(8) The use of DMF had no effect on the product yields.
(9) Without shaking, the cysteine complex yielded C_2H_4 and C_4H_6 (borate buffer) in about equal amounts, probably due to depletion of acetylene in the liquid phase.
(10) A 200-μl sample was taken using a valve-type syringe ("Pressure-Lok"). Thus an aliquot (0.01 l) of the gas phase could be obtained regardless of pressure changes in the vial.
(11) E. I. Stiefel, *Prog. Inorg. Chem.*, in press.
(12) Preparation of the new complexes will be described elsewhere. Satisfactory C, H, N analyses were obtained in all cases. Infrared, NMR, electronic spectra, and conductivity behavior in comparison with $Mo_2O_4(edta)^{2-}$ and $Mo_2O_4(cys)_2^{2-}$ support the structures shown. Abbreviation: pen = penicillamine = 3-mercaptovaline = β,β-dimethylcysteine.
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(18) The nitrogenase preparation used was from *Azotobacter vinelandii*, the specific activity being determined in the presence of excess Fe protein and 10% C_2H_2 in argon. The value reported is for the reaction mixture containing $S_2O_4^{2-}$, ATP, creatine phosphate, creatine phosphokinase, and Mg^{2+} as well as the enzyme. Details of enzyme preparation and purity will be reported elsewhere by E. I. Stiefel and D. Jacobs.

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Novel Thioxo-β-lactams from Thiosulfinates Derived from Penicillin Sulfoxides

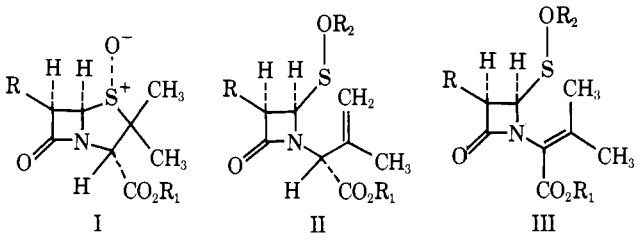
Sir:

Recent publications[1] revealed the utilization of the trimethylsilyl (Me_3Si) group in the isolation and crystallization of β-lactam sulfenic acids II and III (R_2 = H, R_1 = CH_3, *p*-$NO_2C_6H_4CH_2$) generated thermally from penicillin sulfoxides. The Me_3Si group distinguished itself from other acid protecting groups in that it is hydrolyzed readily to permit the generation of the β-lactam sulfenic acids in situ and, therefore, provided a way of studying the chemistry of this reactive species.

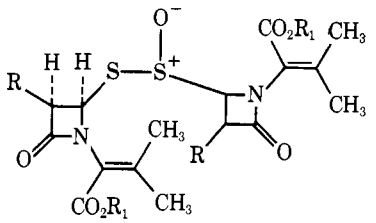
The nucleophilic nature of the sulfur atom in the sulfenic acid is well known;[2] thus, sulfenic acid II (R_2 = H) obtained from hydrolysis of the Me_3Si ester (II, R_2 = Me_3Si) will add to the vinylic double bond under neutral conditions to regenerate the penicillin sulfoxides. However, due to the lack of reactivity of the conjugated double bond of the α,β-unsaturated ester (III) to the intramolecular 1,4 addition,[3] a characteristic intermolecular condensation reaction of the sulfenic acid moiety is allowed to take place.[4] Therefore, when sulfenic acid III (R_1 = CH_3, R_2 = H), generated from its Me_3Si ester (III, R_1 = CH_3, R_2 = Me_3Si) by the treatment of methanol, was allowed to stand at room temperature for several hours, this condensation reaction occurred readily and the resulting thiosulfinate crystallized from chloroform–ether to give a colorless crystalline solid IV (R_1 = CH_3): mp 156–157 °C; $[\alpha]^{27}_D$ +56° ($CHCl_3$); IR ($CHCl_3$) 1795, 1785, 1735, and 1115 cm^{-1}; NMR ($CDCl_3$) δ 2.08 (s, 3 H), 2.15 (s, 3 H), 2.21 (s, 3 H), 2.35 (s, 3 H), 3.76 (s, 3 H), 3.81 (s, 3 H), 5.62 (d, 2 H, *J* = 4.5 Hz), 5.70 (ABq, 2 H, *J* = 4.5 and 34 Hz) and 7.82 (s, 8 H). Similarly, treatment of III (R_1 = CH_3, *p*-$NO_2C_6H_4CH_2$, Me_3Si; R_2 = Me_3Si) in chloroform with methanolic HCl resulted in the instantaneous precipitation of IV (R_1 = CH_3, *p*-$NO_2C_6H_4CH_2$, H, respectively) in high yield.

The thiosulfinate IV (R_1 = CH_3), after brief heating or prolonged standing at room temperature in an inert solvent, produced the novel thioxo-β-lactam V (R_1 = CH_3).[5] This monocyclic thione lactam will not polymerize and can be crystallized from methanol as light yellow prisms, mp 126–127 °C, in 67% yield.[6,7] The presence of an azetidine carbonyl group and a thiocarbonyl carbon in V (R_1 = CH_3) was indicated respectively by an absorption in the IR ($CHCl_3$) at 1835 cm^{-1} and by a chemical shift at 200.5 ppm downfield from tetramethylsilane in the ^{13}C NMR ($CDCl_3$).[8] In addition, the ^{13}C NMR also indicated the presence of $2CH_3$ (δ 22.0, 23.4), $1OCH_3$ (δ 52.3), 1CH (δ 65.7), 2C=C (δ 117.1, 161.8), 1 NC=O (δ 165.9), 1 ester C (δ 167.2), and a phthaloyl group. A ^1H coupled ^{13}C spectrum verified that the thiocarbonyl carbon is within three bonds of only one proton. The proton NMR ($CDCl_3$) of V had signals at δ 2.18 (s, 3 H), 2.42 (s, 3 H), 3.78 (s, 3 H), 5.92 (s, 1 H), and 7.84 (m, 4 H), and was also consistent with the structure.[9] Using the same method, the thioxo-β-lactams (V, R_1 = H, *p*-$NO_2C_6H_4CH_2$) can be prepared from the respective thiosulfinates (IV, R_1 = H, *p*-$NO_2C_6H_4CH_2$).

We theorized that the corresponding thioxo-β-lactam (VI) in the β,γ-unsaturated ester series could be prepared if the sulfenic acid II could be intercepted by an external sulfur nucleophile. Treatment of I (R_1 = CH_3) with *n*-pentyl mercapton afforded a high yield of VII, NMR ($CDCl_3$) δ 5.74 (ABq, 2 H, *J* = 4.5 and 10 Hz), 5.10–5.35 (m, 3 H, characteristic of the vinylic CH_2 and the allylic methine H), 2.32–2.80 (m, 2 H, $-SCH_2-$) and 2.12 (s, 3 H).[10] Subsequent oxidation of VII with *m*-chloroperbenzoic acid–CH_2Cl_2 gave selectively the thiosulfinate VIII, NMR ($CDCl_3$) δ 5.8–6.4 (m, 2 H), 2.8–3.2 (m, 2H, $OSCH_2-$), and 2.0 (s, 3 H).[11] Heating VIII in re-


I

II III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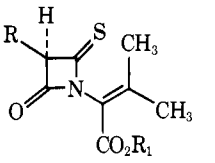
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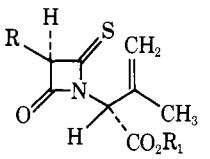
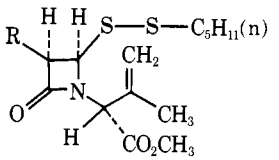
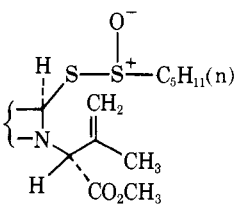

VI


VII


VIII

R = phthalimido
R_1 = CH_3, *p*-nitrobenzyl (*p*-$NO_2C_6H_4CH_2$), H, trimethylsilyl (Me_3Si)
R_2 = H, Me_3Si

fluxing benzene for 1 h and evaporating the solvent afforded the thione VI as a yellow gum: IR ($CHCl_3$) 1825 cm^{-1}; NMR ($CDCl_3$) δ 5.86 (s, 1 H), 5.43 (s, 1 H), 5.21 (m, 2 H), and 1.92 (s, 3 H). Thione VI was obtained in comparable yield to thione V. However, it was less stable than V, and, consequently, purification was achieved by removing the pentyl sulfide byproduct through the used of cellulose preparative thin layer chromatography.

The thione functionality adds a new dimension to β-lactam chemistry. The utilization of the thioxo-β-lactam in the construction of new penicillins and cephalosporins is currently under investigation.

Acknowledgment. The authors wish to express their gratitude to Dr. Jack Baldwin for useful discussions during the preparation of this manuscript and to Mr. J. R. Burgtorf for technical assistance.

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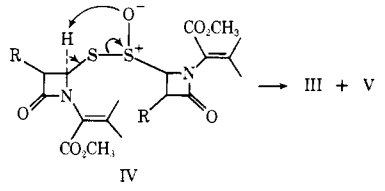
(6) In theory, one could expect only a 50% yield of thione V by pyrolysis of the thiosulfinate IV. However, the 67% yield of thione V can be rationalized by β-elimination of IV giving the thione and regeneration of III (R_2 = H). Sulfenic acid III could subsequently undergo dimerization and β-elimination or simply dehydration to give more thione V.



IV

(7) The chirality of V as reflected at C_3 is the same as C_6 of the starting penicillin. This contention is supported by optical rotation of V: $[\alpha]^{25}_D = -18.2°$ (*c* 0.01, benzene:ethanol = 1:1).
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(9) The mass spectrum of V (R_1 = CH_3) gave the molecular ion peak at *m/e* 358 and other fragments at *m/e* 330 ($M^+ - CO$), 315 ($M^+ - CO - CH_3$), 299 ($M^+ - CO_2CH_3$), 271 ($M^+ - CO_2CH_3 - CO$), 203 ($C_8H_4NO_2CH{=}C{=}S^+$), and 187 ($C_8H_4NO_2CH{=}C{=}O^+$).
(10) The disulfide VII was obtained by heating penicillin sulfoxide I (R = CH_3) in neat *n*-pentylmercaptan at 105 °C under N_2 for 16 h. The exclusive formation of the β,γ-unsaturated ester disulfide was in contrast to the report of Barton and co-workers in which penicillin V sulfoxides reacted with isobutylmercaptan to give the α,β-unsaturated ester disulfide; see D. H. R. Barton, P. G. Sammes, and M. V. Taylor, *Chem. Commun.*, 1137 (1971).
(11) The thiosulfinate VIII was obtained as a mixture of diastereomers. Exclusive oxidation of the pentyl sulfur was probably the result of the deactivation of azetinone sulfur electronically through induction and sterically by the phthalimido moiety which prevents oxidation of that sulfur.

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Molecular Structure of μ-(9-Methyladenine-N^1,N^7)-bis(diisopropyl sulfoxide-*S*)-*trans*-dichloroplatinum(II)[1]

Sir:

The anticarcinogenic chemotherapeutic effect of platinum(II) complexes is thought to be associated, in vivo, with the direct complexation of the platinum complex with the purine and pyrimidine bases of deoxyribonucleic acid.[2,3] Recent experiments have suggested that complexation with the purine bases is more important than with pyrimidine bases.[4]

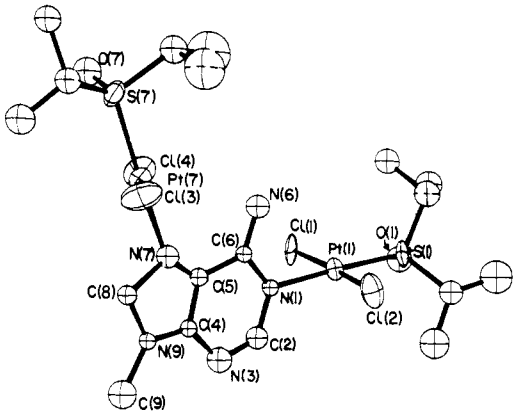

Figure 1.

On the basis of spectroscopic results, it has been suggested that platinum complexes can coordinate to one of the N7, N1, or NH_2-6 positions of adenosine[5,6] and coordination at N7 has been confirmed by x-ray crystallography.[7] In addition, it has been suggested that N1 and N7 positions can be coordinated simultaneously by two different platinum atoms.[6] We report here x-ray crystallographic evidence that confirms this suggestion.

Yellow crystals of the title compound were prepared by the stoichiometric reaction of $K[PtCl_3(\{(CH_3)_2CH\}_2SO)]$[8] with 9-methyladenine in water, the product being crystallized from acetone solution by evaporation at room temperature. Satisfactory analyses were obtained for C, H, S, N, and Cl.

Crystal data: $C_{18}H_{35}Cl_4N_5O_2Pt_2S_2$; M 949.6; monoclinic; space group $P2_1/c$; a = 15.620 (8), b = 17.357 (5), c = 14.05 (2) Å; β = 104.8 (1)°; Z = 4; d_c = 1.71 g cm^{-3}. Intensity data were collected using a Syntex $P\bar{1}$ diffractometer with Mo Kα radiation. The two crystallographically independent platinum atoms were located by direct methods. (The pseudosymmetry between the coordinates of the two platinum atoms precluded a unique solution to the Patterson map.) The other atoms were located by successive electron density difference syntheses. Full-matrix least-squares refinement, with anisotropic temperature factors for Pt, Cl, and S atoms, converged to a conventional R value of 0.069 for 1344 reflections with $I > 3\sigma(I)$.

The molecule is shown in Figure 1. The arrangement of ligand atoms about each platinum atom is essentially a square, the Pt-Cl (Pt(1)-Cl(1), 2.29 (1); Pt(1)-Cl(2), 2.31 (1); Pt(7)-Cl(3), 2.30 (1); Pt(7)-Cl(4), 2.30 (1)), Pt-N (Pt(1)-N(1), 2.08 (3); Pt(7)-N(7), 2.07 (3)); and Pt-S (Pt(1)-S(1), 2.23 (1); Pt(7)-S(7), 2.25 (1)) distances, bond lengths within the bis(isopropyl) sulfoxide group and all angles do not differ significantly from values we have found previously for a similar platinum complex of 1-methylcytosine.[8] Bond lengths and angles within the 9-methyladenine group do not differ significantly from the average values listed by Voet and Rich.[9]

Significant features of the structure are the large dihedral angles between the plane of the 9-methyladenine and the plane of each platinum atom and its four bonded atoms. The adenine-Pt(7) plane angle is 61° and the adenine-Pt(1) plane angle is 89°. Similar large angles have been observed for a platinum-1-methylcytosine complex (84°)[8] and a platinum-2,6-lutidine complex (81°).[10] These large angles are caused by the steric requirements of the groups attached to the carbon atoms adjacent to the bound nitrogen atom, and similar large dihedral angles will occur in any square planar platinum-DNA-base complex. This will undoubtedly cause a marked distortion in a coiled DNA chain, when platinum complexes are bound to the bases. This distortion may well be the reason