

APPLICATION OF THE BERGSON MODEL TO THE OPTICAL PROPERTIES OF CHIRAL DISULFIDES

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Abstract—Bergson developed a simple model to explain the observed red shift of the long-wavelength transition of disulfides as the dihedral angle is reduced from 90° to smaller values. This model is extended here to a calculation of the oscillator strengths and rotational strengths of the $n \rightarrow \sigma^*$ transitions of chiral disulfides. Explicit expressions for the gradient and angular momentum matrix elements for the $n \rightarrow \sigma^*$ transitions as functions of the dihedral angle are presented. Transition monopoles suitable for the calculation of the coupling of disulfide $n \rightarrow \sigma^*$ transitions with other chromophoric groups in complex disulfides are also presented. It is shown that this extension of the Bergson model can account quite well for the observed intensities and rotational strengths of chiral disulfides. The quadrant behavior of the long-wavelength rotational strength derived by Linderberg and Michl and verified experimentally by Ludescher and Schwyzer is observed in our results as well. The observed transitions in the far ultraviolet spectrum of disulfides are assigned to an $n \rightarrow \sigma^*$ transition at 205 nm and a $\sigma \rightarrow \sigma^*$ transition at 190 nm.

In recent years, there has been much interest in the development and application of rules for relating the circular dichroism (CD) and chirality of inherently dissymmetric chromophores.¹⁻³ Although conjugated π -electron systems such as dienes, enones and α -dicarbonyls have been the most thoroughly studied, the disulfide group has also received considerable attention, especially because of its role in molecules of biological importance, e.g., proteins, peptide hormones (oxytocin and vasopressin), coenzymes (lipoic acid) and antibiotics (gliotoxin, aranotin, etc).

An empirical correlation of the sign of the lowest energy CD band and the disulfide chirality was provided by the work of Carmack and Neubert,⁴ of Dodson and Nelson,⁵ and of Claeson.⁶ This empirical rule states that a positive long-wavelength CD band in a disulfide is associated with a right-handed screw sense of the disulfide.

The molecules of known absolute configuration used in this empirical correlation all had dihedral angles with absolute values less than 90° . Linderberg and Michl⁷ were the first to carry out theoretical calculations of the rotational strength of disulfide transitions. Their results suggested that the intrinsic rotational strength of the long-wavelength CD should obey a quadrant rule, i.e., the sign for a right-handed disulfide with a dihedral angle slightly less than 90° should be positive, while one with a dihedral angle slightly greater than 90° should be negative. This reversal in sign does not come about because a particular transition undergoes a sign change, but because the *identity* of the long-wavelength band changes. Linderberg and Michl's

analysis indicated that for a dihedral angle of 90° , the intrinsic rotational strengths of the long-wavelength disulfide transitions should largely cancel, due to their degeneracy.

Recently Ludescher and Schwyzer⁸ have verified the quadrant behavior of disulfides. They have shown that a right-handed disulfide with a dihedral angle of 120° does indeed have a negative long-wavelength CD band, in agreement with Linderberg and Michl's predictions.⁷

In this paper, the simple model for disulfides successfully used by Bergson^{9,10} to account for the dihedral angle dependence of the absorption band positions is applied to calculating the intrinsic rotational strengths of the disulfide $n \rightarrow \sigma^*$ transitions. The Bergson model was used in a qualitative way by Linderberg and Michl,⁷ but their quantitative calculations used CNDO (complete neglect of differential overlap) wavefunctions. There are several reasons for presenting here the results from this calculation based on the Bergson model. First, it is of interest to see how far one can take this model which has been so useful in interpreting absorption spectra.^{9,10} Second, the wavefunctions used here can be written in a simple form, leading to analytical expressions for the energies and electric and magnetic dipole transition moments as trigonometric functions of the dihedral angle. This makes it much easier to visualize how the rotational strengths and transition wavelengths vary with dihedral angle. Third, this model provides a useful basis for treating the coupling of disulfide transitions with transitions in other chromophoric groups in complex molecules.

Method

We consider the non-bonding orbitals of the disulfide as symmetry-adapted linear combinations of sp^3 hybrids. Denoting the two hybrid orbitals on S_1 as h'_3 and h'_4 , and those on S_2 as h_3 and h_4 , we have the following linear combinations:

$$\begin{aligned} n_1 &= \frac{1}{2}(h'_3 - h'_4 - h_3 + h_4) & a_2 \\ n_2 &= \frac{1}{2}(h'_3 + h'_4 - h_3 - h_4) & b_1 \\ n_3 &= \frac{1}{2}(h'_3 + h'_4 + h_3 + h_4) & a_1 \\ n_4 &= \frac{1}{2}(h'_3 - h'_4 + h_3 - h_4) & b_2 \end{aligned}$$

We have also indicated the symmetry of each orbital in the planar *cis* conformation (C_{2v}). When the disulfide is skewed, the symmetry is reduced to C_2 . For skewed disulfides, n_1 and n_3 belong to the a representation and n_2 and n_4 belong to the b representation in C_2 symmetry.

If we denote the sp^3 hybrids on S_1 and S_2 directed along the disulfide bond as h'_1 and h_1 , respectively, the σ^* orbital can be written as

$$\sigma^* = \frac{1}{\sqrt{2}}(h'_1 - h_1)$$

which is of b_1 symmetry in C_{2v} and b symmetry in C_2 .

It is useful to examine the electric and magnetic dipole-allowed character of the various $n \rightarrow \sigma^*$ transitions in the planar *cis* geometry. This geometry serves as a convenient reference point, especially for the common case of acute dihedral angles.

It also serves as a valuable check on the expressions for the electric and magnetic dipole transition moments as a function of dihedral angle, in that these expressions must have the proper limiting value as $|\varphi| \rightarrow 0$. The directions of the electrically (μ) and magnetically (m) allowed transitions in the planar *cis* geometry are indicated in Fig 1.

We consider the S—S bond to be skewed by twisting the R_1 — S_1 bond through an angle of φ with respect to the group R_2 — S_2 . The angle φ is defined as positive for a clockwise rotation from the eclipsed conformation looking along the S—S bond from S_2 toward S_1 . Thus, a positive $\varphi < 180^\circ$ corresponds to a right-handed screw sense for the disulfide.

The hybrid orbitals of interest on S_1 and S_2 are as follows:

$$h'_1 = \frac{1}{2}s' - \frac{\sqrt{3}}{2}p_x'$$

$$\begin{aligned} h'_3 &= \frac{1}{2}s' + \frac{\sqrt{3}}{6}p_x' + \left(\frac{\sqrt{6}}{6}\cos\varphi - \frac{\sqrt{2}}{2}\sin\varphi\right)p_y' \\ &+ \left(\frac{\sqrt{6}}{6}\sin\varphi + \frac{\sqrt{2}}{2}\cos\varphi\right)p_z' \end{aligned}$$

$$\begin{aligned} h'_4 &= \frac{1}{2}s' + \frac{\sqrt{3}}{6}p_x' + \left(\frac{\sqrt{6}}{6}\cos\varphi + \frac{\sqrt{2}}{2}\sin\varphi\right)p_y' \\ &+ \left(\frac{\sqrt{6}}{6}\sin\varphi - \frac{\sqrt{2}}{2}\cos\varphi\right)p_z' \end{aligned}$$

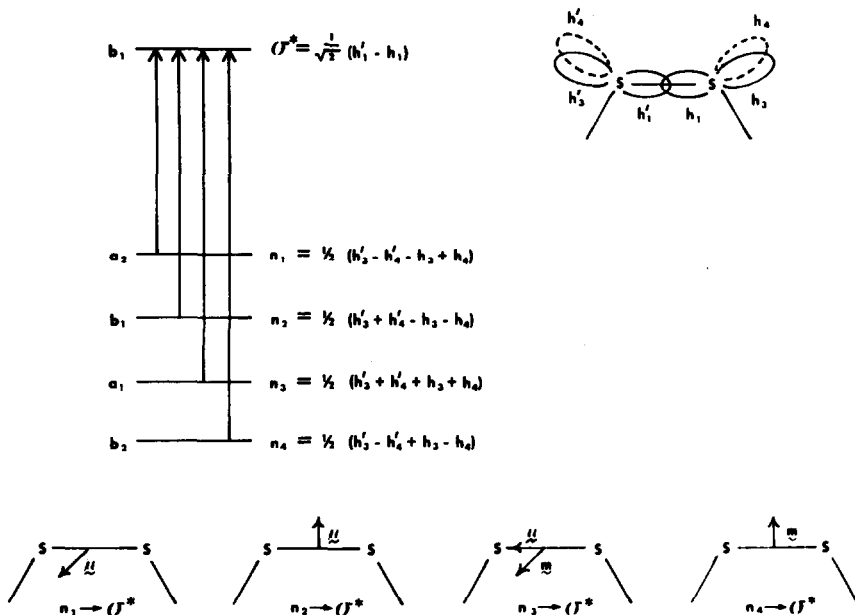


Fig 1. Representation of hybrid orbitals used as a basis set, the energy level scheme and the allowed transitions for the *cis* conformation. The symmetry designations are for the C_{2v} symmetry of the planar *cis* conformation. The vectors μ and m represent, respectively, electrically- and magnetically-allowed transitions.

$$h_1 = \frac{1}{2}s + \frac{\sqrt{3}}{2} p_x$$

$$h_3 = \frac{1}{2}s - \frac{\sqrt{3}}{6} p_x + \frac{\sqrt{6}}{6} p_y + \frac{\sqrt{2}}{2} p_z$$

$$h_4 = \frac{1}{2}s - \frac{\sqrt{3}}{6} p_x + \frac{\sqrt{6}}{6} p_y - \frac{\sqrt{2}}{2} p_z$$

where we have denoted orbitals centered on S_1 by primes and those on S_2 are unprimed.

Matrix elements of the ∇ and $rx\nabla$ operators were derived, using the hybrid orbitals as a basis set, as a function of φ . These were then combined to obtain the matrix elements for the $n_1 \rightarrow \sigma^*$, $n_2 \rightarrow \sigma^*$, etc. transitions. Formulae for these matrix elements are given in Table 1.

In order to evaluate the matrix elements given in Table 1, the two-center ∇ and $rx\nabla$ integrals over orbitals on the sulfur atoms must be calculated. Integrals of this type, involving Slater orbitals of principal quantum number 2, have been worked out previously and expressions for them are available in the literature. However, we are interested in Slater orbitals with $n = 3$. Following the procedure of Moscovitz,¹¹ expressions were obtained for the integrals involving the operator ∇ . We denote the integral $\int s' \nabla s d\tau$ by $(s's)$, etc.

$$(s's) = -\frac{R^6}{16} \frac{\xi^7}{45} \left\{ 2[(2A_2 - A_0)B_4 - 2A_4B_2 + A_4B_0] + \frac{\zeta R}{2} [A_1B_6 - (2A_3 + A_1)B_4 + (A_5 + 2A_3)B_2 - A_5B_0] \right\} \quad (1a)$$

$$(s'x) = \frac{R^6}{16} \frac{\xi^7}{15\sqrt{3}} \left\{ 2[A_3B_4 - (A_5 + A_1)B_2 + A_3B_0] + \frac{\zeta R}{2} [A_2B_6 - (2A_4 + A_0)B_4 + (A_6 + 2A_2)B_2 - A_4B_0] \right\} \quad (1b)$$

$$(s'y) = (s'z) = -\frac{R^6}{32} \frac{\xi^7}{15\sqrt{3}} \left\{ (3A_3 - 5A_1)B_4 + (A_5 + 3A_1)B_2 - (3A_5 - A_3)B_0 + \frac{\zeta R}{2} [(A_2 - A_0)(B_4 - B_6) + (A_6 - A_4)(B_2 - B_0)] \right\} \quad (1c)$$

$$(x'x) = -\frac{R^6}{16} \frac{\xi^7}{15} \left\{ (2A_4 - A_2 + A_0)B_4 - (A_4 + 4A_2 - A_0)B_2 + (A_4 + A_2)B_0 + \frac{\zeta R}{2} [A_3(B_6 - B_0) + (A_5 + A_3 + A_1)(B_2 - B_4)] \right\} \quad (1d)$$

$$(x'y) = (x'z) = -\frac{R^6}{32} \frac{\xi^7}{15} \left\{ (2A_4 - 3A_2 + A_0)B_4 - (3A_4 - 4A_2 + A_0)B_2 + (A_4 - A_2)B_0 + \frac{\zeta R}{2} [(A_3 - A_1)B_6 - (A_5 + A_3 - 2A_1)B_4 + (2A_5 - A_3 - A_1)B_2 - (A_5 - A_3)B_0] \right\} \quad (1e)$$

Table 1. Matrix elements of the ∇ and $rx\nabla$ operators^a

Matrix element	x-component	y-component	z-component
$(\psi_0 \nabla \psi_{n_1}^*)$	0	$\left[\frac{a}{9}\zeta - b(s'y) + a(x'y) \right] \frac{\sin \varphi}{2}$	$\left[-\frac{a}{9}\zeta + b(s'z) - a(x'z) \right] \frac{(1 + \cos \varphi)}{2}$
$(\psi_0 \nabla \psi_{n_2}^*)$	0	$\left[-\frac{b}{9}\zeta + \frac{a}{3}(s'y) - b(x'y) \right] \frac{(1 + \cos \varphi)}{2}$	$\left[-\frac{b}{9}\zeta + \frac{a}{3}(s'z) - b(x'z) \right] \frac{\sin \varphi}{2}$
$(\psi_0 \nabla \psi_{n_3}^*)$	$-\frac{2}{9}\zeta - \frac{1}{2}(s's) - \frac{\sqrt{3}}{3}(s'x) - \frac{(x'x)}{2}$	$\left[\frac{b}{9}\zeta - \frac{a}{3}(s'y) + b(x'y) \right] \frac{(1 - \cos \varphi)}{2}$	$\left[-\frac{b}{9}\zeta + \frac{a}{3}(s'z) - b(x'z) \right] \frac{\sin \varphi}{2}$
$(\psi_0 \nabla \psi_{n_4}^*)$	0	$\left[\frac{a}{9}\zeta - b(s'y) + a(x'y) \right] \frac{\sin \varphi}{2}$	$\left[\frac{a}{9}\zeta - b(s'z) + a(x'z) \right] \frac{(1 - \cos \varphi)}{2}$
$(\psi_0 rx\nabla \psi_{n_1}^*)$	0	$[a + b[s'z] - a[x'z]] \frac{(1 - \cos \varphi)}{2}$	$[-a + b[s'y] - a[x'y]] \frac{\sin \varphi}{2}$
$(\psi_0 rx\nabla \psi_{n_2}^*)$	0	$\left[-b - \frac{a}{3}[s'z] + b[x'z] \right] \frac{\sin \varphi}{2}$	$\left[-b + \frac{a}{3}[s'y] - b[x'y] \right] \frac{(1 - \cos \varphi)}{2}$
$(\psi_0 rx\nabla \psi_{n_3}^*)$	0	$\left[-b - \frac{a}{3}[s'z] + b[x'z] \right] \frac{\sin \varphi}{2}$	$\left[b - \frac{a}{3}[s'y] + b[x'y] \right] \frac{(1 + \cos \varphi)}{2}$
$(\psi_0 rx\nabla \psi_{n_4}^*)$	0	$[-a - b[s'z] + a[x'z]] \frac{(1 + \cos \varphi)}{2}$	$[-a + b[s'y] - a[x'y]] \frac{\sin \varphi}{2}$

^a $a = \sqrt{6}/2, b = \sqrt{2}/2.$

$$(y'y) = (z'z) = \frac{R^6 \zeta^7}{32 \cdot 15} \left\{ (2A_4 - 3A_2 + A_0)B_4 \right. \\ - (3A_4 - 4A_2 + A_0)B_2 + (A_4 - A_2)B_0 \\ + \frac{\zeta R}{2} [(A_3 - A_1)B_6 - (A_5 + A_3 - 2A_1)B_4 \\ \left. + (2A_5 - A_3 - A_1)B_2 - (A_5 - A_3)B_0] \right\}. \quad (1f)$$

Here R is the bond length in atomic units; ζ is the orbital exponent;

$$A_n = A_n(\zeta R) = \int_1^\infty e^{-\zeta R x} x^n dx;$$

$$\text{and } S_p \equiv S_p(\zeta) = \int_{-1}^{+1} x^p dx = \frac{2}{n+1} \text{ (n even)}.$$

The integrals involving the operator $rx\nabla$ were evaluated following the methods of Moscovitz¹¹ and Hansen.¹² The integral $\int s'rx\nabla y dz$ is denoted by $[s'y]$, etc.

$$[s'y] = -[s'z] = \frac{1}{2} S_{s'x} \quad (2a)$$

$$[x'y] = -[x'z] = S_{x'x} - \frac{R}{2} (x'y) \quad (2b)$$

Here, $S_{s'x}$ is the overlap integral between the s orbital on S_1 and the p_x orbital on S_2 , and similarly for $S_{x'x}$. The angular momentum matrix elements were evaluated with respect to the center of the disulfide bond.

Numerical values of the two-center integrals were determined from Equations (1) and (2), using a S—S bond length of 3.9327 a.u. = 2.0816 Å and $\zeta = 1.817$. These numerical values are given in Table 2.

Rotational strengths for the four $n \rightarrow \sigma^*$ transitions were calculated from the matrix elements using the expression¹¹

$$R_{0 \rightarrow i} = -\frac{e^2 \hbar^3}{2m^2 c E} (\psi_0 | \nabla | \psi_i) \cdot (\psi_i | rx\nabla | \psi_0). \quad (3)$$

Here e , \hbar , m and c are, respectively, the electronic charge, Planck's constant divided by 2π , elec-

tronic mass and the velocity of light. E is the energy of the electronic transition $0 \rightarrow i$. If E is expressed in electron volts and ∇ in Å^{-1} ($rx\nabla$ is dimensionless), $R_{0 \rightarrow i}$ can be found in units of Debye-Bohr magnetons (DBM = 0.9273×10^{-38} cgs units) from the following expression:

$$R_{0 \rightarrow i} = \frac{36 \cdot 5964}{E} (\psi_0 | \nabla | \psi_i) \cdot (\psi_i | rx\nabla | \psi_0). \quad (4)$$

Oscillator strengths can be calculated from the gradient operators using the equation:

$$f_{0 \rightarrow i} = \frac{5 \cdot 0843}{E} (\psi_0 | \nabla | \psi_i)^2. \quad (5)$$

In order to calculate the rotational and oscillator strengths, we need not only the ∇ and $rx\nabla$ matrix elements, but also the energies of the $n \rightarrow \sigma^*$ transitions. In the Bergson model^{9,10} we are using here, it is assumed that the energy differences between the various $n \rightarrow \sigma^*$ transitions arise from differences in the n orbital energies and not in the Coulomb and exchange integrals, and that the σ^* orbital energy is independent of the dihedral angle.

We note that orbitals n_1 and n_4 are actually π -type orbitals made up only of sulfur 3p orbitals, since the s contributions to the sp^3 hybrids on each center cancel. Orbitals n_2 and n_3 are σ -type orbitals with a good deal of $3s$ character. As a first approximation, let us neglect the energy difference between sulfur $3s$ and $3p$ orbitals, and assume that the core integrals over the n orbitals are simply proportional to the overlap integrals

$$S_{n_1 n_1} = 1 - \cos \varphi S_{y'y} \quad (6a)$$

$$S_{n_2 n_2} = 1 - \frac{1}{2} \cos \varphi S_{y'y} \quad (6b)$$

$$S_{n_3 n_3} = 1 + \frac{1}{2} \cos \varphi S_{y'y} \quad (6c)$$

$$S_{n_4 n_4} = 1 + \cos \varphi S_{y'y}. \quad (6d)$$

Here we have neglected the small contributions of σ -type overlap ($S_{\sigma\sigma} = 0.004$ vs. $S_{y'y} = 0.1175$). This simple picture then predicts that the $n\sigma^*$ transitions should be equally spaced on an energy scale and separated by $\frac{1}{2} k \cos \varphi S_{y'y}$ where k is the proportionality factor between the resonance integral and the overlap integral. We then place the center of gravity of the n orbitals at 4.96 eV, corresponding to a wavelength of 250 nm, which is where the $n\sigma^*$ transition(s) of open-chain disulfides ($\varphi \cong \pm 90^\circ$) are located (e.g., for $(\text{CH}_2)_2\text{S}_2$, $\lambda_{\text{max}} \cong 250 \text{ nm}$).¹³ The proportionality constant k can be calibrated using the energy of the long-wavelength transition of gliotoxin ($\varphi = 12.3^\circ$, the average of two molecules in the unit cell¹⁴) at 337 nm.¹⁵ This gives $k = -10.3 \text{ eV}$ and $kS_{y'y} \cong -1.32 \text{ eV}$.

This picture of four evenly spaced $n \rightarrow \sigma^*$ transitions is certainly an unrealistic one. The two types of lone pair orbitals—the π -type and the σ -

Table 2. Two center integrals used in evaluating ∇ and $rx\nabla$ operators^a

$(s's) = -0.1790 \text{ i}$	$(x'x) = 0.2770 \text{ i}$
$(s'x) = -0.1741 \text{ i}$	$(x'y) = -0.1206 \text{ j}$
$(s'y) = 0.0780 \text{ j}$	$(x'z) = -0.1206 \text{ k}$
$(s'z) = 0.0780 \text{ k}$	
$[s'y] = 0.1500 \text{ k}$	$[x'y] = 0.0944 \text{ k}$
$[s'z] = -0.1500 \text{ k}$	$[x'z] = -0.0944 \text{ k}$

^aGradient matrix elements in atomic units. Matrix elements for $rx\nabla$ operator are dimensionless.

type are not equivalent in energy. The σ -type n orbitals are considerably lower in energy and thus give rise to $n \rightarrow \sigma^*$ transitions at higher energies than the π -type. This problem will be discussed subsequently, but for the present, because of the uncertainties in the exact energies of the σ -type n orbitals and hence the position of $n_2 \rightarrow \sigma^*$ and $n_3 \rightarrow \sigma^*$ transitions, we have used the energies calculated from the simple model for computing rotational and oscillator strengths. Since these energies are certainly too low for the $n_2, n_3 \rightarrow \sigma^*$ transitions, the corresponding R and f values will be upper limits.

The calculated rotational strengths are presented in Fig 2 and the oscillator strengths in Fig 3 as functions of the dihedral angle.

We are also interested in treating the coupling of the disulfide chromophore with other chromophores in complex molecules. This can be done using the Kirkwood¹⁶ approximation, as extended by Tinoco.¹⁷ In Tinoco's formulation, the coupling of two transition charge densities is calculated using transition monopoles. The transition monopole charges are defined by the integral

$$q_{loa} = \int \phi_a \phi_b d\tau_1 \quad (7a)$$

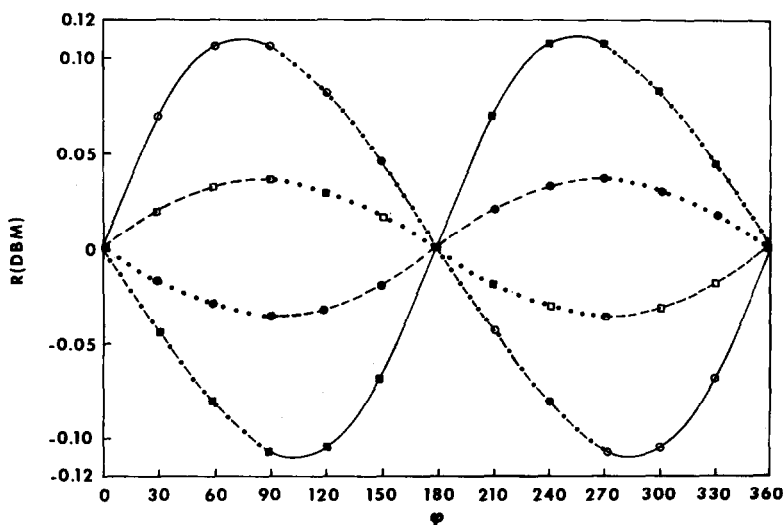


Fig 2. Rotational strengths of the $n \rightarrow \sigma^*$ transitions as a function of φ , the dihedral angle of the disulfide. The relative wavelengths are represented by various types of lines. In order of decreasing wavelength: —, — —, ···, — · —. The symbols represent the nature of the transitions: 0, $n_1 \rightarrow \sigma^*$; □, $n_2 \rightarrow \sigma^*$; ●, $n_3 \rightarrow \sigma^*$; ■, $n_4 \rightarrow \sigma^*$.

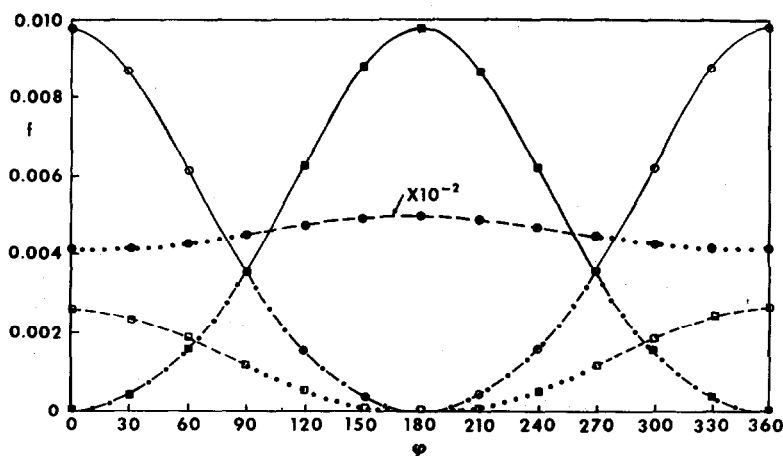


Fig 3. Oscillator strengths of the $n \rightarrow \sigma^*$ transitions as a function of φ , the dihedral angle of the disulfide. The meaning of the types of lines and symbols is the same as for Fig 2. Note that for the $n_3 \rightarrow \sigma^*$ transition, the oscillator strength has been multiplied by 0.01.

where the integral is taken over a restricted region of space in which the basis function ϕ_a and ϕ_b have the same sign. The position of the i th monopole is given by

$$r_{\text{loa}} = \frac{\int \mathbf{r} \phi_a \phi_b d\tau_i}{\int \phi_a \phi_b d\tau_i} \quad (7b)$$

In applying this method to the $n\sigma^*$ transitions of the disulfide, we encounter monopoles of several types: $s \rightarrow s$, $s \rightarrow p$, $p_x \rightarrow p_y$, and $p_x \rightarrow p_x$. The charges and positions for these various types of transition monopoles between Slater orbitals with $n = 3$ are indicated in Table 3. The monopole posi-

Table 3. Charges and positions of monopoles

Type	Position		Charge ^c
	General ^a	Sulfur ^b	
$s \rightarrow p_x^d$	$\pm(7/3\zeta) i$	$\pm 1.0396 i$	$\pm\sqrt{3}/4$
$p_x \rightarrow p_y^e$	$(\pm) \left(\frac{21\pi}{32\zeta} \right) (i \pm j)$	$(\pm) 0.9186 (i \pm j)$	$\pm 1/2\pi$
$p_x \rightarrow p_x^f$	$\pm(21/8\zeta) i$	$\pm 1.1695 i$	$\pm 1/2$

^aIn atomic units ($a_0 = 0.52917 \text{ \AA}$). ζ is the Slater orbital exponent.

^bFor the semi-empirical value $\zeta = 1.188$ determined for sulfur. In \AA units.

^cIn units of the electron charge.

^dSimilarly for $s \rightarrow p_y$, $s \rightarrow p_z$.

^eSimilarly for $p_x \rightarrow p_z$, $p_y \rightarrow p_z$.

^fSimilarly for $p_y \rightarrow p_y$, $p_z \rightarrow p_z$.

tions depend on the effective charge, ζ , of the Slater orbital. In accordance with previous work,³⁸ we have used a semi-empirical ζ value rather than the Slater value for calculating interchromophore interactions. The semi-empirical ζ value is determined by equating the one-center Coulomb integral for p orbitals determined from valence state ionization potential (VSIP) and electron affinity (VSEA) data to the theoretical value for a Slater p orbital, which is directly proportional to the parameter ζ . Using Hinze and Jaffe's¹⁹ VSIP and VSEA data, together with Weiss *et al.*'s²⁰ method for calculating the one-center Coulomb integral of doubly-occupied orbitals, we obtain $(pp|pp)_{\text{se}} = 9.00 \text{ eV}$. For Slater $3p$ orbitals, the theoretical one-center Coulomb repulsion integral is given by

$$(pp|pp)_{\text{th}} = 7.5746 \zeta \quad (8)$$

This leads to $\zeta_{\text{se}} = 1.19$. We have assumed that the same semi-empirical orbital exponent holds for the $3s$ orbital as for the $3p$.

The monopole charges for the various transitions are given in Table 4 in the form of coefficients of the basic monopoles, $q_{s's'}$, $q_{s'x'}$, etc. In addition to

the transitions from the ground state to the $n_i \rightarrow \sigma^*$ excited states, transitions between these excited states are included. These must be considered in a full treatment of the coupling of the disulfide transitions with other chromophores in complex molecules.

RESULTS AND DISCUSSION

The Bergson model^{9,10} considering its simplicity, has been remarkably successful in treating disulfide $n \rightarrow \sigma^*$ transitions. The extension described in this paper to a quantitative treatment of rotational and oscillator strengths is also surprisingly good for the low-energy transitions. However, as mentioned above, the assumption which we have used concerning the energies of the σ -type n orbitals is not a reasonable one.

CD studies^{4,5} of disulfides incorporated in 6-membered ring systems, where $|\varphi| \cong 60^\circ$, show only one transition at wavelengths above 250 nm, rather than the two transitions predicted by the picture outlined above. Diketopiperazine disulfides such as gliotoxin, where $|\varphi| \cong 10^\circ$, do show two long-wavelength transitions,¹⁵ one at about 350 nm and the other at about 320 nm. At one time, we assigned the 320 nm band of gliotoxin to the $n_2 \rightarrow \sigma^*$ transition and argued that the failure to observe the $n_2 \rightarrow \sigma^*$ transition in 1,2-dithiane systems was due to the smaller splittings for larger dihedral angles and the relative weakness of this transition. We are now confident that the 320 nm band of gliotoxin is due to a charge-transfer transition.²¹

Additional evidence that the picture of four evenly spaced $n \rightarrow \sigma^*$ transitions in disulfides is not correct is provided by recently published data from photoelectron spectroscopic studies of 1,2-dithianes.²² These data show only two high-lying levels, with a spacing which is appropriate for the n_1 and n_4 orbitals, i.e., the π -type lone pair MO's.

Thus, two types of lone pair MO's should be considered—the π -type (n_3 and n_4) and the σ -type (n_2 and n_3), with the latter lying at lower energies because of their $3s$ -character. The exact positioning of these σ -type orbitals relative to the π -type is quite uncertain at present. Yamabe *et al.* have performed an INDO-type calculation on H_2S_2 ²³ and $(\text{CH}_3)_2\text{S}_2$ ²⁴ for dihedral angles of 0° , 45° and 90° . They found that the π -type orbitals behave approximately as the simple theory would predict, with the center of gravity remaining approximately constant and a splitting which increases as one goes from $\varphi = 90^\circ$ to 45° to 0° . However, the σ -type lone pair orbitals behave quite differently. Their center of gravity moves upward in energy and the splitting decreases as we go from 90° to 0° . As a consequence, the calculations of Yamabe *et al.* suggest that while for larger dihedral angles (open-chain disulfides and 1,2-dithianes) there is an appreciable gap between the π -type and σ -type non-bonding

Table 4. Monopole coefficients for disulfide $n \rightarrow \sigma^*$ transitions^a

	Q_{ss}	Q_{sx}	Q_{sy}	Q_{sz}	$Q_{x'x'}$	$Q_{x'y'}$	$Q_{x'z'}$	$Q_{y'y'}$	$Q_{y'z'}$	$Q_{z'z'}$	$Q_{x''x''}$	$Q_{x''y''}$	$Q_{x''z''}$	$Q_{y''y''}$	$Q_{y''z''}$	$Q_{z''z''}$	Q_{yz}	Q_{zx}	Q_{zy}	
$(\psi_0 q \psi_{n1}^*)$			$-b \sin \varphi$	$b \cos \varphi$	$b \cos \varphi$	$a \sin \varphi$	$-a \cos \varphi$													
$(\psi_0 q \psi_{n2}^*)$	\dagger	$-\frac{\sqrt{3}}{6}$	$\frac{2}{3} \cos \varphi$	$\frac{2}{3} \sin \varphi$	$-\dagger$	$-b \cos \varphi$	$-b \sin \varphi$				\dagger	$\frac{\sqrt{3}}{6}$	$\frac{a}{3}$	$-\dagger$						b
$(\psi_0 q \psi_{n3}^*)$	\dagger	$-\frac{\sqrt{3}}{6}$	$\frac{2}{3} \cos \varphi$	$\frac{2}{3} \sin \varphi$	$-\dagger$	$-b \cos \varphi$	$-b \sin \varphi$				$-\dagger$	$-\frac{\sqrt{3}}{6}$	$-\frac{a}{3}$	\dagger						$-b$
$(\psi_0 q \psi_{n4}^*)$			$-b \sin \varphi$	$b \cos \varphi$	$b \cos \varphi$	$a \sin \varphi$	$-a \cos \varphi$													
$(\psi_{n1}^* q \psi_{n2}^*)$			$b \sin \varphi$	$-b \cos \varphi$	$-b \cos \varphi$	$\frac{2}{3} \sin \varphi$	$-\frac{2}{3} \cos \varphi$	$\frac{\sin 2\varphi}{\sqrt{3}}$												
$(\psi_{n1}^* q \psi_{n3}^*)$			$b \sin \varphi$	$-b \cos \varphi$	$-b \cos \varphi$	$\frac{2}{3} \sin \varphi$	$-\frac{2}{3} \cos \varphi$	$\frac{\sin 2\varphi}{\sqrt{3}}$												
$(\psi_{n1}^* q \psi_{n4}^*)$								$-\frac{\sin 2\varphi}{2}$	$-\frac{\cos 2\varphi}{2}$											
$(\psi_{n2}^* q \psi_{n3}^*)$	$-\dagger$	$-\frac{\sqrt{3}}{6}$	$-\frac{2a}{3} \cos \varphi$	$-\frac{2a}{3} \sin \varphi$	$-\frac{1}{12} \sin \varphi$	$-\frac{2b}{3} \cos \varphi$	$-\frac{2b}{3} \sin \varphi$	$-\frac{\sin 2\varphi}{6}$			\dagger	$-\frac{\sqrt{3}}{6}$	$\frac{2a}{3}$	$-\frac{1}{12}$	$\frac{1}{6}$					$-\frac{2b}{3}$
$(\psi_{n2}^* q \psi_{n4}^*)$																				
$(\psi_{n3}^* q \psi_{n4}^*)$																				

^a $a = \sqrt{6/4}$, $b = \sqrt{2/4}$.

orbitals, for disulfides near the *cis* conformation (e.g., gliotoxin), the σ -type orbitals fall between the widely split π -type orbitals.

In addition, Boyd²⁵ has recently reported extended Hückel calculations on H_2S_2 and $(CH_3)_2S_2$, which lead to yet another picture of the disulfide orbitals. His calculations indicate that for *cis* disulfides, n_1 is the highest filled orbital as expected, but that the next highest orbital is analogous to our n_2 orbital and that it is this orbital which becomes degenerate with the n_1 orbital at $\varphi = 90^\circ$, rather than the n_4 orbital. His calculations indicate that the n_4 orbital is rather strongly bonding in the *cis* conformation and becomes more so as the dihedral angle increases. Although Boyd's calculations, which include the effect of sulfur 3d orbitals, give oscillator strengths in qualitative accord with experiment, we shall see that our picture also is capable of explaining the observed disulfide bands. Further experimental results, particularly polarization data and photoelectron spectra, will be required to decide among these conflicting assignments.

All of the theoretical treatments are in agreement concerning the nature of the long wavelength transition for $|\varphi| < 90^\circ$, which is $n_1 \rightarrow \sigma^*$ in our notation. Bergson^{9,10} originally showed that his model explains the marked red shift in the long-wavelength transition as the dihedral angle decreases from 90° . In recent years, many more data have become available for disulfides with small dihedral angles. In Fig 4 the calculated dihedral angle dependence for the long-wavelength band is compared with experimental results. It can be seen that the model does indeed work very well for predicting the position of the long wavelength transition.

The transition observed by Carmack and Neubert⁴ and by Dodson and Nelson⁵ at ca 240 nm in 1,2-dithianes we assign to the $n_4 \rightarrow \sigma^*$ transition. The greater sensitivity of this band to external perturbations, commented on by Carmack and Neubert,⁴ was attributed by Linderberg and Michl⁷ to the fact that it is closer in energy to perturbing transitions in other chromophoric groups. Another factor which emerges from our treatment is that unlike the $n_1 \rightarrow \sigma^*$ transition, the $n_4 \rightarrow \sigma^*$ has a large magnetic dipole transition moment. Thus, like the carbonyl $n\pi^*$ transition, the $n_4 \rightarrow \sigma^*$ transition can acquire a large rotational strength through electric dipole transition components induced by external perturbations.

At present, we cannot definitely assign the other two $n \rightarrow \sigma^*$ transitions in any disulfides. This point will be discussed more fully below after the oscillator strength calculations have been considered.

Let us now consider the intrinsic rotational strengths of the disulfide $n \rightarrow \sigma^*$ transitions. Linderberg and Michl⁷ used the Bergson^{9,10} model

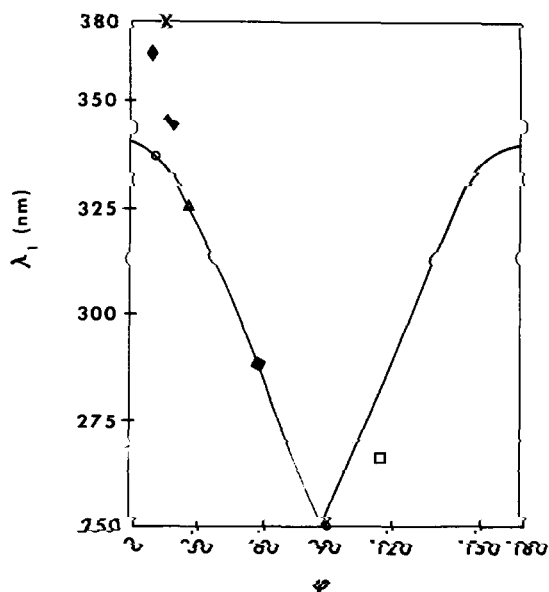


Fig 4. Comparison of the wavelengths of the lowest energy transition observed for disulfides of various dihedral angle with the calculated φ dependence. The symbols represent data for: \circ , cystine²⁶ and $(CH_3)_2S_2$ ¹³; \blacklozenge , dithianes⁵; \blacktriangle , thioctic acid⁶ and brugine (A. F. Beecham *et al. Tetrahedron Lett.* 15, 1785 (1968)); \blacktriangle , arantoin¹⁵; \bullet , gliotoxin¹⁵; \blacktriangledown , sporidesmin (R. Nagarajan, personal communication); X, chaetocin (*ibid.*); \square , [2,7-cystine]-gramicidin S⁸.

in a qualitative way to deduce a quadrant rule for the $n\sigma^*$ transitions as a function of dihedral angle. They did not proceed with a quantitative treatment 'because' 'The model does not permit absolute sign predictions because of uncertainty in the sense of the electric dipole transition moment. . . .'⁷ Linderberg and Michl then carried out CNDO calculations on H_2S_2 to provide a quantitative basis for their predicted quadrant behavior.

However, the sense of the electric dipole transition moment is arbitrary in any MO calculations, as is the sense of the magnetic dipole transition moment. It is the scalar product of the two transition moments which determines the rotational strength, and as long as care is taken to preserve the proper phase relationship between the two, the Bergson model should give qualitatively correct results for the absolute sign of the rotational strengths.

This is indeed the case, as can be seen from Fig 3. The longest wavelength $n_1 \rightarrow \sigma^*$ transition is predicted to have a positive rotational strength for φ between 0° and 90° (right-handed helices) and a negative rotational strength for φ between 270° and 360° (left-handed helices). This is in accord with the empirical rule formulated by Carmack and Neubert⁴ and by Dodson and Nelson,⁵ and with the theoretical CNDO calculations of Linderberg

and Michl.⁷ It also agrees with the generalized sign rule for chromophores of C_2 symmetry propounded by Wagniere and Hug.^{1,2} Their rule states that the long wavelength Cotton effect of a right-handed chromophore is negative for a transition of A symmetry and positive for one of B symmetry. The Bergson model used here leads to B symmetry for the longest wavelength transitions in disulfides with $|\varphi| < 90^\circ$ and A symmetry for those with $|\varphi| > 90^\circ$.

The Bergson model, when applied quantitatively, also predicts a quadrant behavior, as anticipated by Linderberg and Michl.⁷ That is, for φ between 90° and 270° , the longest wavelength transition (now the $n_4 \rightarrow \sigma^*$) gives a positive rotational strength for a right-handed screw sense. This quadrant behavior has recently been verified in an elegant way by Ludescher and Schwyzer,⁸ who have synthesized an analogue of gramicidin S with a disulfide bridge across the cyclodecapeptide ring. Models indicate a dihedral angle of *ca* 120° for this disulfide and NMR studies show that the disulfide is right-handed. The long-wavelength CD band is negative, in agreement with a quadrant rule.

Beyond the qualitative agreement with experiment, the application of the Bergson model leads to numerical values for the rotational strengths for the long-wavelength band which are in semi-quantitative agreement with experiment. This is illustrated in Table 5, where experimental rotational strengths for several disulfides are compared with the theoretical values. (Unfortunately, quantitative rotational strengths have only been reported for $\varphi = \pm 60^\circ$ and $\varphi = \pm 120^\circ$, which according to the theory should all have the same absolute values.) The agreement is very satisfactory for the long-wavelength band. For the short-wavelength band, the agreement is satisfactory for 1 and 2, but not for the remaining compounds. This can probably be attributed to the coupling of the higher energy $n \rightarrow \sigma^*$ transitions with other chromophores.

Oscillator strengths were also calculated for the

$n \rightarrow \sigma^*$ transitions as a function of dihedral angle. Comparison with the two quantitative reports of intensity again shows qualitative agreement for the long-wavelength transitions. Carmack and Neubert⁴ reported anisotropy factors as well as rotational strengths, from which oscillator strengths can be calculated. For their compounds, with $|\varphi| \cong 60^\circ$, the long-wavelength band had an oscillator strength of 0.01 while we calculate $f = 0.006$ for the $n_1 \rightarrow \sigma^*$ transition. The band at about 240 nm had an oscillator strength of 0.003 as compared to the calculated value for the $n_4 \rightarrow \sigma^*$ transition of $f = 0.0016$. Thompson *et al*¹³ report an oscillator strength of 0.031 for the 250 nm band dimethyldisulfide. This band corresponds to a superposition of the $n_1 \rightarrow \sigma^*$ and $n_4 \rightarrow \sigma^*$ transitions, whose total oscillator strength is calculated to be 0.0072. In both the $\varphi = 60^\circ$ and the $\varphi = 90^\circ$ cases, the model gives oscillator strengths of the right order of magnitude, but too small by factors of 2–4. Thus, for the transitions involving the π -type lone pair orbitals the Bergson model gives a reasonable representation of the absorption intensity as well as the rotational strength.

However, the model does run into difficulties with the transitions involving the σ -type lone pairs. The calculated oscillator strengths for the $n_3 \rightarrow \sigma^*$ transitions lead to an improbably large value, $f \cong 0.4\text{--}0.5$. The dominant contribution to this large oscillator strength is the x-component of the gradient operator, i.e., the component along the S—S bond. Since the x-component of the magnetic dipole operator vanishes for all φ , this has no effect on the calculated intrinsic rotational strengths, although it will affect calculations involving the coupling of disulfide transitions with transitions in other chromophoric groups.

Thompson *et al*¹³ have reported the absorption spectrum of dimethyldisulfide down to 180 nm. In addition to the weak 250 nm band, they observed a shoulder at about 210 nm ($f = 0.028$) and a strong band at 195 nm ($f = 0.303$). They also comment that the 195 nm band is blue-shifted by solvents of increasing polarity. Coleman and Blout²⁶ have

Table 5. Comparison of experimental^a and calculated^b rotational strengths

	φ (deg)	λ_1 (nm)	R_1 (exp)	R_1 (calc)	λ_2 (nm)	R_2 (exp)	R_2 (calc)
1	-60	290	-0.21	-0.11	241	+0.11	+0.08
2	+60	287	+0.16	+0.11	238	-0.14	-0.08
3 (in CH_2Cl_2)	+60	288	+0.16	+0.11	241	-0.065	-0.08
3 (in H_2O)	+60	282	+0.15	+0.11	238	-0.041	-0.08
4	+120	272	-0.13	-0.11	230	+0.63	+0.08

^aIn DBM. Data for compounds 1–3 are from Ref. 4. Compound 1 is (9S, 10S)-*trans*-2,3-dithiadecalin. Compound 2 is (4R,5R)-4,5-isopropylidenedioxy-1,2-dithiane. Compound 3 is (4R,5R)-4,5-dihydroxy-1,2-dithiane. Data for compound 4, which is [2,7-cystine]-gramicidin S, is from Ref. 8.

^bIn DBM. The calculated value for R_1 is that for the $n_1 \rightarrow \sigma^*$ transition and that for R_2 is the $n_4 \rightarrow \sigma^*$ transition.

studied both the absorption and the CD of cystine in the far UV. Their absorption spectrum of cystine agrees well with that of 2,2'-dithiodiethanol which they used as a model compound, except for a larger absorption by cystine in the 210–220 nm region attributable to the carboxylate $n\pi^*$ transition. The absorption spectra of both cystine and 2,2'-dithiodiethanol show a definite inflection at about 187 nm, which presumably corresponds to the 195 nm band of dimethyldisulfide in the gas phase. Although Coleman and Blout do not comment on the point, their spectrum of 2,2'-dithiodiethanol does appear to exhibit a poorly developed shoulder at about 205 nm, which would correlate with the 210 nm band of dimethyldisulfide.

These bands observed in disulfides with dihedral angles of about 90° may be assignable to the $n_2 \rightarrow \sigma^*$ (200–210 nm band) and to the $n_3 \rightarrow \sigma^*$ (187–195 nm band) transitions. This assignment would be consistent with the calculations of Yamabe *et al.*²⁴ Their calculated orbital energies for $\varphi = 90^\circ$ would lead us to expect the $n_2 \rightarrow \sigma^*$ transition about 1 eV higher in energy than the degenerate $n_1, n_4 \rightarrow \sigma^*$ transitions which lie at 250 nm, and the $n_3 \rightarrow \sigma^*$ transition would then occur at about 2 eV above the 250 nm band. This would place the $n_2 \rightarrow \sigma^*$ transition at 6 eV (207 nm) and the $n_3 \rightarrow \sigma^*$ transition at 7 eV (177 nm).

However, although the assignment of the 190 nm band to the $n_3 \rightarrow \sigma^*$ transition would be consistent with the calculated intensity of that transition, it is difficult to assign the 205 nm band to the $n_2 \rightarrow \sigma^*$ transition, for its observed intensity¹³ ($f_{\text{obs}} = 0.028$) is almost 25 times that calculated ($f_{\text{calc}} = 0.0012$).

A more plausible interpretation would be that the 190 nm band is the disulfide $\sigma \rightarrow \sigma^*$ transition and the 205 nm band is the $n_3 \rightarrow \sigma^*$ transition, while the $n_2 \rightarrow \sigma^*$ transition is either overlaid by the more intense $n_2 \rightarrow \sigma^*$ transition or is at somewhat longer wavelengths but is not seen because of its low intensity. This implies that the theory is overestimating the $n_3 \rightarrow \sigma^*$ intensity. It is not unreasonable that this should be the case with this simple theory. The principle sources of the large intensity are the large one-center contributions of the $s \rightarrow p$ type. There is good reason^{13, 25, 27, 28} to believe that sulfur 3d orbitals participate in the σ^* orbital to an appreciable extent. Since atomic $s \rightarrow d$ transitions are electrically forbidden, their participation would tend to reduce the calculated oscillator strength. Participation of d orbitals might also explain the underestimation of the oscillator strengths for the $n_1 \rightarrow \sigma^*$ and $n_4 \rightarrow \sigma^*$ transitions, since atomic $p \rightarrow d$ transitions are electrically allowed.

For disulfides with small dihedral angles, the calculations of Yamabe *et al.*²⁴ would indicate that the $n_2 \rightarrow \sigma^*$ and $n_3 \rightarrow \sigma^*$ transitions should occur at about 1.5–1.7 eV above the long-wavelength $n_1 \rightarrow \sigma^*$ transitions. This would place them at

about 5.2 eV, in the 230–240 nm region. In the CD spectrum of diketopiperazine disulfide systems,^{16, 29} there is a very strong band at about 235 nm. This band undoubtedly has a large contribution from peptide $n\pi^*$ transitions, but the large magnitude may contain contributions from other transitions. The absorption spectrum of glutathione³⁰ does show appreciable absorption ($\epsilon \approx 3500$) in the 235 region, but no maximum or inflection. However this region is overlapped by a diene band at longer wavelengths and the diketopiperazine $\pi\pi^*$ transitions as well as diene transitions at shorter wavelengths. It is therefore possible that one or two disulfide transitions of moderate intensity may occur in the 235 nm region disulfides near the *cis* conformation, but further studies will be required to settle this question.

In summary, the Bergson model is very successful in accounting for the dihedral angle dependence of the long wavelength disulfide absorption bands, and also can account satisfactorily for their intensity and rotational strength. The location of the $n \rightarrow \sigma^*$ transitions arising from the σ -type n orbitals is uncertain, but we have suggested that for dihedral angles near 90° , one of these transitions (the $n_3 \rightarrow \sigma^*$) is observed at about 205 nm while the band at about 190 nm is probably the disulfide $\sigma \rightarrow \sigma^*$ transition. The success of this model for simple disulfides leads us to believe that it will be useful in treating disulfide transitions in more complex molecules containing other chromophores. Indeed, calculations on diketopiperazine disulfides²¹ indicate that this is the case.

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