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Ab-initio MCSCF Study of the Homolytic S-S Bond Dissociation in Disulphides, Thiosulphinates and α-Disulphoxides.

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Abstract: The geometrical and electronic properties of RSSR, RS(O)SR and RS(O)S(O)R (with R=H,CH_3) molecules and the energy profile for S-S bond cleavage were calculated with *ab-initio* MO MCSCF wavefunctions at 3-21G* level. The results show that the electronic structure of α–disulphoxides is more likely that of two paired radicals with net spin population localized on the oxygen atoms. Also in terms of bond-length and bond-index the S-S bond in α–disulphoxides appears to be much weaker than in the other molecules, as also confirmed by the calculated bond dissociation energy (DE) which turns out much lower than expected for a true S-S bond.

The disulphide linkage has a role in stabilising the tertiary structure of proteins. The S-S bond acts as a cross-link between two separate polypeptide chains or between loops of a single chain: this linkage can thus affect the conformational structure of proteins[1].

In recent years considerable experimental and theoretical efforts have been addressed to the investigation of molecules which contain the S-S unit in order to clarify the structural and conformational features of this bond. Moreover, oxidative processes such as autoxidation or induced by chemical oxidants, often cause marked changes in the protein structure and these changes can be correlated with oxidation of the disulphide bridge[2].

The oxidation of simple disulphides has been widely studied and the ultimate product is the corresponding sulphonic acid which arises through S-S bond scission[2]. The possible structure of intermediate disulphide dioxides has generated considerable controversy, the question being whether they have the thiosulphonate structure (4), or the isomeric α-disulphoxide structure (3), the latter never being isolated and only recently observed at low temperature[3].

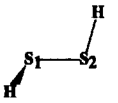
R-S-S-R	R-S(O)-S-R	R-S(O)-S(O)-R	R-S(O)$_2$-S-R
(1)	(2)	(3)	(4)

Theoretical calculations[4] and comparisons based on IR and Raman spectra of a number of related oxygen-sulphur compounds[5] have shown that the thiosulphonate (4) is considerably more stable than the isomeric *vic*-disulphoxide structure (3).

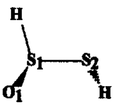
Although the chemistry of α-disulphoxides is relatively unknown, it seems reasonable to postulate that formation of (3) is a preliminary step in the oxidation of (1) and rearrangement to (4) occurs through homolytic S-S bond cleavage and head-to-tail recombination of the radicals[4].

In some recent studies, direct[3] and indirect[6] evidence for the formation of (3) has been definitely acquired. The stability of this chemical species appears, however, to be rather low and, up to now, the highest stability has been observed for α-disulphoxides obtained in the electrophilic oxidation of bridged bicyclic thiosulphinates[7].

Comparative theoretical studies of the stability of the S-S bond in disulphides and in their oxygenated forms have not been performed with accurate approaches and this paper aims to fill the gap with a report on thermal homolytic bond dissociation in compounds **1** - **3** with R = H, CH_3 by employing *ab-initio* MO calculations with a multiconfigurational (MCSCF) wavefunction model.



(5 a)



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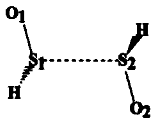
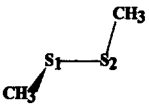
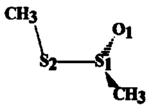


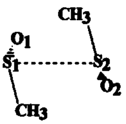
(7 a)



(5 b)



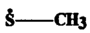
(6 b)



(7 b)

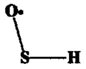
$^2\Pi$

(8 a)



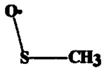
$^2A'$

(8 b)



$^2A''$

(9 a)



$^2A''$

(9 b)

Bond dissociation energies will be evaluated as total energy change (DE) for the reaction:

$$A\text{-}B \rightarrow A^{\cdot} + B^{\cdot}$$

For the α-disulphoxide only the diastereoisomer RS was considered: the diastereoisomer SS is less stable as shown in a previous work on the conformational properties of these molecules at SCF/6-31G* level[8].

The radicals formed in the homolytic bond dissociation of these molecules also appear to be involved in natural processes or in reactions of practical utility ranging from those occurring in biological systems to hydrogenation processes on coal[9]. The radicals RS· and RSO· were then investigated and results relative to the ground state structure are here reported.

Theoretical method

To avoid the breakdown of the Hartree-Fock model when describing the homolytic bond breaking and to tackle the electronic structure of molecules that are likely to be poorly described by a single-determinant wave-function, a multiconfiguration wavefunction model was used. All calculations were carried out with the CAS (complete active space) MCSCF method on an AIX/6000 workstation, employing the GAUSSIAN 92[10] and HONDO 8[11] packages.

In order to obtain a wavefunction which can correctly describe S-S bond breaking in the ground singlet state, the valence (active) space must include the σ and σ^* orbitals associated with the S-S bond. To obtain this valence space we found it convenient to use as initial orbitals those of the two isolated fragments (10 Å was assumed as the infinite distance). These orbitals were then used as starting point for the MCSCF procedure.

The total molecular energy was evaluated along the bond breaking coordinate in order to have details of the energy profile for this process. The S-S bond distance was adopted as reaction coordinate. For each fixed value of this distance the geometry was optimized with respect to all the remaining internal coordinates using MCSCF gradient procedure.

As starting geometries the conformational ground states at SCF/6-31G* level[8] were chosen and the MCSCF procedure applied at 3-21G* level. The ground states of the isolated radicals RS· and RSO· were also localized at MCSCF/3-21G* level employing the gradient method.

From *ab-initio* wavefunctions an APS population analysis[12] was performed in order to obtain a classical interpretation of electronic configurations of each molecule. The estimate of the bond-dissociation energy was performed as the difference between the energy of the molecule in its equilibrium geometry and that calculated at infinite distance (10 Å).

Results and discussion

Calculated bond lengths corresponding to the equilibrium structure of each molecule are reported in Table 1. A comparison between these results and those obtained from the normal SCF procedure[4,8] is also reported. The calculated equilibrium distances increase in the order (5)<(6)<(7) and for the α-disulphoxide (7) the bond length is noticeably longer than for (5) and (6). This result should indicate that α-disulphoxides are consistently less stable than disulphides and thiosulphinates.

The comparison between MCSCF and SCF results shows that the S-S bond is longer in the former approach, markedly for α-disulphoxide. A rationalization of the consistently different results of the two approaches together with a deeper insight into the structural factors affecting the relative stabilities of these compounds may be sought in the analysis of the relative weights of electronic configurations.

Tab. 1

Molecule	Bond	Bond length (Å)		
		MCSCF	$SCF^{4,8}$	Exptl.
5a	S-S	2.108	2.057	2.055^{b}
5b	S-S	2.090	2.053^{a}	2.038^{c}
6a	S(O)-S	2.125	2.104	2.108^{d}
6b	S(O)-S	2.097	2.094^{a}	
7a	S(O)-S(O)	3.831	2.144	
7b	S(O)-S(O)	4.313	2.147^{a}	

[a] 6-31G* basis set. [b]Ref. 13. [c]Ref.14. [d]Ref.15: referred to S-*p*-tolyl *p*-toluenethiosulphinate.

Tab. 2

	Configuration weights		
	2 0	**1 1**	**0 2**
5a	0.986	0.0	0.014
5b	0.987	0.0	0.013
6a	0.980	0.008	0.012
6b	0.988	0.0	0.011
7a	0.575	0.0	0.425
7b	0.495	0.0	0.504

The values are reported in Table 2 and represent the electronic configurations obtained by distributing two electrons on σ and σ* orbitals of the valence space, that is **2 0**, **1 1** and **0 2**. For disulphide (**5**) and thiosulphinate (**6**) the weights of the structure with two electrons on the σ orbital are near unity, and the contribution of excited electronic structures is quite small. For α–disulphoxide the structures **2 0** and **0 2** have nearly the same contribution, the excited electronic structure **0 2** being energetically close to the structure **2 0**, the only one taken into account in SCF calculations. For molecules of this type, simple SCF calculations cannot reproduce their chemical and structural properties.

From the APS[12] population analysis we evaluated the net spin population on atoms at equilibrium geometries. These values are reported in Table 3 for S and O atoms.

Tab. 3

APS population analysis: net spin populations (n.s.p) on O and S atoms.

	n.s.p S_1	n.s.p S_2	n.s.p O_1	n.s.p O_2
5a	0.066	0.066	-	-
5b	0.059	0.059	-	-
6a	0.045	0.010	0.065	-
6b	0.040	0.002	0.048	-
7a	0.119	0.119	0.879	0.879
7b	0.142	0.142	0.852	0.852
8a	1.000	-	-	-
8b	0.980	-	-	-
9a	0.128	-	0.872	-
9b	0.141	-	0.854	-

For disulphide (**5**) and thiosulphinate (**6**) the net spin population on S and O atoms is close to zero, all electrons being paired as lone-pairs or bonding electrons. For α–disulphoxide (**7**) these values show an unexpected electronic configuration: two electrons are unpaired and principally localized on O atoms. Furthermore these values are very close to those of the radicals (**9a,b**). This should indicate that the electronic configuration of this molecule is markedly non-bonding: α–disulphoxide strongly resembles two isolated radicals kept at equilibrium distance.

From APS population analysis[12] for each molecule and radical at equilibrium distances bond indices were also evaluated. These values for the S-S and S-O bonds are reported in Table 4.

For disulphide and thiosulphinate the S-S bond index is near to unity whereas for α–disulphoxide this value is smaller. This confirms that (**7**) is better described by almost isolated fragments which cannot lead to an S-S linkage but, more likely, to a sort of complex of van der Waals cluster type.

As regards the S-O bond indices and equilibrium bond lengths a considerable double bond character is found in the case of the thiosulphinate molecule yet for α-disulphoxide the bond order is close to unity. Once more the values for (**7a,b**) are very close to those of the radicals (**9a,b**).

In terms of classical electronic configuration a further insight on the structure of these molecules can be obtained from the sum of bond indices for each atom, which can be associated with a classical parameter such as the valence of atoms. The values are reported in Table 5 for S and O atoms.

Tab.4

APS population analysis: bond indices (B.I.) and optimized bond lengths (r).

	B.I. (S-S)	B.I. (S-O)	r(S-O) (Å)
5a	0.897	-	-
5b	0.909	-	-
6a	0.783	1.526	1.486
6b	0.809	1.423	1.512
7a	0.004	1.056	1.602
7b	0.019	1.077	1.590
8a	-	-	-
8b	-	-	-
9a	-	1.068	1.590
9b	-	1.077	1.590

Tab. 5

APS population analysis: sum of bond indices on S and O atoms.

	B.I S_1	B.I S_2	B.I O_1	B.I O_2
5a	1.830	1.830	-	-
5b	1.841	1.841	-	-
6a	3.147	1.871	1.768	-
6b	3.068	1.865	1.693	-
7a	1.975	1.975	1.086	1.086
7b	1.981	1.981	1.123	1.123
8a	0.950	-	-	-
8b	0.947	-	-	-
9a	1.982	-	1.098	-
9b	1.975	-	1.122	-

In compound (**5**), each S atom involves nearly two electrons (these values often underestimate the classical value[12]); for thiosulphinate (**6a,b**) one S atom involves more than three electrons, while the second sulphur atom only two electrons. The oxygen atom involves nearly two electrons, owing to the significant double bond character of the S-O linkage (**6a,b**). The electronic configuration of α-disulphoxide, in a classical view, can thus be described with each S atom involving only two electrons, one of these with the R group and a second one with the oxygen atom. The oxygen atoms involve only one electron, the second remaining unpaired and strongly localized.

The energy profiles calculated as a function of the S-S bond distance are represented in Figure 1 for derivatives with R = H. Inspection of these figures shows that the ground state potential energy curves for bond breaking are Morse-like curves.

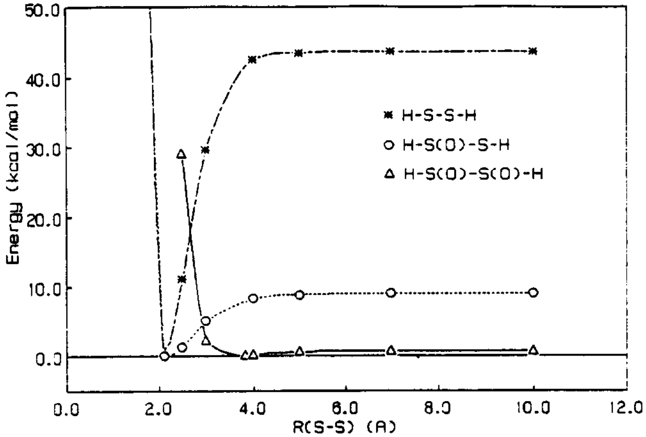


Fig. 1 MCSCF dissociation energy curves of disulphide (**5a**), thiosulphinate (**6a**) and α-disulphoxide (**7a**)

The values of the dissociation energy (DE) are reported in Table 6. These values are, as a general rule, underestimated with respect to dissociation energies (reported in parentheses), though they show a remarkable improvement with respect to those calculated at SCF/3-21G* level (~30 kcal/mol for **5a**[4]). As regards α-disulphoxide, a DE close to 1.0 kcal/mol should more properly be considered as an energy associated with a stabilizing interaction between two approaching molecules than with a proper bond.

Tab. 6

Values of the dissociation energies (DE) for the molecules examined.

Compound	DE (kcal/mol)	Compound	DE (kcal/mol)
5a	43.6(66)[b]	5b	43.5(74)[b]
6a	9.0	6b	18.0
7a	0.7	7b	1.0

[b] Ref.16.

The effect of H->CH_3 substitution on the calculated DE values is negligible for disulphides and for α–disulphoxides (slightly stabilizing) but rather significant for thiosulphinate: the energy for cleaving the bond increases about twice. The methyl group seems to decrease the net spin population on O atoms strengthening the S-S bond. Moreover, while the methyl group increases the bond index in all the derivatives, only the DE for thiosulphinate is significantly affected. The effect on S-S bond distances is to decrease their values for (**5**) and (**6**) and to increase it for (**7**).

To clarify the effect of R groups on the structural and reactional features of these molecules it is nevertheless necessary to analyse the effect of a larger set of substituents.

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