Figure 1. Molecular structure of **21**.
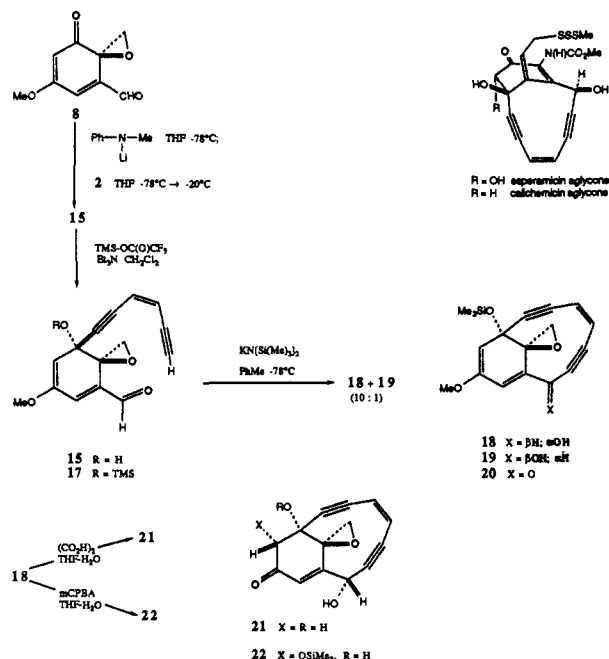
2^5 to a THF solution (−78 °C) of the protected **8**, followed by workup, afforded a 50–60% yield of **15**.[7b] This compound was converted to its trimethylsilyl derivative **17** (70% yield), as shown.

Reaction of a toluene solution of **17** with potassium hexamethyldisilazide (toluene −78 °C, 20 min) afforded a 52% yield[11] of a 10:1 ratio of **18:19**. The somewhat unstable ketone **20**, obtained by oxidation[9] of **19**, upon reduction with potassium triisopropoxyborohydride, afforded alcohol **18**, thus allowing for "retrieval" of the minor cyclization product. The stereochemistry of **18** (and therefore **19**) initially surmised from NMR (NOE) measurements was fully established by X-ray crystallographic determinations of compounds **21** and **22**. These products were obtained in 90% and 50% yields, respectively, by hydrolysis or oxidation of **18** as shown.[12] It will be noted that **21** represents a highly functionalized version of calicheamicin. The siloxyketone **22** contains the additional oxygen required for esperamicin, though an inversion at carbon 4 would be required.

The crystal structures of both **21** and **22** are the first obtained in the esperamicin–calicheamicin series wherein the enediyne and bridgehead olefin functionalities are present. The molecular parameters of the two compounds are very similar. An ORTEP view and some of the more interesting data for compound **21** are provided in Figure 1. This compound has many interesting

(11) This yield is based on 18% recovered starting material. The ratio reflects predominant attack of the acetylide on the S-trans conformer of the enal. When the reaction was performed in THF with lithium hexamethyldisilazide as base, a 2.5:1 ratio of **18:19** ensued.

(12) The X-ray crystallographic analysis indicated a transfer of the trimethylsilyl group from the oxygen at C_5 to the newly introduced oxygen at C_4.

features. The distortion of the acetylenic bond angles is substantial relative to the only modest deviations in the connecting C_8–C_9 vinylene unit. The distance between C_6 and C_{11} is compressed[14] to 3.44 Å. Bonding between these centers is assumed to occur during the bioactivation process.[1,2] Also noteworthy are the deviation from planarity of the enediyne[15] and the boat-like conformation of the cyclohexenone. The C_3 oxygen is tipped syn to C_{13}, and the deviation from planarity of the enone is 17°.

The results of continuing research in this area will be disclosed in due course.

(13) Cf. dibenzo-1,5-cycloocta-3,7-diyne has acetylenic bond angles of 155.8°: Destro, R.; Simonetta, M. *J. Am. Chem. Soc.* **1975**, *97*, 658. Benzocyclodeca-3,9-diyne has a $C_{2,3,4}$ bond angle of 166.7° and a $C_{3,4,5}$ bond angle of 176.3°: Bennet, M. J.; Smith, R. A. *Acta Crystallogr., Sect. B:* **1977**, *33B*, 1123.

(14) In an analogous acyclic system, 1,2-bis(trimethylstannylacetylene)-benzene, the distance between the distal acetylene carbons is 4.17 Å: Adiwidjaja, G.; Grouhi-witte, G. *J. Org. Met. Chem.* **1980**, *91*, 188.

(15) The torsion angles of $C_{5-6-7-8}$, $C_{6-7-8-9}$, $C_{7-8-9-10}$, $C_{8-9-10-11}$, and $C_{9-10-11-12}$ are −38°, −7°, −2.8°, −8°, and −23°, respectively.

Dependence of Disulfide Vibrational Frequencies on Internal Rotation Geometry: An ab Initio and Normal Mode Study of Dimethyl Disulfide

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Correlations of disulfide vibrational frequencies, such as the S–S [ν(SS)] and C–S [ν(CS)] stretch modes, with the internal rotation angles associated with this group have been the subject of numerous investigations since Lord and Yu noted the conformation dependence of these modes in the Raman spectra of proteins.[1] We have completed ab initio force constant and normal mode calculations as a function of τ(SS), the CS–SC dihedral angle, on dimethyl disulfide, the simplest of a series of such molecules that we are studying, that provide a rigorous basis for evaluating some of these relationships.

There have been contradictory claims regarding the dependence of ν(SS) on τ(SS). According to Sugeta and co-workers,[2–4] ν(SS) is independent of τ(SS), a conclusion supported by Bastian and Martin.[5,6] On the other hand, Van Wart, Scheraga, and co-workers initially proposed[7] that ν(SS) varies linearly with τ(SS) in the range of 0 to ~90°, subsequently, on the basis of CNDO/2[8]

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(5) Bastian, E. J., Jr.; Martin, R. B. *J. Phys. Chem.* **1973**, *77*, 1129–1133.
(6) Martin, R. B. *J. Phys. Chem.* **1974**, *78*, 855–856.
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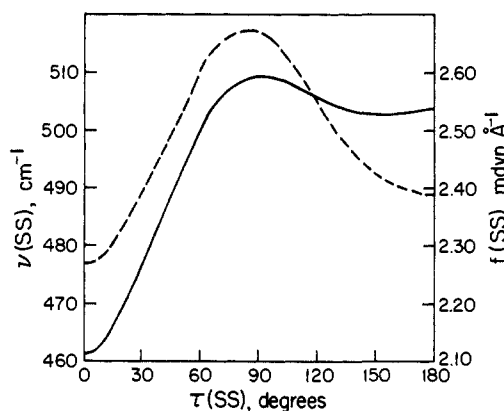
Figure 1. Variation of the S–S stretch force constant, f(SS) (— — —), and the S–S stretch frequency, ν(SS) (—), with the S–S dihedral angle, τ(SS), in dimethyl disulfide, as determined from ab initio and normal mode calculations.

and experimental[9] studies, asserting[9–11] that ν(SS) varies linearly with τ(SS) only in the range of 0–60°, being invariant in the range of 60–85° and expected to decrease in the 120–180° region. In contrast to Sugeta's normal mode calculation with a modified Urey–Bradley force field,[4] Kuptsov and Trofimov[12] showed that, even with an invariant f(SS)[4] (the S–S stretching force constant), a valence force field leads to a small variation in ν(SS) with τ(SS). In any case, there is general agreement[4,11] that in a CCSSCC moiety ν(SS) does depend on the τ(CS), the CC–SS dihedral angles.

Both the earlier CNDO/2[8] as well as more recent ab initio[13] calculations have shown that r(SS), the S–S bond length, varies with τ(SS), thus showing that f(SS) must also change. Of course, ν(SS) depends on the geometry as well as on f(SS), and therefore frequency estimates[8,11] based only on force constant trends cannot be completely reliable. The results of our ab initio and normal mode studies shed light on these issues.

Calculations were done with the 3-21G* basis set at the Hartree–Fock level. Analytical techniques were used to obtain force constants in cartesian coordinates, and these were then transformed to internal and symmetry coordinates. As usual,[14] force constants were scaled to match calculated with observed frequencies. Diagonal force constants were scaled according to internal coordinate types, six scaling factors being optimized to fit 15 observed frequencies.[15] Off-diagonal force constants were scaled with the geometric average of the diagonal scale factors.[14]

For each τ(SS), the geometric parameters were obtained from an ab initio geometry optimization. Ab initio force constants were calculated for the stationary energy conformers, viz., cis ($\tau = 0°$), gauche ($\tau = 85.17°$), and trans ($\tau = 180°$). The f(SS) for other values of τ (30°, 60°, 120°, 150°) were obtained from the empirical formula relating f and r,[16] viz., $f = c/(r - d)^2$. First, the c and d parameters were obtained by optimizing the fit of the ab initio f and r to this relation. From this, the f at other values of r could be obtained from the ab initio optimized geometries. Since it is more convenient to have a correlation between f and τ, we obtained this by using a Fourier expansion, viz., $f = f_o + \frac{1}{2}\sum_n f_n(1 - \cos n\tau)$. Having seven values, we used $n = 6$ for f(SS); for the

other force constants we used the three ab initio values, and therefore $n = 2$. The scaled force constants were used to calculate frequencies and potential energy distributions, the unscaled force constants being used to calculate infrared and Raman intensities. Our vibrational assignments are consistent with those of Sugeta[4] for the gauche conformer; the average deviation between observed and calculated frequencies is 0.3%, and the observed relative band intensities are well predicted.

The results show that some of the force constants (such as f(CS)) do not change appreciably with τ(SS), while others do and are not a simple function of this dihedral angle. For example, Figure 1 shows the variation of f(SS) with τ(SS), indicating that it goes through a maximum near the gauche conformer. On the other hand, f(CSS) decreases monotonically in the 0–120° region and is then constant to 180°. The off-diagonal force constants all change significantly with τ(SS), in some cases changing sign.

The frequencies, as noted above, depend on the geometry as well as the force field. In Figure 1 we show the variation of ν(SS) with τ(SS). In the 0–85° range it follows the trend of f(SS), but in the region of 85–180° kinematic factors obviously counter the force constant trend, as previously recognized,[12] and ν(SS) decreases slightly (compared to a much larger decrease predicted from CNDO/2 calculations[8]). This variation is similar to that observed experimentally by Van Wart and Scheraga,[9] keeping in mind that in dimethyl disulfide there is no effect of τ(CS) on ν(SS). The changes in ν_s(CS) (symmetric stretch) and ν_a(CS) (antisymmetric stretch) with τ(SS) are relatively small (~ 10 and ~ 15 cm^{-1}, respectively), but the changes in ν_a(CSS) and ν_s(CSS) (~ 100 and ~ 50 cm^{-1}, respectively) are quite large, and while generally similar to previous results[4] are significantly different in detail.

Geometry optimization calculations on diethyl disulfide show a variation of r(SS) with τ(SS) similar to that in dimethyl disulfide, and therefore a similar variation in f(SS) is expected. We are also examining the effect of τ(CS) on the disulfide group frequencies. We believe that such ab initio methods offer a good possibility of elucidating the obviously complex dependence of disulfide vibrations on the internal rotation geometry of this group.

The Enzymatic Baeyer–Villiger Oxidation: Enantioselective Synthesis of Lactones from Mesomeric Cyclohexanones

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In a synthetic project directed toward the syntheses of the 3-acyltetramic acid antibiotics (e.g., tirandamycin[1]), we envisioned ketone **1** as a potential precursor.[2] The planned sequence involved the transformation of **1** into the ϵ-lactone **2** by using a peracid mediated Baeyer–Villiger oxidation. Because of the inherent mirror plane in **1**, chirality would not be established until after the oxygen atom had been inserted between the carbonyl group and one of the α-carbon atoms. If one could discriminate between the two enantiotopic carbon atoms flanking the carbonyl, then when the oxygen atom was inserted, a product which would be entirely one or highly enriched in one enantiomeric form would be produced. Insertion of the oxygen into the right-hand side of

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