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An *ab initio* MO study on the disulfide bond: properties concerning the characteristic S–S dihedral angle

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Abstract. The characteristics of disulfide groups concerning the S-S dihedral angle are represented by *ab initio* SCF calculations using the split-valence 6-31G(*) basis set. It is shown that the hyperconjugation between the S-H bond and the electron pair on the other sulfur plays an important role in determining the characteristic S-S dihedral angle. The S 3d orbitals do not participate in such characteristics. The nature of the S-S bond is compared with that of the O-O bond. The S-S bond length varies largely depending on the S-S dihedral angle. This is related to the frequency-conformation correlation of the disulfide group.

Key words: Disulfide bond — Hyperconjugation interaction — Overlap population — Frequency-conformation correlation

1. Introduction

In activities and functions of proteins, the conformation of the disulfide bond (S-S bond) plays important roles. Although much theoretical work has been done which concentrates on the rotational barriers about the S-S bond [1-10], several problems are left unresolved.

Concerning the factors determining the characteristic S-S dihedral angle of about 90°, two kinds of interpretations have been presented: One is the hyperconjugation between the S-H bond and the electron pair on other sulfur [11] and the other is the participation of S 3d orbitals in accepting the unshared electrons from the neighbouring S atom [12].

Here, we investigate the nature of the S-S bond in comparison with the O-O bond, using the *ab initio* molecular orbital method with a large basis set, double zeta plus polarization. To clarify whether and how the S 3d orbital participates in the bonding, the analysis is presented by dividing the overlap populations into sp components and d components.

On the other hand, it is important to ascertain the frequency-conformation correlation of disulfide group, because this can be used to determine the conformations of cystine residues in proteins based on their Raman spectra. There have been controversial debates as to the nature of this correlation. Van Wart et al. [13, 14] proposed a nearly linear relationship between the S-S stretching frequency and the S-S dihedral angle. On the contrary, by use of normal coordinate calculations, Sugeta et al. [15, 16] showed that the S-S stretching frequency did not depend on the S-S dihedral angle but depended on the torsional isomerism about the C-S bond. Our analyses shed light on this problem: it becomes clear that the conformation of the S-S bond correlates with the frequencies observed in laser-Raman spectra.

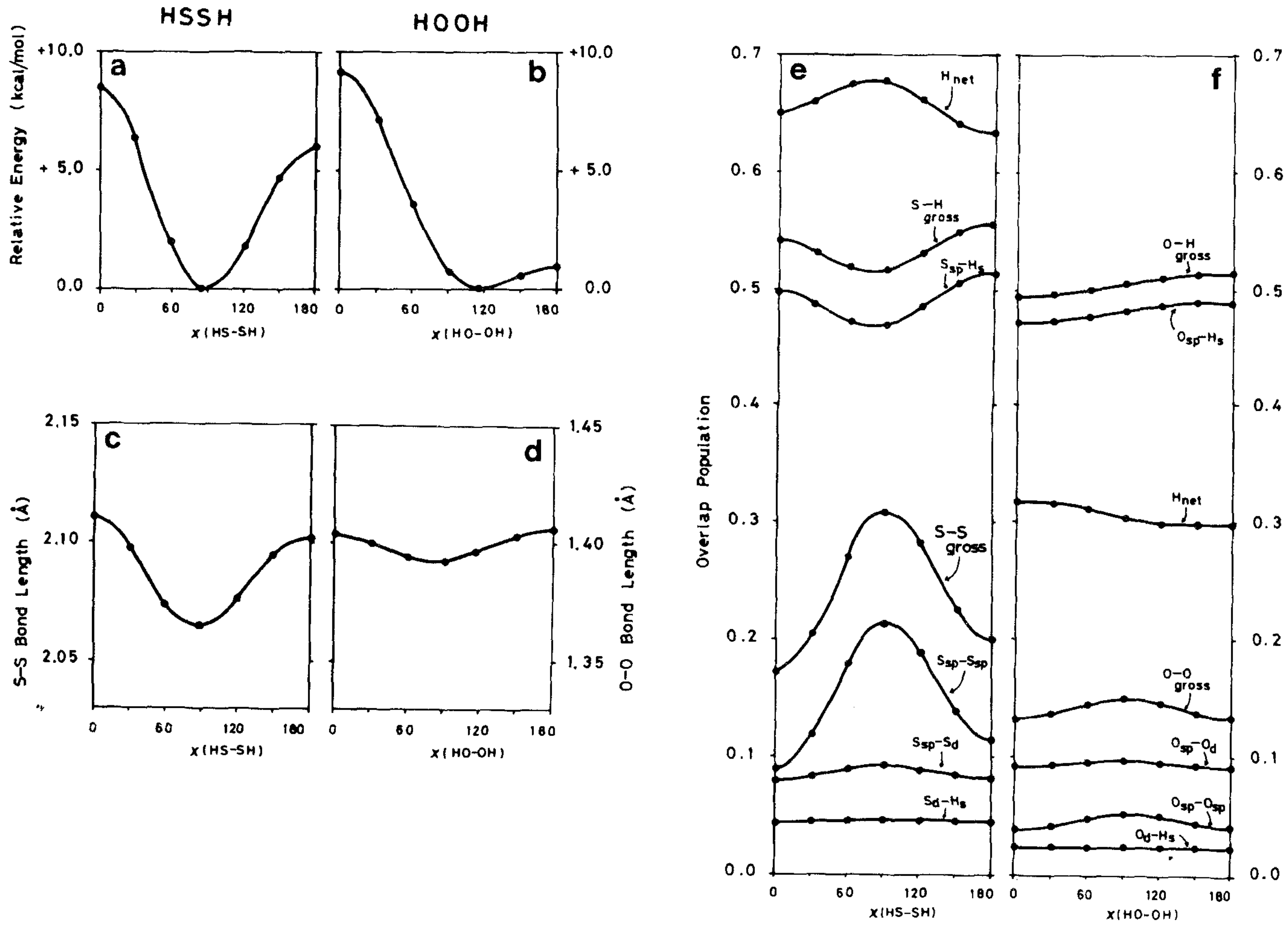
2. Methods

Ab initio calculations were carried out with the IMSPACK [17] and GAUSSIAN 80 [18] program systems. Gradient techniques [19] were used to determine molecular geometries at the single-determinant Hartree-Fock level. The split-valence 6-31G basis set [20, 21] was used, augmented with a set of six d functions, $\zeta_d = 0.65$ on sulfur atom and $\zeta_d = 0.8$ on oxygen atom.

HSSH and CH_3SSCH_3 are examined to determine the characteristics for rotation around the S-S bond. For the comparison, the same procedure is performed for HOOH. The conformational parameters are fully optimized, in each case.

3. Results and discussion

In order to investigate the origin of the characteristic S-S dihedral angle and the participation of the S 3d orbital in the S-S bond, the overlap populations [22] are analysed by dividing them into sp components and d components. For the comparison, the same procedure was performed for HOOH. The relative energies, S-S and O-O bond lengths and various overlap populations are shown as functions of S-S and O-O dihedral angles for HSSH and HOOH, respectively, in Fig. 1 and Tables 1-4. The variation in the S-S bond length correlates well with the stability of HSSH. The gross overlap population of the S-S bond also shows a similar correlation, as has already been pointed out [1, 2, 10]. Furthermore, by analysing each component of the overlap population, it becomes clear (Tables 3 and 4 and Fig. 1) that the sp component plays an important role in determining the dependence of the overlap population on the S-S dihedral angle. The overlap population of S_{sp}-S_d is almost independent of the S-S dihedral angle and the variation is comparable to that of O_{sp}-O_d. This denies the possibility that the S 3d orbitals participate in the characteristic structure by accepting the unshared electrons from the neighbor S atom.



13007 **Fig. 1.** The calculated relative energies (**a** and **b**), the S–S and O–O bond lengths (**c** and **d**) and various overlap populations (**e** and **f**) as functions
13008 of the S–S and the O–O dihedral angles for HSSH and HOOH, respectively

Table 1. Geometries[a] and relative energies[b] of HSSH for various dihedral angles

χ(HSSH)	0.0	30.0	60.0	89.84 (90.8)[c]	120.0	150.0	180.0
R(S-S)	2.111	2.097	2.073	2.064 (2.058)	2.077	2.095	2.102
R(S-H)	1.327	1.328	1.329	1.330 (1.345)	1.328	1.327	1.327
α(SSH)	98.20	98.52	99.14	99.14 (98.1)	97.65	95.58	94.63
Relative energy	+9.15	+7.36	+3.57	+0.71	0.0	+0.57	+0.95

[a] χ denotes dihedral angle. R denotes bond length. α denotes bond angle. Bond lengths in angstroms and bond angles in degrees

[b] Relative energies in kcal/mol

[c] Values in parentheses are experimental [23]

Table 2. Geometries[a] and relative energies[b] of HOOH for various dihedral angles

χ(HOOH)	0.0	30.0	60.0	90.0	116.01 (120.2)[c]	150.0	180.0
R(O-O)	1.404	1.400	1.395	1.393	1.397 (1.463)	1.403	1.406
R(O-H)	0.949	0.950	0.950	0.950	0.949 (0.967)	0.949	0.949
α(OOH)	106.7	106.0	104.5	103.1	102.1 (99.3)	100.9	100.6
Relative energy	+9.15	+7.36	+3.57	+0.71	0.0	+0.57	+0.95

[a] χ denotes dihedral angle. R denotes bond length. α denotes bond angle. Bond lengths in angstroms and bond angles in degrees

[b] Relative energies in kcal/mol

[c] Values in parantheses are experimental [24]

Table 3. Net atomic populations of S and H atoms and overlap populations and their components in HSSH for various dihedral angles

χ(HS-SH)	0.0	30.0	60.0	89.84	120.0	150.0	180.0
S	15.766	15.759	15.742	15.734	15.744	15.758	15.763
H	0.651	0.660	0.677	0.679	0.662	0.641	0.634
S-S gross	0.172	0.204	0.273	0.310	0.282	0.226	0.200
S_{sp}-S_{sp}	0.089	0.118	0.179	0.214	0.190	0.139	0.115
$S_{sp}-S_d$	0.080	0.083	0.090	0.092	0.089	0.084	0.082
S_d-S_d	0.003	0.003	0.003	0.003	0.003	0.003	0.003
S-H gross	0.542	0.533	0.519	0.517	0.533	0.551	0.556
S_{sp}-H_s	0.499	0.489	0.473	0.471	0.488	0.507	0.513
S_d-H_s	0.044	0.044	0.046	0.046	0.045	0.044	0.044

Table 4. Net atomic populations of O and H atoms and overlap populations and their components in HOOH for various dihedral angles

χ(HO-OH)	0.0	30.0	60.0	90.0	116.01	150.0	180.0
O	8.168	8.168	8.170	8.175	8.182	8.188	8.190
H	0.316	0.316	0.313	0.304	0.295	0.285	0.282
O-O gross	0.132	0.137	0.146	0.150	0.147	0.137	0.133
O_{sp}-O_{sp}	0.038	0.041	0.048	0.052	0.050	0.043	0.040
O_{sp}-O_d	0.092	0.093	0.096	0.097	0.095	0.092	0.091
O_d-O_d	0.002	0.002	0.002	0.002	0.002	0.002	0.002
O-H gross	0.495	0.497	0.502	0.507	0.511	0.513	0.513
O_{sp}-H_s	0.473	0.474	0.478	0.484	0.488	0.491	0.491
O_d-H_s	0.023	0.023	0.023	0.023	0.023	0.022	0.022

Winnewisser et al. [11] suggested that there is the hyperconjugative interaction between the S-H bond and the electron pair on the other sulfur, which causes the partial S-S double bonding at the expense of some S-H bonding and puts a positive charge on the S atom, as is shown below, qualitatively;

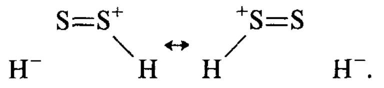


Figure 1 gives the quantitative basis to this scheme; near the S-S dihedral angle of 90°, where the total energy shows a minimum, each of the sp component of the S-H overlap population and the net atomic population of S atom shows a minimum, and each of the net atomic population of H atom and the sp component of the S-S overlap population shows a maximum (Fig. 1 and Table 3).

This hyperconjugative interaction can be interpreted in terms of the stabilizing interaction between the S-H σ^* orbital and the lone pair on the other sulfur (the p orbital), as shown in Fig. 2A. The interaction results in the double bonding character of the S-S bond (Fig. 2B). This scheme of hyperconjugation is similar to the case of XCH_2-CH_2^- [25]. The hyperconjugative interaction in the case of the S-S bond is larger than the case of CH_3-CH_2^-, because the difference of the electronegativities between S atom and H atom are smaller than that between C atom and H atom.

Here, it is interesting to compare the nature of the S-S bond with that of the O-O bond, because the characteristic O-O dihedral angle is not 90°. In the case of the O-O bond, the O-O bond length shows a minimum and the sp component of the O-O overlap population shows a maximum, at the O-O dihedral angle of 90°. However, the degree of the variation is much lower than the case of the S-S bond. The sp component of the O-H overlap population shows a maximum and the net atomic population of H atom shows a minimum at the O-O dihedral angle of 180°; but the degrees of variations are low. A number of studies have been done on the O-O bond [24, 26]; it is well known that the O-O dihedral

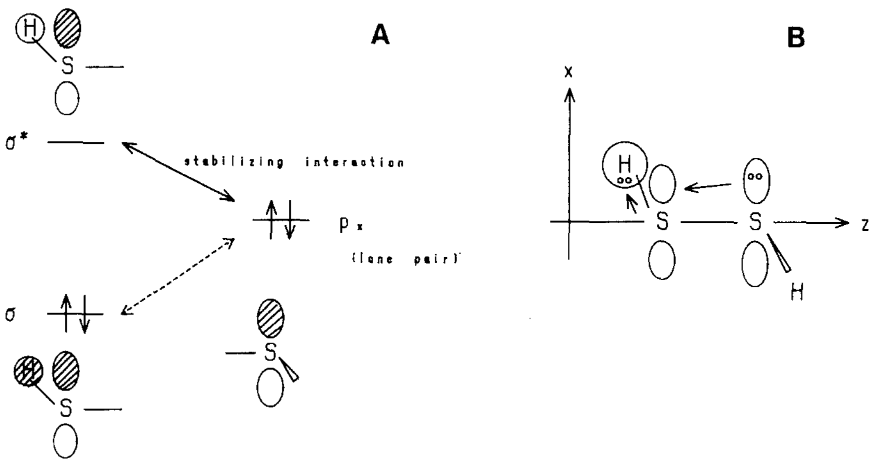
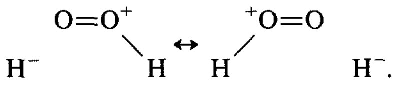


Fig. 2. A Schematic representation of the interaction between the σ-type orbitals of a S-H bond and the p orbital corresponding to the lone pair of the other S atom. B Schematic representation of the resultant change of electron density

angle for the most stable structure in HOOH is about 120° and that in CH_3OOCH_3 is 180°. The difference of the conformation between the O-O compound and the S-S compound may be due to the difference in the electronegativities between O atom and S atom. Because the electronegativity of O atom is much larger than that of H atom, the hyperconjugation, as is shown below, cannot be brought about;



$$\begin{array}{cccccc} & \mathrm{O{=}O^+} & & & \mathrm{^+O{=}O} & \\ & & \diagdown & \leftrightarrow \quad \diagup & & \\ \mathrm{H^-} & & \mathrm{H} & \mathrm{H} & & \mathrm{H^-}. \end{array}$$

Incapability of this hyperconjugation may be the reason for the difference of the nature between the O-O bond and the S-S bond, as is shown in Fig. 1.

For a better model of cystine residue in protein, CH_3SSCH_3 is examined: the calculated geometries and the relative energies for various S-S dihedral angles are listed in comparison with the experimental values, in Table 5. The *cis* (S-S dihedral angle: 0°) and *trans* (180°) barrier heights for CH_3SSCH_3 were experimentally estimated to be 6-12 kcal/mol [27], although the *cis* and *trans* barriers were not individually identified. The result of our calculations is in good agreement with the experimental estimate, and shows that the height of the *cis* barrier is higher than that of the *trans* barrier.

As is shown in Tables 1 and 5, the S-S bond length varies largely, depending on the S-S dihedral angle, and correlating with the stability of the molecule. In Fig. 3, the S-S bond length of CH_3SSCH_3 is plotted as a function of the S-S dihedral angle. Figure 3 is drawn to facilitate the comparison between the S-S bond length and the S-S stretching frequency (instead of the manner of Fig. 1c). Van Wart et al. [13, 14] showed from the observed spectra that the reduction in the S-S stretching frequency in the strained disulfide varied almost monotonically with their values of the CS-SC dihedral angle below about 65°. Figure 3 gives the

Table 5. Geometries[a] and relative energies[b] of CH_3SSCH_3 for various dihedral angles

χ(CSSC)	0.0	30.0	60.0	87.29 (84.7)[c]	120.0	150.0	180.0
R(S-S)	2.112	2.091	2.061	2.052 (2.038)	2.067	2.086	2.092
R(S-C)	1.813	1.813	1.815	1.817 (1.810)	1.816	1.814	1.812
R(C-H)	1.078	1.079	1.079	1.078 (1.097)	1.078	1.079	1.079
R(C-H′)	1.078	1.077	1.078	1.079	1.078	1.078	1.079
R(C-H″)	1.081	1.081	1.081	1.081	1.081	1.080	1.080
α(SSC)	106.4	105.2	103.8	103.2 (102.8)	101.8	99.42	98.27
α(SCH)	112.3	112.1	111.2	110.8 (108.9)	110.9	111.2	111.1
α(SCH′)	112.3	111.8	111.5	111.5	111.4	111.1	111.1
α(SCH″)	105.0	105.6	106.6	106.8	106.7	106.7	106.9
χ(SSCH)	62.46	58.49	54.60	58.00	59.92	61.21	61.27
χ(SSCH′)	−62.46	−65.69	−68.42	−64.46	−62.53	−61.32	−61.27
χ(SSCH″)	180.0	176.6	173.3	176.8	178.3	179.6	180.0
Relative energy	+11.36	+7.70	+1.98	0.0	+2.12	+4.80	+5.72

[a] χ denotes dihedral angle. R denotes bond length. α denotes bond angle. Bond lengths in angstroms and bond angles in degrees

[b] Relative energies in kcal/mol

[c] Values in parentheses are experimental [23]

reliable theoretical basis to their conclusion; the calculated S-S bond length increases as the S-S dihedral angle varies from near 90° to 0°. The increase of the bond length is consistent with weakening of the bond, and this results in lowering of the force constant for S-S stretching motion. Sugeta [16] carried out a normal mode analysis for several disulfides, with the assumption that the force field and the structural parameters except the S-S dihedral angle were independent of conformation, and showed that the S-S stretching frequency did not depend on the S-S dihedral angle. His assumption, however, needs to be reexamined, because the S-S bond length and the SSC angle vary depending on the S-S dihedral angle, as is shown in Table 5.

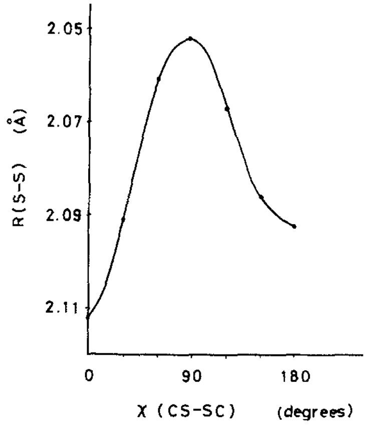


Fig. 3. The calculated S-S bond length (R(S-S)) of CH_3SSCH_3 as a function of the S-S dihedral angle (χ(CS-SC))

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