bond dissociation energy for the S=O bond in alkyl sulfones,[27] BDE = +470.0 kJ mol^{-1}, it was possible to determine the enthalpy of formation in the gas phase of sulfoxide **10** (a hygroscopic compound not amenable for experimental calorimetric measurements), $\Delta_f H^\circ_m$(**10**) = $-$174.0 kJ mol^{-1} (Fig. 10).

6. 1,3-Dithiane sulfoxide and 1,3-dithiane sulfone

Section 3 in this review discussed the thermochemical evidence that indicates the lack of significant $n_S \rightarrow \sigma^*_{C\text{–}S}$ hyperconjugation in the S–C–S segment. An interesting question is whether hyperconjugative $n_S \rightarrow \sigma^*_{C\text{–}SO_2}$ interaction will be operative in the 1,3-dithiane sulfone derivative **12**. Indeed, the highly electronegative SO$_2$ sulfonyl group should lead to a lower-energy $\sigma^*_{C\text{–}SO_2}$ orbital with better accepting properties. (Fig. 11). Thus, double bond–no bond stereoelectronic stabilization in 1,3-dithiane sulfone **12** should be manifested in a more negative enthalpy of formation.

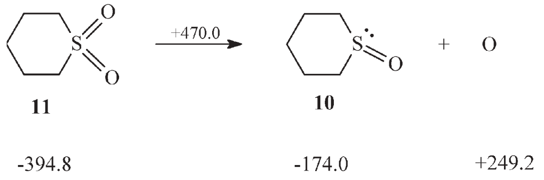


Fig. 10 Enthalpies of formation in the gas phase for thiane sulfoxide **10** and thiane sulfone **11**.

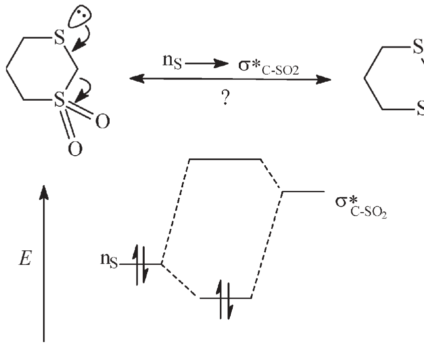


Fig. 11 1,3-Dithiane sulfone **12** could benefit from $n_S \rightarrow \sigma^*_{C\text{–}SO2}$ hyperconjugation.

The enthalpies of combustion and sublimation of 1,3-dithiane sulfone **12** were measured in order to determine the gas-phase enthalpy of formation, $\Delta_f H^\circ_m$(**12**) = -326.3 ± 2.0 kJ mol^{-1}.[28] Comparison of this value with those previously recorded for thiane sulfone **11** ($\Delta_f H^\circ_m$ = $-$394.8 kJ mol^{-1}), thiane **3** ($\Delta_f H^\circ_m$ = $-$63.5 kJ mol^{-1}), and 1,3-dithiane **6** ($\Delta_f H^\circ_m$ = $-$2.7 kJ mol^{-1}) shows that the enthalpy of formation of 1,3-dithiane sulfone **12** is less exothermic than expected; that is, a destabilization worth 7.7 kJ mol^{-1} is evident (Fig. 12).

To get information that could help understand the nature of the destabilizing effect in 1,3-dithiane sulfone **12** that apparently counterbalances the $n_S \rightarrow \sigma^*_{C\text{–}SO_2}$ stabilizing interaction, the charge distribution in the compounds of interest was analyzed by means of the NBO method[20] (Fig. 13). Most significant is the very large positive charge created at sulfur upon oxidation, from values ranging +0.22 to +0.25 in thioethers **3** and **6** to +2.47 and +2.46 in the sulfones **11** and **12**.[28] The very large exothermic **3** to **11** process ($\Delta\Delta_f H^\circ_m$ = $-$331.3 kJ mol^{-1}) reflects in part the overriding electrostatic attraction with the negative C(3,5) carbons. By contrast, in 1,3-dithiane sulfone **12**, some of the attractive electrostatic stabilization is offset by a repulsive electrostatic interaction between sulfurs.

Analogous 1,3-dithiane monosulfoxide **13** was also examined,[29] with particular attention given to potential thermochemical or computational manifestations of electrostatic (*e.g.*, S$^{\delta+}$—$^{\delta+}$S(O) repulsion or S$^{\delta+}$—$^{\delta-}$O=S attraction, Scheme 4a) and stereoelectronic interactions[7,24] (*e.g.*, $n_S \rightarrow \sigma^*_{C\text{–}S(O)}$ or $\sigma_{S\text{–}C} \rightarrow \sigma^*_{S\text{–}O}$ hyperconjugation, Scheme 4b,c).

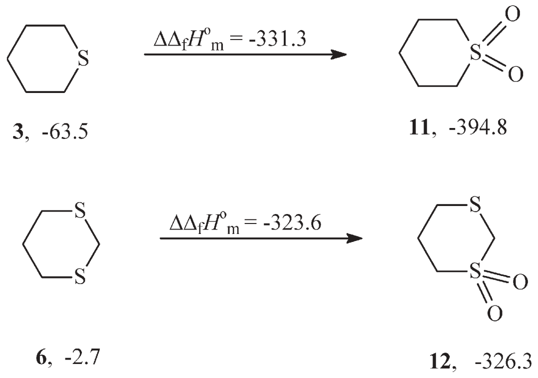


Fig. 12 Differences is the enthalpy of formation ($\Delta\Delta_f H^\circ_m$, in kJ mol^{-1}) for the conversions **3** into **11** and **6** into **12**.

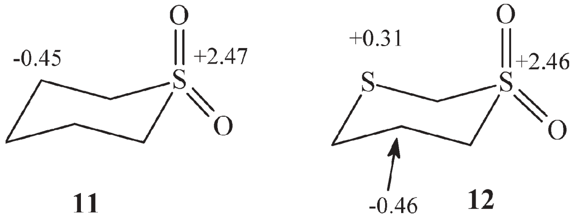
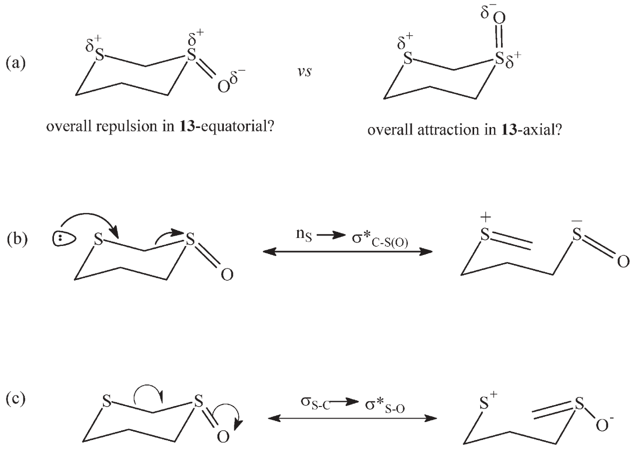


Fig. 13 NBO charges [MP2(FULL)/6–31G(d) level] at selected heavy atoms in sulfones **11** and **12**.



Scheme 4

The experimental enthalpy of formation in the gas phase of 1,3-dithiane sulfoxide **13**, $\Delta_f H^\circ_m = -98.0 \pm 1.9$ kJ mol^{-1},[29] is to be compared with that of 1,3-dithiane **6**, $\Delta_f H^\circ_m = -2.7 \pm 2.3$ kJ mol^{-1}. It is appreciated that the **6** to **13** oxidation process is exothermic by 95.3 kJ mol^{-1} (Fig. 14a). By contrast, oxidation of thiane **3** to thiane oxide **10** is significantly more exothermic, $\Delta\Delta_f H^\circ_m = -110.5$ kJ mol^{-1} (Fig. 14b).

In order to explain the lower than anticipated enthalpy of formation for 1,3-dithiane sulfoxide **13**, we proceeded to compare its molecular and electronic structure with those of 1,3-dithiane **6**, the sulfone analog **12**, and thiane sulfoxide **10** (Fig. 15).

In contrast with thiane oxide **10** that is more stable in the axial conformation (Scheme 5a), 1,3-dithiane monosulfoxide **13** adopts preferentially the equatorial conformation (Scheme 5b). According to high level [MP2(FULL)/6–31G(3df,2p)] calculations,[29] the conformer with the oxygen atom in the axial position (**13**-axial in Scheme 5b) is 7.1 kJ mol^{-1} higher in energy. This gas-phase estimate is in fair agreement with the experimentally obtained value, $\Delta G^\circ_{298K} = 2.7$ kJ mol^{-1} in methanol.[24] The higher energy of **13**-axial relative to **13**-equatorial has been ascribed to a repulsive interaction between the lone electron pairs at sulfur and oxygen in the axial sulfinyl group. (Scheme 5b).

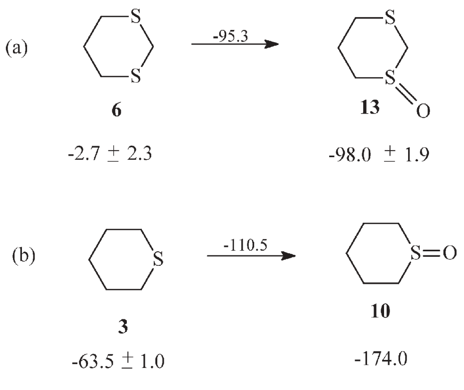


Fig. 14 Differences in the enthalpy of formation ($\Delta\Delta_f H^\circ_m$, in kJ mol^{-1}) for (a) the conversion of 1,3-dithiane **6**, into sulfoxide **13**, and (b) the conversion of thiane **3** into sulfoxide **10**.

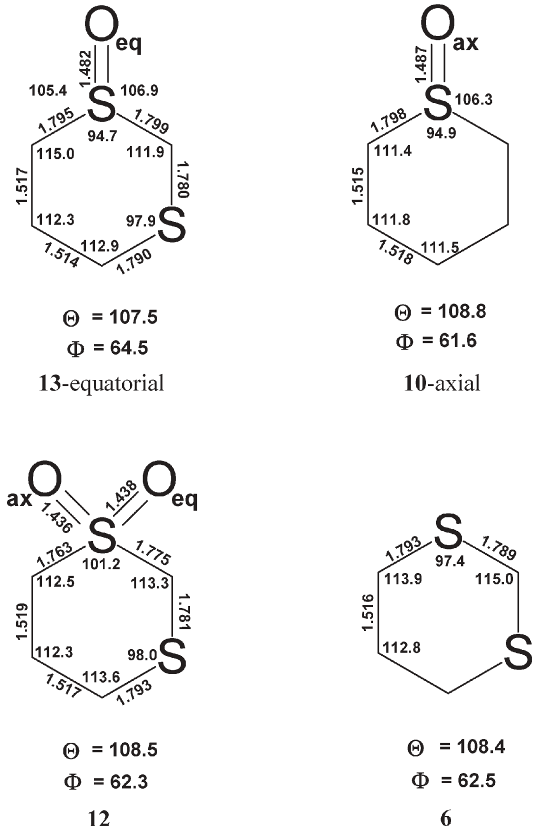
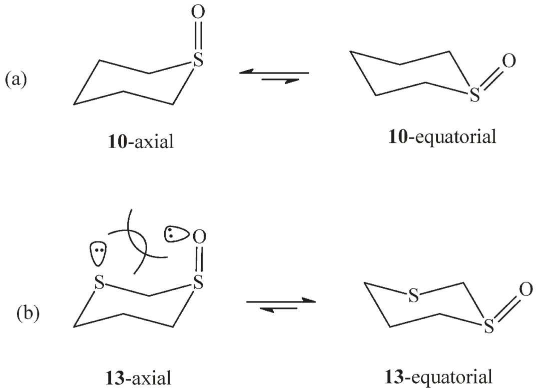


Fig. 15 MP2(FULL)6–31G(3df,2p)-calculated structures of 1,3-dithiane sulfoxide **13**, 1,3-dithiane **6**, 1,3-dithiane sulfone **12** and thiane sulfoxide **10**. Bond distances in Ångstroms, and bond angles in degrees, Θ and Φ are the valence and torsional angles.



Scheme 5

The structural data summarized in Fig. 15 is in line with expectation from $n_S \rightarrow \sigma^*_{C\text{–}S(O)}$ hyperconjugation in **13** (Scheme 5b) since comparison with the structural data for 1,3-dithiane **6** shows a shortening of the S(3)–C(2) bond length (from 1.789 Å in **6** to 1.780 Å in **13**) and a lengthening of the C(2)–S(1) bond (from 1.789 Å in **6** to 1.799 Å in **13**) (Fig. 15).

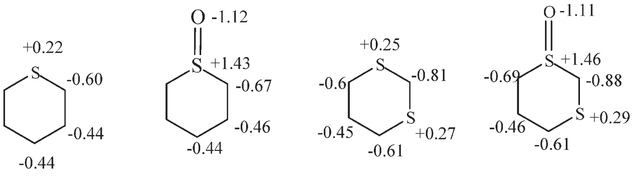
On the other hand, the structural data in Fig. 15 helps discard the possibility of $\sigma_{S\text{–}C} \rightarrow \sigma^*_{S\text{–}O}$ hyperconjugation in **13**-equatorial since one would expect the S–O bond length in

13 significantly longer relative to **10**. In fact, the calculated S–O bond length in sulfoxide **13** (1.482 Å) is slightly shorter than that calculated for reference sulfoxide **10** (1.487 Å).

It is evident that the stabilization gained from the apparent $n_S \rightarrow \sigma^*_{C-S(O)}$ hyperconjugative interaction in **13** is more than counterbalanced by a repulsive interaction that is reflected in its small experimental enthalpy of formation ($\Delta_f H^\circ_m(g) = -98.0$ kJ mol^{-1}). To get information that could help understand the nature of the destabilizing effect in 1,3-dithiane sulfoxide **13** that apparently counterbalances the $n_S \rightarrow \sigma^*_{C-S(O)}$ stabilizing interaction, the charge distribution in the compounds of interest was analyzed by means of the natural bond orbital (NBO) method of Weinhold *et al.*[20] In Fig. 16 we have collected the natural atomic charges (the nuclear charges minus summed natural populations of the natural atomic orbitals on the atoms) at the heavy atoms for the compounds of interest.[29]

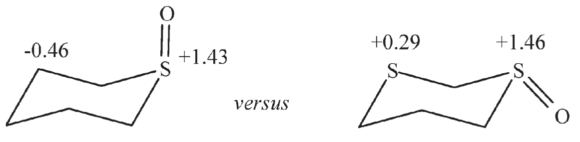
Most significant is the very large positive charge generated at sulfur upon oxidation, from values between +0.24 and +0.27 in thioethers **3** and **6** to +1.43 and +1.46 in sulfoxides **10** and **13**. Indeed, the large experimentally observed **3** to **10** process ($\Delta\Delta_f H^\circ_m = -110.5$ kJ mol^{-1}, Fig. 14b), reflects the substantial electrostatic attraction between positive sulfur (q = +1.43, Scheme 6) and the negative C(3,5) carbon in sulfoxide **10** (q = −0.46, Scheme 6). In contrast, in 1,3-dithiane sulfoxide **13**, the attractive electrostatic stabilization is offset by a repulsive electrostatic interaction between sulfurs (q = +1.46 and +0.29, Scheme 6).

Fig. 17 summarizes the thermochemical data for the oxidation of thiane **3** and 1,3-dithiane **6**. As discussed in the present paper, the oxidation of 1,3-dithiane **6** to sulfoxide **13** is much less exothermic than the oxidation of thiane **3** to sulfoxide **10**, and this observation is explained in terms of electrostatic repulsion between sulfurs. In contrast, the oxidation of 1,3-dithiane sulfoxide **13** to sulfone **12** is more exothermic than the corresponding oxidation of thiane sulfoxide **10** to thiane sulfone **11**, probably as the result of the $n_S \rightarrow \sigma^*_{C-SO_2}$ stabilizing interaction that is possible in **12** but not in **11**. This interpretation implies that most of the energetic cost of the electrostatic repulsion between sulfurs is paid in the initial sulfide to sulfoxide oxidation step. Nevertheless, the overall conversion of thiane **3** to sulfone **11** is more favorable than the overall conversion of 1,3-dithiane **6** to sulfone **12** (−331.3 kJ mol^{-1} and 323.6 kJ mol^{-1}, respectively). Thus electrostatic repulsion between positive sulfurs in sulfone **12** seems to dominate over the stabilizing stereoelectronic effect.



3 **10**-axial **6** **13**-equatorial

Fig. 16 Natural charges obtained from NBO analysis at the MP2(FULL)/6–31G(3df,2p) level, located at the heavy atoms in thiane **3**, thiane oxide **10**-axial, 1,3-dithiane **6**, and 1,3-dithiane sulfoxide **13**-equatorial.



10-axial **13**-equatorial

Scheme 6

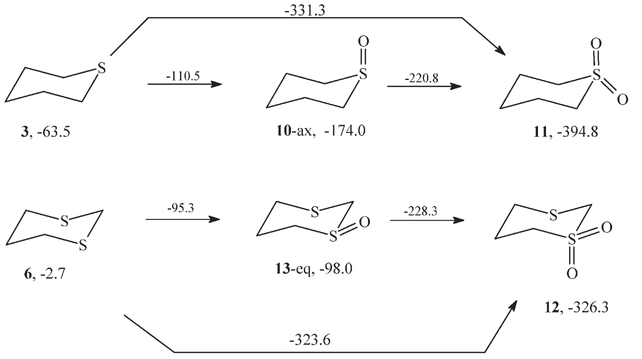


Fig. 17 Thermochemical data ($\Delta_f H^\circ_m$ and $\Delta\Delta_f H^\circ_m$, in kJ mol^{-1}) for the oxidation processes **3** → **10** → **11** and **6** → **13** → **12**.

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