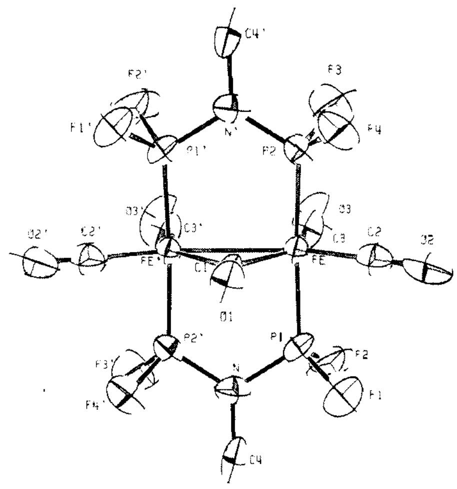


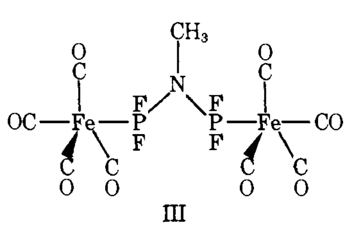
Figure 2. ORTEP drawing of the structure of $[CH_3N(PF_2)_2]_2Fe_2(CO)_5$ (II).

the ultraviolet irradiation of equimolar quantities of $Fe(CO)_5$ and $CH_3N(PF_2)_2$ in diethyl ether.

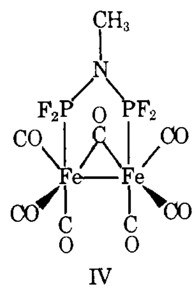
The complex $[CH_3N(PF_2)_2]_2Fe_2(CO)_5$ (II) forms orthorhombic crystals from mixtures of 1:1 *n*-hexane-dichloromethane: space group *Pccn*; $a = 10.061$ Å, $b = 9.269$ Å, $c = 19.876$ Å; $Z = 8$. Least-squares refinement using the 978 observed reflections ($R = 0.0411$, $R_w = 0.0414$) indicates the structure depicted in Figure 2 with a twofold axis passing through the bridging carbonyl group and the midpoint of the iron-iron bond. The iron-iron distance is 2.661 (1) Å corresponding to an iron-iron bond. The coordination polyhedron around each iron atom can be derived by appropriate distortions from an octahedron or trigonal bipyramid depending upon whether a coordination position is allocated to the metal-metal bond.

Of particular interest is a comparison between the iron coordination polyhedra in I and II as an indication of the effect of the metal-metal bond in II (see Figures 1 and 2). In $[CH_3N(PF_2)_2]_2Fe_2(CO)_5$ (II) the phosphorus-iron-phosphorus angles are 172.5 (1)° which is close to the 180° required for the collinear apical positions in an octahedron or trigonal bipyramid. However, in $[CH_3N(PF_2)_2Fe(CO)_3]_2$ (I) the phosphorus-iron-phosphorus angles are reduced to 153.9 (2)° since the nonbonding iron-iron distance in I is larger than the bite of the $CH_3N(PF_2)_2$ ligand. Thus the repulsion between the nonbonded iron atoms in I forces the five-coordinate iron(0) atoms to adopt the unusual square pyramidal geometry instead of the more usual trigonal bipyramidal geometry. The ability of the simple nonbonded interaction to change the coordination polyhedron of a five-coordinate system is a further indication of the relative nonrigidity of this coordination number and the small energy difference between the trigonal bipyramid and the square pyramid.

Bimetallic iron carbonyl complexes have also been obtained in which only one $CH_3N(PF_2)_2$ ligand bridges the pair of iron atoms. Thus the reaction of $Fe_2(CO)_9$ with $CH_3N(PF_2)_2$ in diethyl ether at 25 to 35 °C gives a mixture of yellow liquid $CH_3N(PF_2)_2[Fe(CO)_4]_2$ (III) (infrared ν(CO) in pentane 2090 (m), 2023 (s), 1996 (s), 1985 (s), and 1976 (s) cm^{-1}) and red-orange $CH_3N(PF_2)_2Fe_2(CO)_7$ (IV) mp 75-77 °C (infrared ν(CO) in pentane 2090 (m), 2040 (s), 2025 (s), 1995 (vs), 1982 (m), and 1805 (s) cm^{-1}) in III:IV ratios ranging from 3:1 to 10:1. Those two compounds can be readily separated by column chromatography on Florisil in hexane solution. The proposed structure of IV is analogous to that reported[7] for the closely related complex $CH_2[P(C_6H_5)_2]_2Fe_2(CO)_7$.



III



IV

Acknowledgment. We are indebted to the Air Force Office of Scientific Research for partial support of this work under Grant AFOSR-75-2869. One of us (J.G.) is indebted to the Program of Cultural Cooperation between the U.S.A. and Spain administered by the Fulbright Commission of Spain for a Fellowship.

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(8) University of Georgia Graduate Fellow, 1976-1977.

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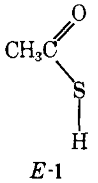
Dynamic Nuclear Magnetic Resonance Spectroscopy. Carbon-Sulfur p-p π-Bonding and Conformational Equilibria in Thioacetic Acid

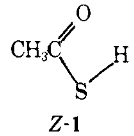
Sir:

Much information about the conformational preferences and carbon-nitrogen π-bonding in amides has been obtained from dynamic nuclear magnetic resonance studies of these compounds,[1] but similar studies of π-bonding between carbon and other heteroatoms have been rare.[2] Application of this method to the bonding in thiol acids is of particular interest because previous studies of carbon-sulfur π-bonding in related systems, using other methods, have resulted in opposite conclusions. The majority[3] of studies cited in a review[4] of divalent sulfur bonding seem to indicate that the mesomeric effect is greater for oxygen than for sulfur.[5] Evidence for the reverse order is presented in this work. In addition, the conformational equilibrium described here has not been detected in previous infrared[6] or electron diffraction studies[7] of thioacetic acid (**1**).

Two planar conformations (*E*-**1** and *Z*-**1**) are possible for the -SH tautomer of thioacetic acid, as shown below. Several bond lengths and bond angles have been reported,[7] but the O-C-S-H dihedral angle was not determined, and the possibility of *E* and *Z* isomers was not discussed. Infrared spectra



E-**1**



Z-**1**

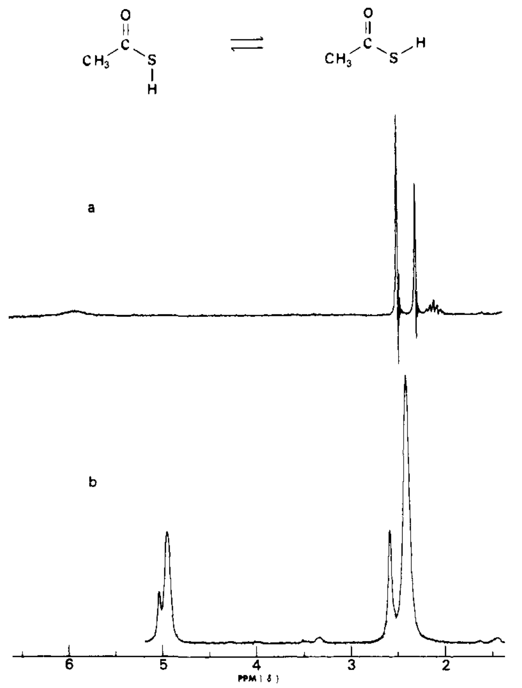


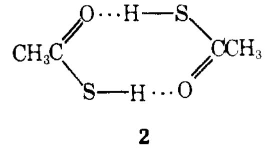
Figure 1. ^{1}H NMR spectra (60 MHz) of thioacetic acid (**1**): (a) 34 mg of **1** in acetone-d_6 (390 mg) at −50 °C. (The sample was prepared at low temperature to minimize the formation of an impurity (see text).) (b) 89 mg of **1** in CHClF$_2$ (total volume, ca. 0.56 mL) at −150 °C.

of the acid in the gas phase at high temperatures were interpreted in terms of an equilibrium between -OH and -SH tautomers;[6b] at room temperature, only a small amount of the -OH tautomer was believed to be present. Evidence for monomeric and two types of dimeric species of the -SH form has been obtained from IR spectroscopy.[6e,f,h] The predominant associated species in CCl$_4$ solution at room temperature was suggested[6e] to be an open dimer of the SH···O type. The results of a variable temperature IR study[6f] of the compound dissolved in a 1:1 mixture of two Freon solvents were interpreted in terms of a mixture of open and cyclic dimers of the *Z* configuration. Normal coordinate calculations have been carried out[6h] for **1**, and the possible presence of the *E* isomer was considered, but an alternative interpretation of the spectra was favored.

In contrast, both *E* and *Z* isomers of thioformic acid have been identified in the gas phase by microwave spectroscopy,[8] and detailed structural parameters have been reported. Both conformations were found to be planar, and no evidence for the -OH tautomer was found.

The ^{1}H NMR spectrum of **1**[9] at +38 °C in acetone-d_6 solution consists of singlets at δ 2.46 and 5.44, relative to internal tetramethylsilane, for the methyl and -SH protons, respectively. In this solvent, an additional methyl peak gradually appears downfield from the major resonance; this impurity was not identified, but the chemical shift was indistinguishable from that of added diacetyl sulfide. At low temperatures, the methyl resonance broadens and splits (T_c = +17 °C) into two peaks of unequal intensity centered at δ 2.39 and separated by 11.1 Hz at −50 °C.[10] At this temperature, the ratio of areas is 1.5:1, with the downfield isomer predominating (Figure 1a). The ratio of conformations increasingly favors the downfield isomer at higher temperatures, and from a plot of ΔG vs. $1/T$ for several temperatures, the free energy difference at +17 °C is estimated to be 1.9 kcal/mol. The coalescence temperature of a sample containing the same amount of acetone and three times the amount of **1** did not change from +17 °C within experimental error; however, because of the difficulty of accurately determining the coalescence temperature due to the large population ratio (ca. 27:1), this experiment cannot be regarded as conclusive evidence for an intramolecular process for interconversion of methyl sites. If a first-order process is assumed, the rate constant of 16 s^{-1} at +17 °C, determined using complete line shape analysis, corresponds to a free energy of activation of 15.3 kcal/mol for conversion of the minor isomer to the major isomer; the barrier for the reverse process is 17.2 kcal/mol. These barriers should, at least, represent lower limits for the barriers to interconversion of isomers by rotation about the C–S bond. The coalescence temperature for the methyl signals is much lower in CHF$_2$Cl as solvent (−137 °C), indicating that the equilibrium shown in Figure 1 takes place by intermolecular exchange of the acidic proton in this solvent.[11] The ratio of isomers at −150 °C is 3:1 (Figure 1b).

Formation of cyclic dimer **2** was believed to be favored at low temperatures in a mixture of Freon solvents.[6f] If this conclusion also applies to solution in acetone, then a tentative assignment of the *Z* configuration to the isomer with the upfield methyl signal can be made. The narrow line width of the -SH peak of the minor isomer in CHClF$_2$ indicates the absence of a substantial long-range coupling to this proton and provides some support for a similar assignment of conformations in this solvent. A large coupling constant (^4J = 0.6 Hz) was found[12] for the NH proton cis to the carbonyl group in acetamide. This may be due to a "planar W" relationship of the C–H and N–H protons in conformation **3**.[13] Such a relationship is not possible in the *E* configuration of **1**.



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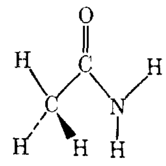

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The high rotational barriers for thioacetic acid demonstrate the large contribution of charged resonance structures in this compound, and comparison with the barrier for acetamide ($\Delta G^{\ddagger}$ = 16.7 kcal/mol)[12] indicates that *carbon-sulfur and carbon-nitrogen p-p π-bonding are of comparable importance in these systems.* Unfortunately, the barriers to isomerism have not been determined for acetic acid by the same method. However, the available evidence indicates that conjugation involving oxygen is less important than for nitrogen; for example, the barriers to interconversion of isomers in *tert*-butyl formate (8.81 and 9.17 kcal/mol)[2c] are lower than for simple amides.[1,14] The present work, in combination with previous studies of rotational barriers, then indicates that π-bonding decreases in the order N $\gtrsim$ S > O. Recent ab initio calculations on $^+$CH$_2$X (X = NH$_2$, OH, SH)[15] have led to similar conclusions, and the effects of overlap and energy differences between interacting orbitals are discussed in detail.

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considered for thiol esters: J. P. Idoux, P. T. R. Hwang, and C. K. Hancock, *J. Org. Chem.*, **38**, 4239 (1973), and references cited therein.

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(9) The thioacetic acid used in this study was obtained commercially from Aldrich Chemical Company or Matheson, Coleman and Bell. The acid was distilled twice before using and stored in a stoppered flask at −20 °C. The content of acetic acid in the purified compound was estimated to be less than 0.5%.

(10) The chemical shifts of the -SH protons were not resolved for the individual isomers in dry acetone-d_6 as solvent. However, in the presence of a trace amount of water, the broad absorption for these protons changed into a sharp peak at δ 5.90 and a broad, overlapping peak. The chemical shifts observed for the acidic proton in thioacetic acid show that the isomers are *E*-**1** and *Z*-**1**, rather than the -OH tautomers, which should absorb at much lower field.

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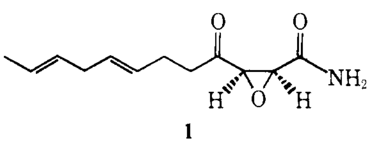
A Total Synthesis of *dl*-Cerulenin: a Novel Fatty Acid Antibiotic and Lipid Synthesis Inhibitor

Sir:

Cerulenin (**1**) was isolated from *Cephalosporium caerulens*, and shown to possess antibiotic[1] as well as lipid synthesis inhibitory properties.[2] The novel structure, **1**, has been assigned on the basis of IR, NMR, and chemical degradative data.[3,4] We have undertaken the total synthesis of cerulenin described herein in hopes of confirming the structural assignment as well as providing a route to the labeled antibiotic for biological studies of current interest[5] and to structural analogues of this novel class of substances.



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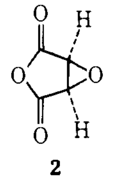
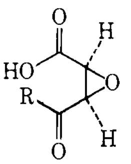


2

We considered initially, that cerulenin might be readily derived from interaction of anhydride **2**[6] already possessing the requisite acyl epoxy acrylate system, and suitably constituted organometallic reagents. However, a variety of reagents under a range of reaction conditions failed to lead to the desired epoxy acrylic acid derivatives, **3**. We turned instead to the preparation of epoxy lactones, **4**, from which cerulenin might be readily derived. The straightforward routes to the class of substances, **4**, such as epoxidation of unsaturated lactones such as **5**, proved unfeasible.[7] Consequently, we investigated indirect methods of production of the key intermediate, lactone **6**.



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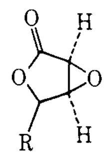

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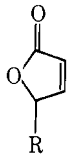

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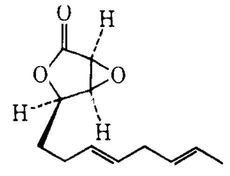
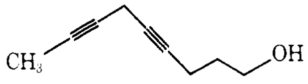


6

Treatment of 4-pentyn-1-ol tetrahydropyranyl ether successively with ethyl magnesium bromide in tetrahydrofuran (THF), cuprous chloride, and 1-bromo-2-butyne afforded, after removal of the protecting group, the air sensitive 1,4 diynol, **7**, as high boiling liquid (bp 70–75 °C (0.08 mm); 67%).[8] Reduction of **7** with lithium (6 equiv) in liquid ammonia, in the presence of *tert*-butyl alcohol (1 equiv) and solid ammonium sulfate (10 equiv) to prevent undesired base catalyzed isomerization and overreduction, produced the trans,trans dienol **8** in quantitative yield. Although few metal-ammonia reductions of 1,4 diynes have been recorded, the foregoing conditions seem generally applicable to the synthesis of trans,trans 1,4-dienes. Oxidation of **8** to the aldehyde **9** (bp 45 °C (0.5 mm) with pyridinium chlorochromate[9] (1.5 equiv) proceeded smoothly (65% yield) and this intermediate was readily purified by distillation.

Treatment of **9** with lithio propargyl alcohol tetrahydropyranyl ether at −78 °C in THF[10] provided the addition product which was hydrolyzed (wet methanol; *p*-toluenesulfonic acid; 20 °C, 4 h), partially reduced (palladium/barium sulfate, quinoline),[11] and selectively epoxidized utilizing vanadyl acetylacetonate/*tert*-butyl hydroperoxide.[12] After purification by chromatography (silica gel) the epoxy diol **10** was obtained in ~50–60% overall yield.[13]



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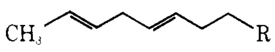
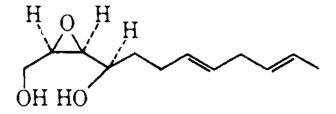


8, R = CH_2OH
9, R = CHO



10

Epoxydiol **10** was then converted to epoxy lactone **6** (bp 120 °C at 0.5 mm); NMR ($CDCl_3$): δ 2.8 (m, 2 H), 3.76 (d, 1 H), 4.1 (m, 1 H), 4.5 (m, 1 H), 5.5 (m, 4 H) utilizing silver carbonate on celite (15 equiv) in refluxing benzene for 2 h (50%).

Aminolysis of lactone **6** (NH_4OH/ether; room temperature) proceeded cleanly to give the amido alcohol **11** in nearly quantitative yield. The final conversion of amido alcohol **11** to cerulenin **1** was effected by treatment with pyridinium chlorochromate (3 equiv in CH_2Cl_2; 25 °C; 2 h).[15] Isolation and purification by successive chromatography (fluorosil; silica gel) provided *dl*-cerulenin (mp 40–42 °C) identical with an authentic sample[16] by comparison of spectral properties (IR–NMR–mass spectra) and thin layer mobility in several solvent systems.

The route seems amenable to the production of optically active cerulenin by resolution of the alcohol derived from **9** and efforts toward this end as well as the synthesis of analogues are under investigation currently.