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S-S AND C-S STRETCHING VIBRATIONS AND MOLECULAR CONFORMATIONS OF DIALKYL DISULFIDES AND CYSTINE

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Raman and infrared spectra of dialkyl disulfides were measured. Correlations of S-S and C-S stretching frequencies to molecular conformations were found for dialkyl disulfides.The molecular structure of cystine in aqueous solution was studied on the basis of the observed S-S and C-S stretching vibrations.

Laser Raman scattering of lysozyme, ribonuclease, and α-chymotrypsin in aqueous solution was measured by Lord and Yu,$^{1)}$ and many Raman lines due to side-chain amino acid residues were observed. For studying conformations of side-chain groups, however, it was necessary to establish correlations between Raman spectra and conformations of side-chain groups. In the present study, infrared and Raman spectra of dialkyl disulfides were studied, in relation with the cystine group in proteins.

The stable conformation about the S-S bond of disulfide groups was established to be gauche, with the internal-rotation angle of $\pm 85^\circ$ for dimethyl disulfide,$^{2)}$ and $\pm 91^\circ$ for hydrogen disulfide.$^{3)}$ Accordingly, the present study was concerned with the internal rotation about the C-S and C-C bonds of disulfide groups C-C-S-S-C-C.

S-S STRETCHING VIBRATIONS OF DIALKYL DISULFIDES

Vibrational spectra of dialkyl disulfides in the liquid state were measured with JEOL Raman spectrometer with an argon-ion laser and Hitachi EPI-G3 and EPI-L infrared spectrophotometer. Fig. 1 shows the observed Raman spectra of dimethyl disulfide, methyl tert-butyl disulfide, and di-tert-butyl disulfide. For any of these three molecules, no rotational isomers are expected other than the molecular conformation with the gauche S-S bond. In fact, only one S-S stretching vibration was observed at 509 cm^{-1} for dimethyl disulfide, at 528 cm^{-1} for methyl tert-butyl disulfide, and at 544 cm^{-1} for di-tert-butyl disulfide. However, two S-S stretching vibrations were observed for disulfides with two primary alkyl groups, including methyl ethyl disulfide (509 and 525 cm^{-1}), diethyl disulfide (509 and 524 cm^{-1}), di-n-propyl disulfide (510 and 523 cm^{-1}), and di-isobutyl disulfide (512 and 526 cm^{-1}). For each of these disulfides, rotational isomers are expected about the C-S bond. Similarly, two S-S stretching vibrations were also observed for disulfides with two secondary alkyl groups, including di-isopropyl disulfide (527 and 542 cm^{-1}) and di-sec-butyl disulfide (526 and 542 cm^{-1}). On the other hand, only one S-S stretching vibration was observed at 543 cm^{-1} for di-tert-amyl disulfide, although rotational isomers about the C-S bond are expected to coexist.

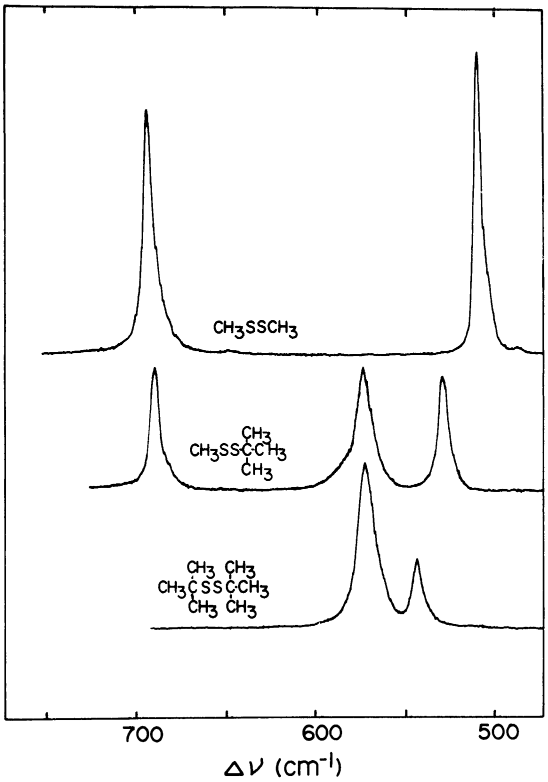


Fig. 1. Raman spectra of dimethyl disulfide, methyl tert-butyl disulfide, and di-tert-butyl disulfide in the liquid state at room temperature.

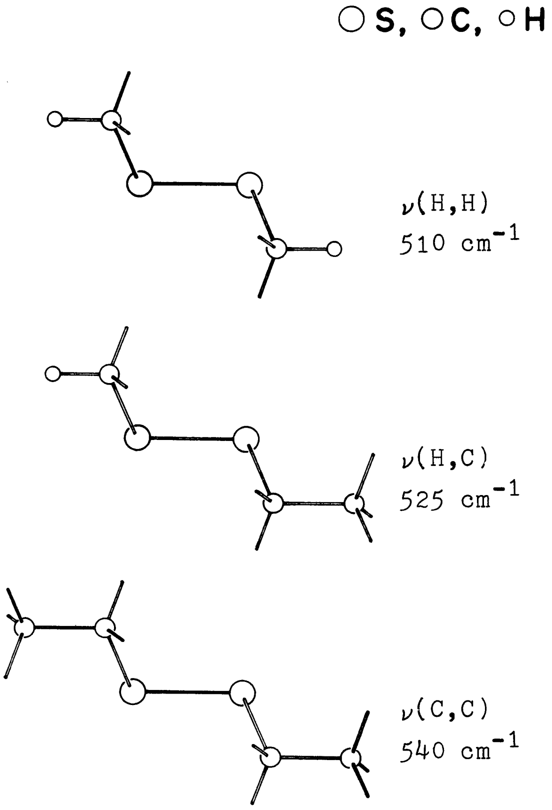


Fig. 2. Characteristic S-S stretching vibrations of alkyl disulfides.

These observations may be explained, as follows, with a new correlation between S-S stretching frequencies and molecular conformations about the two C-S bonds of the disulfide group. As for the internal rotation about the C-S bond of U-C-S-S groups, there is a trans site (U) for atoms bonded to the carbon atom. Since there are two C-S bonds for the U-C-S-S-C-V group, there are two trans sites (U and V) with respect to the central sulfur atoms. The frequencies of S-S stretching vibrations depend upon the atoms U and V. Thus, the S-S stretching vibration lies at about 510 cm^{-1} for the conformation with two hydrogen atoms (U and V), at about 525 cm^{-1} for the conformation with hydrogen atom (U) and carbon atom (V), and at about 540 cm^{-1} for the conformation with two carbon atoms (U and V). These three types of S-S stretching vibrations will be denoted as ν(H,H), ν(H,C), and ν(C,C), respectively (Fig. 2). This new correlation was also confirmed by the normal coordinate treatment of rotational isomers of dialkyl disulfides, including methyl ethyl disulfide, diethyl disulfide, and di-isopropyl disulfide.[4] Because of the vibrational coupling between the S-S stretching mode and S-C-C bending mode of the trans S-S-C-C group, the S-S stretching frequency of the conformation with two carbon atoms (at U and V) is higher, by about 30 cm^{-1}, and the S-S stretching frequency of the conformation with one carbon atom (at V) is higher, by 15 cm^{-1}, than the S-S stretching frequency of the conformation with no carbon atom at U or V.

C-S STRETCHING VIBRATIONS OF DIALKYL DISULFIDES

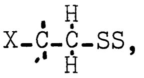
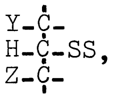
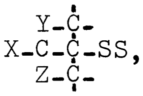
The observed frequencies of the Raman lines due to C-S stretching vibrations of dialkyl disulfide in the liquid state are listed in Table 1. The characteristic CH_3-S stretching vibration is observed at about 690 cm^{-1}. For alkyl disulfide groups -C-C-SS, C-S stretching frequencies are now found to depend upon molecular conformations about the C-C bonds adjacent to the C-S bond, similar to the C-Cl stretching frequencies of alkyl chlorides.[5,6] As for the C-C bond of primary disulfides  $X{-}C{-}\overset{H}{\underset{H}{C}}{-}SS$, there is a trans site (X) with respect to the sulfur atom and C-S stretching frequencies depend upon the atom at the trans site (X). Thus, the C-S stretching vibration lies at 630-670 cm^{-1} (P_H) for the conformation with X=hydrogen (H), but at 700-745 cm^{-1} (P_C) for the conformation with X=carbon (C). For the C-C bonds of secondary disulfides  $\begin{array}{l} Y{-}C{-}\\ H{-}C{-}SS\\ Z{-}C{-}\end{array}$, there are two trans sites (Y and Z) with respect to the sulfur atom, and the C-S stretching vibration lies at 595-635 cm^{-1}(S_{HH}) for the conformation with Y=H and Z=H, but at 650-680 cm^{-1} (S_{CH}) for the conformation with Y=C and Z=H. Finally for the C-C bonds of tertiary disulfides  $\begin{array}{l} \quad\;\; Y{-}C{-}\\ X{-}C{-}C{-}SS\\ \quad\;\; Z{-}C{-}\end{array}$, there are three trans sites (X, Y, and Z) with respect to the sulfur atom, and the C-S stretching vibration lies at about 570 cm^{-1} (T_{HHH}) for the conformation with X=Y=Z=H, but at 615 cm^{-1} for the conformation with X=C and Y=Z=H.

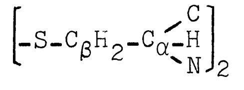
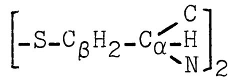
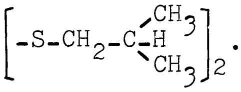
Table 1. Characteristic C-S stretching frequencies (cm^{-1}) of dialkyl disulfides[a)]

Molecule	$\nu(CH_3-S)$	$\nu(-CH_2-S)$		$\nu(>CH-S)$		$\nu(\geq C-S)$	
		P_H	P_C	S_{HH}	S_{CH}	T_{HHH}	T_{CHH}
CH_3SSCH_3	691	-	-	-	-	-	-
$CH_3SSCH_2CH_3$	692	(642 669	-	-	-	-	-
$[-SCH_2CH_3]_2$	-	(640 667	-	-	-	-	-
$[-SCH_2CH_2CH_3]_2$	-	(630 656	(703 731	-	-	-	-
$[-SCH_2CH(CH_3)_2]_2$	-	666	(710 745	-	-	-	-
$[-SCH(CH_3)_2]_2$	-	-	-	(596 625	-	-	-
$[-SCH(CH_3)CH_2CH_3]_2$	-	-	-	(587 618 633	(650 677	-	-
$CH_3SSC(CH_3)_3$	689	-	-	-	-	570	-
$[-SC(CH_3)_3]_2$	-	-	-	-	-	570	-
$[-SC(CH_3)_2CH_2CH_3]_2$	-	-	-	-	-	560	615
Alkyl chlorides[b)]	732	645-690	720-730	605-640	655-675	560-580	610-630

a) Frequencies listed together with parentheses are possibly due to rotational isomers (reference 4).

b) Reference 6.

L-CYSTINE IN SOLUTION

In the hexagonal crystal of L-cystine,[7)] monoclinic crystal of L-cystine dihydrochloride,[8)] and orthorhombic crystal of L-cystine dihydrobromide,[9)] the H-C_α and C_β-S bonds of the  $\left[-S-C_\beta H_2-C_\alpha\begin{smallmatrix}C\\H\\N\end{smallmatrix}\right]_2$ group are in the trans form about the C_α-C_β bond. It may be noted that the  $\left[-S-C_\beta H_2-C_\alpha\begin{smallmatrix}C\\H\\N\end{smallmatrix}\right]_2$ group of cystine derivatives is closely related with di-isobutyl disulfide  $\left[-S-CH_2-C\begin{smallmatrix}CH_3\\H\\CH_3\end{smallmatrix}\right]_2$. Accordingly, for the cystine group with the H-C_α and C_β-S bonds in the trans form, the C-S stretching vibration is expected to lie near the P_H frequency (666 cm^{-1}, see Table 1) of di-isobutyl disulfide. In fact, strong Raman lines were observed[1)] at 680 cm^{-1} for L-cystine, and at 667 cm^{-1} for L-cystine dihydrochloride and L-cystine dihydrobromide in the crystalline state.

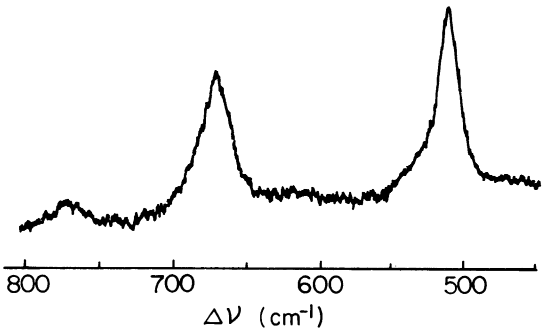


Fig. 3. Raman spectrum of L-cystine in hydrochloric acid solution (2N) at room temperature.

In the present study, however, the Raman spectrum of L-cystine in 2N hydrochloric acid solution was measured as shown in Fig. 3 and observed Raman lines were assigned with reference to the S-S and C-S stretching frequencies of dialkyl disulfides. The strongest Raman line at 510 cm^{-1} corresponds to the ν(H,H) vibration (Fig. 2), indicating that the C_α-C_β and S-S bonds are in the gauche form about the C_β-S bond. The strong line at 670 cm^{-1} corresponds to the P_H vibration of di-isobutyl disulfide, indicating that the H-C_α and C_β-S bonds of L-cystine molecules in solution are also in the trans form about the C_α-C_β bond. These analyses of Raman lines lead to the conclusion that the H-C_α and C_β-S bonds stay in the trans form and also that the C_α-$C_\beta H_2$-S-S-$C_\beta H_2$-C_α group may well be in the right-handed and left-handed gauche-gauche-gauche conformations in solution.

REFERENCES

1) R. C. Lord and N. Yu, J. Mol. Biol., 50, 509 (1970); 51, 203 (1970).
2) D. Sutter, H. Dreizler, and H. D. Rudolph, Z. Naturforsch., 20a, 1676 (1965).
3) G. Winnewisser, M. Winnewisser, and W. Gordy, J. Chem. Phys., 49, 3465 (1968); M. Winnewisser and J. Haase, Z. Naturforsch., 23a, 56 (1968).
4) H. Sugeta, A. Go, and T. Miyazawa, to be published separately.
5) S. Mizushima, T. Shimanouchi, K. Nakamura, M. Hayashi, and S. Tsuchiya, J. Chem. Phys., 26, 970 (1957).
6) J. J. Shipman, V. L. Folt, and S. Krimm, Spectrochim. Acta, 18, 1603 (1962).
7) B. M. Oughton and P. M. Harrison, Acta Cryst., 12, 396 (1959).
8) L. K. Steinrauf, J. Peterson, and L. H. Jensen, J. Am. Chem. Soc., 80, 3835 (1958).
9) J. Peterson, L. K. Steinrauf and L. H. Jensen, Acta Cryst., 13, 104 (1960).

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