Electronic Structure of Lone Pairs. II.[1] Disulfides and Acyl Thiol

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The electronic structure and the electronic transition of three cyclic disulfides, $(CH_2)_3S_2$, $(CH_2)_4S_2$, and $(CH_3)_2S_2$, are calculated by the semi-empirical ASMO SCF method in order to study the interaction of the neighbouring lone pairs of the S–S bond in connection with the ability of reductive scission. It is concluded that the absorption at 2500—3000 Å is the transition of n—σ^* and that the variation in the maximum for the various cyclic disulfides and the chain disulfide are induced by the change in the dihedral angle that a molecule can take. The electronic structure and the reactivity of $(CH_3)_2S_2$, CH_3SSH, and CH_3SCOCH_3 are then discussed on the basis of an extended Hückel calculation. It is suggested that there is the possibility of an interaction between two molecules, R_2S_2, through the S–S bond of each molecule, in the HO of one molecule and in the LV of another.

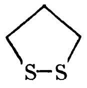
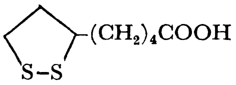
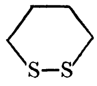
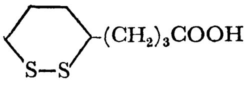
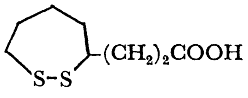
The compounds containing sulfur atoms have some characteristic properties in organic and biological reactions. The S–S bond between two divalent sulfur atoms has a particular role in retaining the tertiary structure of polypeptide as a weak chemical bond. Also, 6,8-thioctic acid is a coenzyme for the decarboxylation of pyruvate to active groups, which through CoA feed carbon atoms into the Krebs cycle; a reductive scission of the S–S linkage of 6,8-thioctic acid to form a dithiol is also involved in the mechanism.[3] Acetyl CoA, $CoASCOCH_3$, is an important biological acetylating reagent, and its C–S bond is a so-called high-energy bond. Though many experimental investigations have been made, there have been only a few discussions of their electronic structures.[4]

Previously we calculated the electronic structure and the electronic interaction of the lone pairs of some azine compounds and quinones.[5] In this connection, in the earlier part of the present paper the electronic structures and electronic transitions of several disulfides, trimethylene-disulfide $(CH_2)_3S_2$ (a model compound of 6,8-thioctic acid), tetramethylene-disulfide $(CH_2)_4S_2$, and dimethyl disulfide $(CH_3)_2S_2$ were investigated by the semi-empirical ASMO SCF method[6] for valence electron systems in order to study the interaction of the neighbouring lone pairs of S–S linkage in connection with the ease of reductive scission. In the later part, the electronic structures of $(CH_3)_2S_2$, CH_3SSH, and CH_3SCOCH_3 (a model compound of $CoASCOCH_3$) are calculated by the extended Hückel method[7] in order to establish the properties of these molecules, based upon the MO theory, and to discuss the reactivity in relation to the lone pair.

I. Dimethyl Disulfide and Cyclic Disulfides

The normal value for the dihedral angle for the S–S bonds of such compounds as S_8, S_2Cl_2,[8] and $(CH_3)_2S_3$[9] is known to be approximately equal to 100° from the X-ray analysis, the measurement of the dipole moment, the IR spectrum, and so on. The dihedral angle of $(CH_3)_2S_2$,[9,10] too, is approximately 90°. On the other

Table 1. Observed transition energies[12] of some disulfides

	 	 	$nH_7C_3\cdot S\text{–}S\cdot nC_3H_7$ 	$H_3C\text{–}S\text{–}S\text{–}CH_3$[9]
λ_{max}(eV)	3.76	4.28	4.96	4.96
Oscillator strength			increase	0.031
ϕ°	~0	~40	~90	90

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[3] P. W. Sadler, *Chem. Rev.*, **60**, 575 (1960); J. D. Watson, "Molecular Biology of the Gene," W. A. Benjamin Inc., New York (1965).

[4] B. Pullman and A. Pullman, "Quantum Biochemistry," Interscience publishers, New York, London (1963): VII.

[5] T. Yonezawa, H. Yamabe, and H. Kato, This Bulletin, **42**, 76 (1969).

[6] H. Konishi, H. Kato, and T. Yonezawa, Symposium of the electronic structure of molecules, Hokkaido, October, 1967; This Bulletin, **42**, 933 (1969).

[7] R. Hoffmann, *J. Chem. Phys.*, **39**, 1397 (1963).

[8] L. Pauling, *Proc. Nat. Acad. Sci.*, **35**, 495 (1949).

[9] S. D. Thompson, D. G. Carroll, F. Watson, M. O. Donnel, and S. P. McGlynn, *J. Chem. Phys.*, **45**, 1367 (1966).

[10] S. P. Stevenson and J. Y. Beach, *J. Amer. Chem. Soc.*, **60**, 2872 (1938).

hand, only a few investigations[9,11] have been performed on the electronic structures and configurations of these compounds in relation to the electronic spectrum. Calvin *et al.*[12] observed the UV spectrum of some cyclic disulfides and *n*-propyl disulfides out of their biological interest in 6,8-thioctic acid (see Table 1). They discussed the variation in the absorption spectra in the 2500—3000Å range of these compounds qualitatively in relation to the ring strain, which may come from the interaction of the two lone pairs of the sulfurs and the shift of the dihedral angle from its stable value of about 90°. Later, Bergson[11] made an attempt to interpret the above observation in terms of a simple molecular orbital theory. That is, he explained it by considering only the interaction between two lone pairs constructed by the 3*p* electrons of the neighbouring sulfur atoms.

Including all the valence electrons, and also taking into account the conformations of these molecules, our calculation in this paper was carried out by the semi-empirical ASMO SCF method for valence electron systems previously proposed by the present authors.[6]

Calculations. By estimating on the base of the molecular model, the dihedral angles of the above cyclic disulfides seem to be in the neighbourhood of 0°, 40°, and 90° for the five-, six-, and seven-membered rings respectively. In order to establish the relation between the dihedral angle and the absorption maximum, shown in Table 1, the electronic structures of dimethyl disulfide with the dihedral angles of 0°, 45°, and 90° are calculated. It is the purpose of these calculations not only to reveal the ϕ dependency (see Fig. 1) of the absorption spectra, but also to carry out a simplified model calculation for the cyclic disulfides. The validity of this simplification is confirmed by the calculation of tri- and tetra-methylene disulfide for the assumed structure of Fig. 1. The bond lengths and bond angles of dimethyl disulfide and the five-membered ring are referred to the compilation by Sutton.[13] They are shown in Table 2. The structure of the six-membered ring is assumed by taking the S–S, S–C, and C–C bond lengths as 2.10Å, 1.78Å, and 1.54Å respectively and the hybridization for all carbon atoms as sp^3. However, the resulting dihedral angle becomes approximately 10°, which is considerably smaller than the expected value.[14] The numberings of the atoms of the five- and six- membered rings are shown in Fig. 1, in which the S_1, S_2, C_3, and C_4 atoms and the S_1, S_2, and C_6 atoms are assumed to be on the same x–y planes. The calculation was carried out by the semi-empirical ASMO SCF method for valence electron systems,[6] in this method the approximation of the zero differential overlap is adopted, and the contribution of 3*d* and 4*s* orbitals of the sulfur atom is neglected.

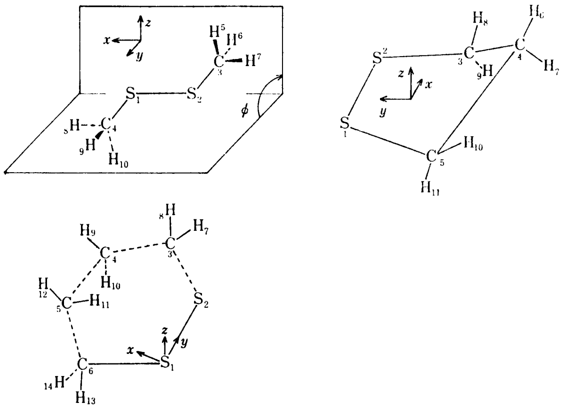

Fig. 1. Models employed for the calculation, coordinate axes and dihedral angle ϕ.

TABLE 2. BOND LENGTHS (IN Å) AND BOND ANGLES (IN DEGREE)

$(CH_3)_2S_2$	S–S	2.04	$(CH_2)_4S_2$	S–S	2.10
	S–C	1.78		S–C	1.78
	C–H	1.09		C–C	1.54
	∠SSC	1.07		C–H	1.09
$(CH_2)_3S_2$	S–S	2.10	CH_3S_2H	S–S	2.04
	S–C	1.84		S–H	1.33
	C–C	1.54		C–H	1.09
	C–H	1.09		∠SSH	95
	∠SSC	97	CH_3SCOCH_3	S–C	1.78
	∠CCC	116.5		C–C	1.54
	∠SCC	109.7		C–O	1.22
dihedral angle[a)]		10		∠CCS	120
				∠CSC	107
			C_2H_6	C–C	1.54
				C–H	1.09

a) Dihedral angle between the x–y plane and the C_3–C_4–C_5 plane (see Fig. 1).

TABLE 3. SOME CALCULATED RESULTS OF $(CH_3)_2S_2$, $(CH_2)_3S_2$, AND $(CH_2)_4S_2$

	$(CH_3)_2S_2$			$(CH_2)_3S_2$	$(CH_2)_4S_2$
	$\phi°=0$	$\phi°=45$	$\phi°=90$		
Difference of the total energy (eV)	1.99	0.64	0.00	—	—
Transition energy (eV)	4.08	4.19	4.81	3.79	4.01
Oscillator strength	0.039	0.043	0.084	0.015	0.034
p_{sr}^{LV} of the S–S p_σ bond	—0.777	—0.772	—0.770	—0.831	—0.762

a) First $n_1 \rightarrow \sigma^*$ transition

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11) G. Bergson, *Arkiv Für Kemi.*, **12**, 233 (1958).

12) J. A. Barltrop, P. M. Hayes, and M. Calvin, *J. Amer. Chem. Soc.*, **74**, 6153 (1952); *ibid.*, **76**, 4343 (1954).

13) L. E. Sutton, "Interatomic Distances of Molecules and Ions," The Chemical Society, London (1958).

14) The dihedral angle of the six-membered ring is considered to be about 40°, assuming a molecular model with somewhat deformed angles of the carbon atom from the sp^3 hybridization. This value (∼40°) seems to be reasonable in view of the UV spectrum (see Table 1). when the sp^3 hybridization is assumed, for convenience in the calculation of the molecular conformation, the dihedral angle becomes about 10°.

Dimethyl Disulfide. The calculated results for the dimethyl disulfide, $(CH_3)_2S_2$, are given in Table 3. The minimum value of the total energy[15] of $(CH_3)_2S_2$ is obtained for the dihedral angle of 90°; this is in accordance with the observation.[10] The calculated transition energies are in good agreement with the experimental values (Table 1). The oscillator strengths increase with the increase in the dihedral angle from 0° to 90°, and run parallel with the experimental values.[12] The lowest vacant orbital (LV) becomes an antibonding orbital of the S–S $p\sigma$ bond. The partial bond orders of the S–S $p\sigma$ bond, $p_{\mathrm{sr}}^{\mathrm{LV}}$,[6] in the lowest vacant orbital are negative and large, and their absolute values increase in the order of 0°, 45°, and 90°. This means that the ring-opening reaction by the means of the nucleophilic reagent occurs more easilly in this order; the five-, six-, and seven-membered rings, this order may be parallel to that of the ring strain of these compounds.[12,16,17] In fact, the ring-opening reaction to form linear polymers is known to take place in this order.[16] It has been reported[18] that 5- and 4- thioctic acids have, respectively, 0.3% and 0.1% pyruvate oxidation activity relative to 6-thioctic acid.

TABLE 4. ATOMIC-CHARGE DENSITY, AO-CHARGE DENSITY OF $(CH_3)_2S_2$ AND BOND ORDER p_{s,p_i} OF THE SULFUR ATOM

ϕ°(degree)		0	45	90	180
Atomic-charge density	S_1	6.126	6.126	6.128	6.183
	C_3	4.142	4.127	4.123	4.115
	$C_3+H_6+H_7+H_8$	6.874	6.873	6.872	6.862
AO-charge density	S_1s	1.664	1.664	1.665	1.665
	x	1.109	1.111	1.110	1.108
	y	1.354	1.356	1.363	1.367
	z	1.998	1.994	1.990	1.998
	S_2s	1.664	1.664	1.665	1.665
	x	1.109	1.105	1.109	1.108
	y	1.354	1.683	1.990	1.367
	z	1.998	1.683	1.364	1.998
	C_3s	0.987	0.982	0.981	0.979
	x	1.110	1.110	1.111	1.108
	y	0.916	0.911	0.904	0.899
	z	1.130	1.124	1.126	1.129
	C_4s	0.987	0.981	0.981	0.979
	x	1.110	1.108	1.108	1.108
	y	0.916	1.014	1.130	0.899
	z	1.130	1.016	0.904	1.129
p_{s,p_i}	S_1s-x	0.260	0.262	0.264	0.261
	s-y	−0.336	−0.335	−0.334	−0.333
	s-z	0.000	0.001	0.000	0.000
	S_2s-x	−0.260	−0.259	−0.263	−0.261
	s-y	−0.336	−0.235	0.002	0.333
	s-z	0.000	−0.240	−0.334	0.000

The atomic orbital (AO) charge densities[6] of the sulfur atom are given in Table 4. For 0°, the electron densities of the p_z AO of the sulfur atom are almost all 2.0; this indicates a lone-pair orbital of the p type. For 90°, the p_z orbital of the S_1 atom (S_1z) and the p_y orbital of the S_2 atom (S_2y) become lone-pair orbitals. That is, the direction of the interacting lone-pair orbitals varies, but almost without changing the absolute value of the population, following the change in the dihedral angle, ϕ. More exactly, one can see in Table 4 that the AO density of the lone pair (S_1z) has a minimum value at 90°, that is, the delocalization of the lone pair is at a maximum. As the dihedral angle increases, the total electron density of the S_1 atom increases and those of the C_3 atom and the CH_3 group, which is a summation of the atomic-charge[6] of the atoms C_3, H_4, H_5, and H_6, decrease. Also, the AO-charge density of S_1y increases and that of C_3y decreases. That is, the electron may migrate from the p_y orbital of the C_3 atom to that of the S_1 atom.[19] The bond orders, s–x and s–y, of the sulfur atom are nearly equal, and that of the s–z is zero for 0°, as is shown in Table 4. The direction of the atomic dipole becomes approximately that of an sp^2-type lone pair. That is, other sp^2-type lone pairs, which result from the delocalization of 3s electrons, are observed. These sp^2-type lone pairs, too, rotate according to the change in the dihedral angle, ϕ.

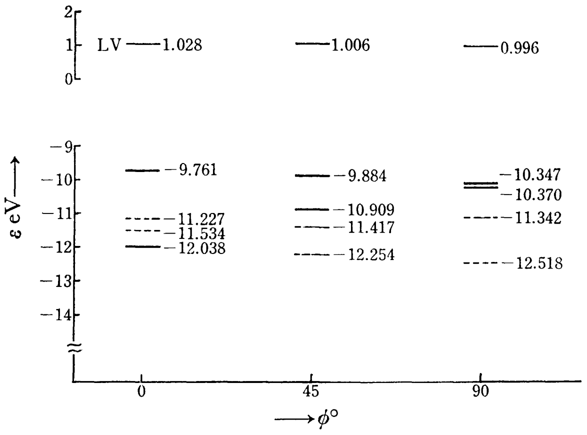

Fig. 2. Lone pair levels and the lowest vacant level of dimethyldisulfide *vs.* dihedral angle ϕ. The heavy lines and the dashed designate the levels of the p-type lone-pair and sp^2-type lone pair, respectively.

The lone-pair levels and the lowest vacant levels of $(CH_3)_2S_2$ for the various ϕ's are illustrated in Fig. 2. The fine line designates the lowest vacant level, while the heavy line and the dashed line designate the lone-pair level of the p type and that of the sp^2 type respectively. It is observed that the splitting of the lone-pair levels of the p type becomes larger in the order of 90°, 45°, and 0°. This may mean that the lone pairs of the p type aligned parallel, as in 0°, have more mutual

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15) The difference of the total energy for 180° is obtained as 0.63 eV.

16) J. G. Affleck and G. Dougherty, *J. Org. Chem.*, **15**, 865 (1950).

17) A. V. Tobolsky, F. Leonard, and G. P. Roeser, *J. Polym. Sci.*, **3**, 604 (1948).

18) M. W. Bullock, J. A. Brockman, Jr., E. L. Patterson, J. V. Pierce, and E. L. R. Stockstad, *J. Amer. Chem. Soc.*, **74**, 3455 (1952).

19) The same tendency has been observed by Morokuma *et al.* in (Ref. 20) their *ab-initio* calculation of H_2O_2; it may also be seen in the report by Pitzer *et al.* (Ref. 21).

20) L. Pedersen and K. Morokuma, *J. Chem. Phys.*, **46**, 3941 (1967).

21) W. E. Palke and R. M. Pitzer, *ibid.*, **46**, 3948 (1967).

interaction than those in an orthogonal form, as in 90°.

Trimethylene Disulfide and Tetramethylene Disulfide. The calculated results for trymethylene disulfide, $(CH_2)_3S_2$, tetramethylene disulfide, $(CH_2)_4S_2$, are given in Table 3. The transition energies of the n–σ^* of $(CH_2)_3S_2$ show a better agreement with the observed value than in the preceding, simplified calculation, in which the dimethyl disulfide of the dihedral angle 0° corresponds to the observed value of $(CH_2)_3S_2$. The first n–σ^* transition of $(CH_2)_4S_2$ is 4.01 eV; it is the transition from the next highest occupied lone-pair level of a p type to the lowest unoccupied level.[22] As has been mentioned previously, the dihedral angle of the assumed structure is smaller than the expected angle[14] (See Table 1). Therefore, the obtained transition energy should become smaller than the experimental value. The calculated oscillator strength of $(CH_2)_3S_2$ is larger than $(CH_2)_4S_2$, showing a parallelism with the experimental value. Judging from the value of p_{rs}^{LV}, LV is an antibonding orbital of the S–S $p\sigma$ bond. This is compatible with the fact that the scission of the S–S bond of 6,8-thioctic acid is induced by light. The atomic-charge density,[6] the AO charge density,[6] and the partial bond orders of the s–x, s–y, and s–z of the sulfur atom are shown in Table 5. For $(CH_2)_3S_2$, two lone pairs of the p type in the z direction are parallel, and the lone pairs of the sp^2 type lie in a nearly orthogonal form; those of the sp^2 type, too, are approximately orthogonal.

TABLE 5. ATOMIC-CHARGE DENSITY, AO-CHARGE DENSITY AND BOND ORDER, p_{s,p_i}, OF THE S_1 ATOM OF $(CH_2)_3S_2$ AND $(CH_2)_4S_2$

		$(CH_2)_3S_2$	$(CH_2)_4S_2$
Atomic-charge density		6.148	6.181
AO-charge density	s	1.716	1.679
	x	1.308	1.405
	y	1.126	1.101
	z	1.999	1.996
p_{s,p_i}	S–x	−0.294	−0.330
	S–y	−0.286	−0.238
	S–z	−0.000	0.003

From the results of our calculation, it may be concluded that the absorption of 2500—3000Å is an n–σ^* transition and that the variation in the absorption maximum for various cyclic disulfides and a chain disulfide are induced by the change in the dihedral angle, ϕ, of the molecule.

II. Chemical Reactivity of $(CH_3)_2S_2$, CH_3SSH, and CH_3SCOCH_3

It has been noted that the E–H method[17] is a tolerable approximation in some cases for discussing the reactivity.[23] Sometimes, the E–H method gives more reasonable results for use in the interpretation of the reactivity, compared to the semiempirical ASMO SCF method, particularly in the calculation of the interaction of two molecules.[24] Therefore, we employed the E–H method in discussing the chemical reactivity of $(CH_3)_2S_2$, CH_3SSH, CH_3SCOCH_3, and the proton affinity of the S–S bond. It will be established later that a discussion similar to those given by the E–H calculation regarding the reactivity of $(CH_3)_2S_2$ and the cyclic interaction of two $(CH_3)_2S_2$ molecules is also possible on the basis of SCF calculations.

In the E–H calculation,[7] the resonance integral, H_{rs}, is evaluated by $H_{rs}=1/2\ KS_{rs}(H_{rr}+H_{ss})$, putting $K=1.75$, where S_{rs} is the overlap integral between two AO's, X_r and X_s. The Coulomb integrals, H_{rr}'s are given in Table 6.

TABLE 6. H_{rr}'s IN THE EXTENDED HÜCKEL CALCULATION (eV)

	1s	2s	2p	3s	3p
H	−13.60	—	—	—	—
C	—	−21.43	−11.42	—	—
O	—	−35.30	−15.45	—	—
S	—	—	—	−20.08	−13.32

$(CH_3)_2S_2$; First we will report the results for $(CH_3)_2S_2$, although the molecular orbital interpretation of the reactivity is carried out analogously to that for H_2O_2, previously reported by the present authors.[23] The highest occupied orbital (HO) and the next highest occupied orbital (NHO) are almost degenerate lone-pair MO's. The AO populations[26] of S_2y and S_1z

TABLE 7. SOME AO POPULATIONS AND PARTIAL AO BOND POPULATIONS, p_{rs}^{HO} AND p_{rs}^{LV} IN HO AND LV OF $(CH_3)_2S_2$

		HO
AO population	S_2y	1.084
	S_1z	0.289
p_{rs}^{HO}	S_1x–S_2x	−0.013

		LV
AO population	S_1x, S_2x	0.563
	S_1y, S_2z	0.159
p_{rs}^{LV}	S_1x–S_2x	−0.859

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[22] The orbital sequence of the 1 one-pair MO's of $(CH_2)_4S$ is slightly different from that of $(CH_3)_2S_2,\phi=45°$, shown in Fig. 2. The highest occupied level (—9.131 eV) of $(CH_2)_3S_2$ is the one connected with the sp^2-type lone pair, which is anomalously high compared to the highest occupied level of $(CH_2)_3S_2$ in various dihedral angles and $(CH_2)_3S_2$. The next highest occupied level (—9.905 eV) becomes the one connected with the p-type lone pair. The transition energies and the oscillator strengths, Osc., of these n(p type)-σ^* and n(sp^2 type)-σ^* transitions of $(DH_2)_4S_2$ are obtained as follows:

n(p type)-σ^* ; 4.01 eV, Osc.=0.034 (See Table 2)

n(sp^2 type)-σ^* ; 4.78 eV, Osc.=0.224

[23] T. Yonezawa, O. Yamamoto, H. Kato, and K. Fukui, *Nippon Kagaku Zasshi*, **87**, 26 (1966); This Bulletin, **40**, 307 (1967).

[24] In the MO calculation of the system composed of NH_3 and HCHO, by changing it the intermolecular distance or the mutual angle, is changed the E-H calculation gives more reasonable results than the SCF method (Ref. 25).

[25] H. Yamabe, H. Kato, and T. Yonezawa, "Electronic Structure of Lone Pairs IV. Transannular Interaction of Some Mesocycles," (to be published in This Bulletin)

[26] K. Morokuma, H. Kato, T. Yonezawa, and K. Fukui, This Bulletin, **38**, 1263 (1965).

in HO, which are almost equal to those of S_1z and S_2y in NHO respectively, have large values, as is shown in Table 7. This means that a cation attack takes place in the lone-pair direction. LV is an antibonding orbital of the S–S $p\sigma$ bond, and AO populations of S_1x and S_2x are large. This means that the anion attack should takes place at the S atom of the S_2 atom from the outside of the S–S bond[27] and that the S–S $p\sigma$ bond is ready for scission. Then, in the absence of steric hindrance, the molecule having the S–S bond will be able to receive the nucleophilic and the electrophilic interaction from two directions at the same time in a mutually perpendicular way.[26] This property causes the S–S bond to be susceptible to ionic scission.[28] A similar discussion can also be made in the case of the SCF calculation of $(CH_3)_2S_2$, presented in the preceding section.

Possibility of a Cyclic Interaction of two Disulfides. The existence of a O_4 molecule has been known;[30] it seems to be an associated form of two O_2 molecules, in which two O_2 molecules are held together by bonds much weaker than an ordinary covalent bond. In our calculation of $(CH_3)_2S_2$, we notice the possibility of a cyclic interaction between two molecules, R_2S_2, through the S–S bond of each molecule, employing the HO of one molecule and the LV of another.[31] Figures 3(A) and (B) show two kinds of the interaction of $(CH_3)_2S_2$ molecules (I, II); only the atoms S and C are illustrated. Figure 3(A) shows the interaction between the HO of the molecule I and the LV of the molecule II,[32] while Fig. 3(B) shows the interaction between the LV of the molecule I and the HO of the molecule II, which is the reverse of that of Fig. 3(A). The relevant MO coefficients of the p_y orbitals[32] are also shown.[33] The S_1–S_2 and the S_1–C_4 bonds of the I and II molecule are placed in the same plane, and the S_2–C_3 bond is directed upwards from the x–y plane. As has been pointed out by Fukui *et al.*,[31] the most favorable conditions for a cyclic interaction include the same symmetry in the corresponding orbitals of the two molecules. This condition is satisfied in the above case.[34,35]

If a II molecule has a conformation which is a mirror image[36] of that of the I molecule, other forms of the interaction may be constructed.

Furthermore, not only the interactions in the completely-square forms, such as in Figs. 3(A),3(B),3′(A),[34] and 3″(A),[34] but also those in the oblique forms are possible.[37] An example, which is an oblique form of Fig. 3′(A),[34] is shown in Figs. 4(A) and 4(B), where the interaction is denoted by the dotted line. In Fig. 4(A), interaction is assumed between the p_y AO (lone-pair AO) in the HO of one molecule and the p_y AO in the LV of another molecule. At the same time, the inverse interaction, as in Fig. 4(B), is also possible, in which the HO and LV in Fig. 4(A) are replaced by the LV and HO respectively. By the superposition of these two interactions, the interaction between disulfides will become stronger. An interaction of this type may be expected in a crystal of disulfides.[37]

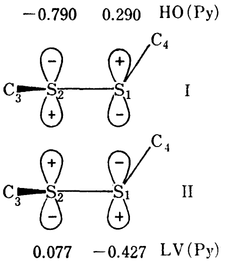

Fig. 3′(A)

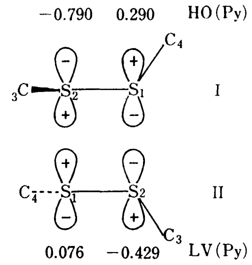

Fig. 3″(A)

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[27] Because, in the inner part of the S–S bond, the mutual signs of the S_1x and S_2x are antagonistic, the AO's largely cancel out and the MO develops to the outside of the S–S bond, as has been pointed out by Fukui *et al.* in their work on H_2O_2 (Ref. 23).

[28] In the ionic scission of the S–S bond, the approach of a nucleophile or an electrophile, for the capture of positive or negative scission products, becomes easy (Ref. 29).

[29] H. L. Yakel, Jr., and E. W. Hughes, *Acta Cryst.*, **7**, 291 (1954).

[30] L. Pauling, "The Nature of the Chemical Bond," 3rd Ed., Cornell University Press, (1960); Chap. 10.

[31] K. Fukui and H. Fujimoto, This Bulletin, **39**, 498 (1966).

[32] The p_y orbital of the S_2 atom in HO is a lone-pair orbital. The numbering of the atoms and the coordinate axes for each $(CH_3)_2S_2$ molecule are the same as those of Fig. 1.

[33] In the preceding section it has been shown that a disulfide such as $(CH_3)_2S_2$, is most stable at the dihedral angle of 90°. It has been pointed out by Fukui (in a private communication) that this stabilization at 90° partially due to the intramolecular interaction between the S_2y AO(lone-pair AO) in the HO and the S_2y AO in the LV.

[34] From the point of view of orbital symmetry, another type of cyclic interaction may be expected, as in Fig. 3′(A), as may its inverse form (not shown) constructed in a way similar to that of Fig. 3(B). However, in this case, as the lone pairs of the S_2 atoms of the molecules I and II lie in a line on the same plane, this cyclic form is less probable. The other form of the interaction between the p_y AO(Ref. 33) in the HO of the molecule I and the p_z AO in the LV of the molecule II is also possible, as in Fig. 3″(A) and as in its inverse form. That is, the molecule II of Fig. 3(A) is rotated about its S–S axis. Then, in Fig. 3″(A), the S_1–C_4 bond of the molecule I and the S_2–C_3 bond of the molecule II are placed on the same plane. The S_2–C_3 bond of the molecule I is directed upwards from the plane of the paper, and the S_1–C_4 bond of the molecule II, downward from the plane. However, this type of its interaction is also not very probable, because the lone pairs of the S_1 atoms of the molecules I and II lie on a line.

[35] In the case of the SCF calculation, too, there is a possibility of a cyclic interaction when the s orbitals (their NO coefficients are 0.309 and —0.307) are used instead of the p_y AO in the LV of the molecule II of Fig. 3(A) and the molecule I of Fig. 3(B). In this calculation, as a form of cyclic interaction, some rotation about its S–S axis is permited for each molecule, I and II, because the s orbital is spherically symmetric.

[36] B. M. Oughton and P. M. Harrison, This Bulletin, **2**, 396 (1959); *ibid.*, **10**, 497 (1957).

[37] Yakel *et al.* describe, in their report about the X-ray analysis of *N,N′*-diglycyl-L-cystine dihydrate, that the van der Waals contacts (or the distances) between molecules related by the b-axis repeat are significantly lower than the normal value (Ref. 29). It is to be expected from the discussion in this section that not only the hydrogen bond (Ref. 29), but also the interaction between the S–S bonds may induce the smaller distance of the repeat. Oughton *et al.*, in their study of the structure of hexagonal L-cystine, also pointed out the close van der Waals contacts between each sulfur atom and its non-bonded neighbouring atoms (Ref. 36). Takagi *et al.* have reported that the CD spectrum of L-cystine hydrochloride indicates interaction between the neighbouring S–S bonds (Ref. 38).

[38] T. Takagi, N. Ito, and T. Isemura, The 23rd Annual Meeteing of the Chemical Society of Japan, April, 1970.

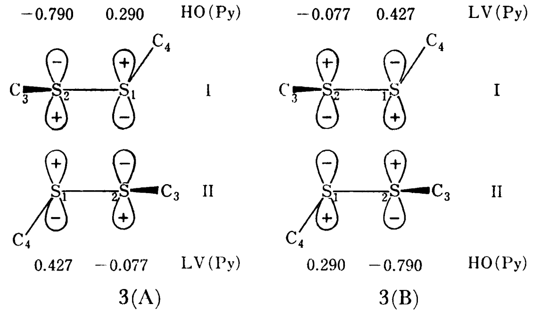

Fig. 3. Cyclic interaction of two disulfides. (A); Interaction between *py* AO in HO of the molecule I and *py* AO in LV of the molecule II. (B); Interaction between *py* AO in LV of the molecule I and *py* AO in HO of the molecule II (Ref. 24).

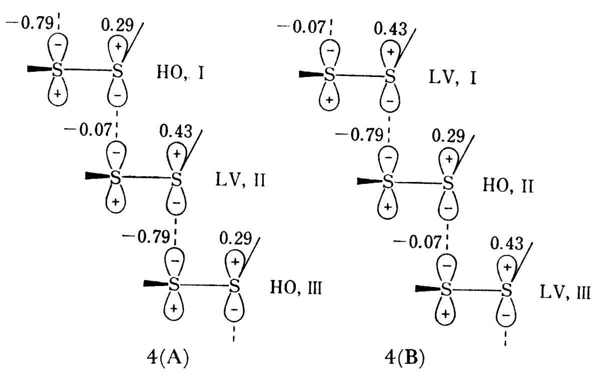

Fig. 4. Interactions in the oblique form.

Proton Affinity of the S–S Bond. Hughes described, in his review,[29] that the outstanding reactive characteristic reactivity of the S–S bond is its ability to undergo ionic (heterolytic) scission in reactions with nucleophilic reagents, and that ionic scission takes place also upon the attack of such electrophilic reagents such as sulfide-forming metal cations and proton. The S–S bond also acts as a chemical bond, are which undergoes ionic scission easily, holding a tertiary structure of polypeptide through a CyS–CyS linkage. Disulfide and dithiol interconversion is a conspicuous property of a S–S bond. In contrast with this, hardly no ionic scission of a C–C bond takes place. These properties of the S–S bond may be due partly to the lone pair of the sulfur and partly to the 3*d* orbitals of the sulfur. In this paper, only the contribution of the lone pair will be discussed.

TABLE 8. PROTON AFFINITY OF A S–S BOND

	direction of a proton approach	atomic population of proton	$\Delta q^{a)}$	ΔE(eV)$^{b)}$
$(CH_3)_2S_2$	case I	0.999	0.966	−4.75
	case II	0.776	0.383	−2.90
C_2H_6	case III	0.525	0.315	−1.72
	case IV	0.526	0.301	−1.85

a) The difference of atomic population, *q*, between two atoms of Fig. 4.

$\Delta q = q(S_1) - q(S_2)$ for $(CH_3)_2S_2$

$\Delta q = q(S_1) - q(C_2)$ for C_2H_6

b) ΔE is a difference of total energies of two forms, as $\Delta E = E(\text{protonated form}) - E(\text{neutral form})$

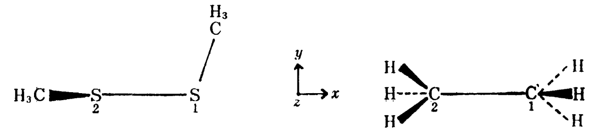

Fig. 5. Conformations and the numbering of the atoms of $(CH_3)_2S_2$ and C_2H_6.

In a case of a proton attack, the following two points must be considered. First, a proton will approach more easily to the S–S bond in a lone-pair direction than to a bond with no lone pairs such as a C–C bond. Second, when a proton approaches one of the lone pairs of the sulfurs, change transfers from the lone pair to the proton and the polarization of the S–S bond will be induced. This polarization may become one step to a heterolytic scission. The protonated form of $(CH_3)_2S_2$ is calculated in Table 8. The calculated results for protonated C_2H_6, in which hardly any ionic scission takes place, are cited in the same table for comparison. In the calculation, the proton is placed 2Å from the S–S bond, first in the lone-pair direction (case I) and then in the *z* direction to the center of the S–S bond (case II). As for C_2H_6, a proton is placed 2Å from the C–C bond, first in the *z* direction to the C_1 atom of the C–C bond in Fig. 5 (case III), and then to the center of the C–C bond (case IV). When a proton approaches from a lone-pair direction, the atomic population[26] of the proton is the largest (0.999) and the stabilization energy, ΔE, of the protonated form is the largest (−4.75 eV). The difference in the atomic population[26] between the S_1 atom and the S_2 atom (0.996) is considerably larger than that between the C_1 atom and the C_2 atom (0.315). That is, when a proton approaches the S–S bond, a larger inclination of the charge distribution is induced that in an approach to the C–C bond. The energy of the LV of $(CH_3)_2S_2$ (−0.53 eV) is lower than that of C_2H_6 (3.21 eV), such as in the case of H_2O_2.[23] This means that $(CH_3)_2S_2$ is more apt to accept a nucleophilic attack than C_2H_6, as described before.

Reaction of Aralkyl Hydrodisulfide. Tsurugi *et al.* have given a series of reports[39] about the reaction of

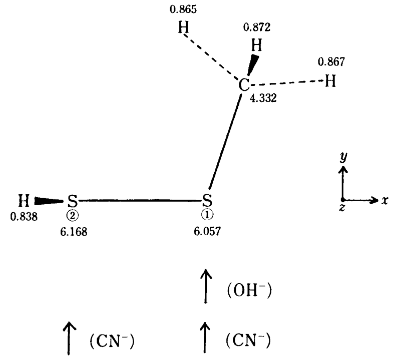

Fig. 6. Conformations and the numbering of the atoms of CH_3SSH are shown together with its atom populations. Arrows show the usual position of an anion attack.

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[39] "Organic Sulfur Compounds," ed. by N. Kharasch, Pergamon Press New York (1961), Chap. 9, 35, *etc.*; T. C. Bruice, *J. Amer. Chem. Soc.*, **81**, 5444 (1959).

TABLE 9. SOME AO POPULATIONS AND PARTIAL AO BOND POPULATION, P_{sr}^{LV}, IN LV OF CH_3SSH

		LV
AO population	S_1x	0.684
	S_2x	0.531
P_{rs}^{LV}	S_1x-S_2x	0.450

aralkyl hydrodisulfide, RSSH, with various anions. They concluded in one of their papers that, in the absence of steric hindrance, the weaker nucleophiles, such as hydroxide and sulfite ions, attack exclusively the sulfenyl sulfur of benzyl hydrodisulfide. Stronger nucleophiles,[39] such as cyanide and thiolate ions, attack both sulfenyl and sulfhydryl sulfur atoms. We calculated the electronic structure of CH_3SSH, as a model compound. The adopted conformation of the compound is shown in Fig. 6, together with the obtained atomic population. The S_1, S_2, and C_3 atoms are placed on the x–y plane, and the H_7 atom, on the x–z plane, while the dihedral angle is assumed to be 90°. The bond lengths and bond angles are given in Table 2. The AO populations of S_1z and S_2y are 1.996 and 1.989 respectively; they should be lone-pair AO's. The AO populations of S_1x and S_2x in LV are large, as is shown in Table 9, they become antibonding orbitals of the S–S $p\sigma$ bond. That is, an anion attack occurs along the S–S bond from the outside. Furthermore, in LV, the AO population of the S_1x is larger than that of the S_2x, though the difference between them is small. Therefore, the S_1 atom is more susceptible to the anion attack than the S_2 atom. This accounts for the experimental facts that weak nucleophiles attack the S_1 atom, while strong nucleophiles attack both the S_1 and S_2 atoms.

Reactions of Acyl Thiol. There have been several reviews[40,41] about various reactions of acyl thiol and the thiol ester, with particular attention payed to their role in biochemistry. As has been described before, $CoAS$-$COCH_3$ is an acetylating intermediate and its C–S bond is a high energy bond.[3] We calculated the electronic structure of CH_3COSCH_3, as a model compound. The assumed conformation of the compound is shown in Fig. 7, together with the atomic population. The S_1, C_2, O_3, C_4, and C_5 atoms are all assumed to be on the same x–y plane. The bond lengths and bond angles are given in Table 2. The AO populations are shown in Table 10, while those of the main p orbitals in HO and LV are shown in Table 11. HO(−12.69 eV) is a π-type lone-pair MO, largely localized at the S_1z AO, which is a lone-pair AO of the sulfur atom. This lone-pair level localized at the sulfur atom become higher than that localized at the oxygen atom. Therefore, a cation attack must take place at S_1z AO, this is in agreement with the experimental results The LV is an antibonding π-type MO largely localized at the C_2z AO. The partial AO bond populations of C_2z–O_3z and C_2z–S_1z in LV are −0.352 and −0.276 respectively. Therefore, an anion attack must take place at the C_2z AO in LV. This accounts for the several reactions[42] reviewed by Bruice,[39] in which an inter- or intra-molecular nucleophilic attack on the carbon atom of acyl thiol or the acyl thiol ester by a lone pair of a nitrogen atom or a sulfur atom is often essential. The energy of LV (−8.47 eV)is remarkably lower than those of CH_3SSH (−0.79 eV) and $(CH_3)_2S_2$ (−0.53 eV). This shows that CH_3SCOCH_3 is very apt to accept an anion attack.

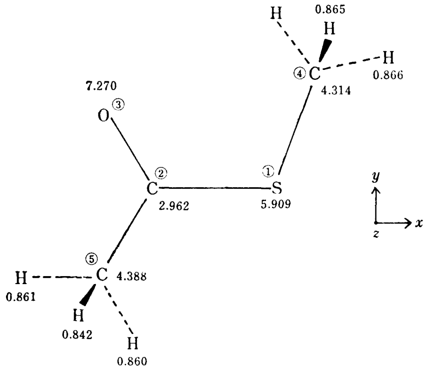

Fig. 7. Conformation and the numbering of the atoms of CH_3SCOCH_3 are shown together with its atom populations.

TABLE 10. AO POPULATION OF CH_3SCOCH_3

AO		AO	
S_1s	1.495	C_4s	1.163
x	1.241	x	1.111
y	1.421	y	0.932
z	1.753	z	1.108
C_2s	1.053	C_5s	1.172
x	0.748	x	1.091
y	0.636	y	1.035
z	0.526	z	1.090
O_3s	1.768		
x	1.906		
y	1.790		
z	1.806		

TABLE 11. SOME AO POPULATIONS IN HO AND LV OF CH_3SCOCH_3

	S_1z	C_2z	O_3z	C_4z	C_5z
LV	0.244	1.465	0.192	0.005	0.009
HO	1.275	0.141	0.078	0.226	0.016

One of the authors(H.Y.) wishes to express her hearty thanks to Professor Kenichi Fukui of Kyoto University for his kind advice in the discussion on the reactivity.

The calculation was carried out on a HITAC 5020 computer at the computation center of the University of Tokyo.

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40) S. Kawamura, T. Nakabayashi, T. Kitao, and J. Tsurugi. *et al.*, *J. Org. Chem.*, **31**, 4174 (1966); *ibid.*, **30**, 2707, 2711 (1965); *ibid.*, **31**, 4171 (1966), *etc.*

41) A. L. Parker and N. Kharash, *Chem. Rev.*, **59**, 583 (1959).

42) See Ref. 40; for example, p. 421 (Eq. (1)), p. 430 (Eq. (38)), p. 431 (Eq. (39)), p. 433 (Eq. (43)), p. 437 (Eq. (57)), and p. 438 (Eq. (58)).