talline $BzPh_3P^+$ salt of this anion was isolated (IV)[13] and its properties (Table I) suggest a structure similar to that already known for the dithiocarbamate–iron nitrosyl complexes.[3a] The epr spectrum of this complex at $-80°$ consists of a typical triplet with $g = 2.0332 \pm 0.0005$ and $A_{N^{14}} = 14.3 \pm 0.1$ G. These values, as well as the magnetic moment (Table I), compare well with those of other similar nitrosyl complexes in which variations in $g$ and $A$ values seem to reflect the extent of electron delocalization in addition to ring size[14] effects. The magnitude of $A_{N^{14}}$ was used as a probe to investigate the changes brought about by chelation at the oxygen sites of the dithiooxalate ligands. An acetone solution of IV in the presence of excess $SnCl_4$[15] gave a spectrum with $A_{N^{14}} = 12.8 \pm 0.1$ G. This value and the well-resolved tin hyperfine splittings indicate electron delocalization away from the iron atom, and are in agreement with the observed ligand-field characteristics of II and III above.

Unlike other dithiooxalate complexes, I undergoes a reversible one-electron oxidation in dichloromethane at $+0.12 \pm 0.01$ V *vs.* Ag|AgI with $Bu_4NClO_4$ as the supporting electrolyte.[16] (Figure 1). Chemical oxidation with $I_2$ in nitromethane occurs readily, and upon dilution with ether, crystals of V (Table I) formed. The magnetic moment of 4.03 BM is very similar to that of the corresponding square-pyramidal[17] dithiocarbamate iron halides,[18] in which the Fe(III) ion is found in the uncommon $^4A_2$ ground state. Refluxing of I in $CH_2Cl_2$ over a 12-hr period resulted in the formation of VI (Table I), which could be isolated as a brown crystalline material with epr and ir spectra very similar to those of V. The structure of VI, and the nature of the presumed bridging dithiooxalate ligand, are uncertain at present.

Cyclic voltammetry of I in the presence of iodide ion or $(Et)_2NH$, in dichloromethane, has shown that the reversible character of the wave changes as a function of the scanning potential. Thus, when the voltage scan rate is greater than 10 V $sec^{-1}$, the reduction part of the wave corresponding to the process

$$[Fe(Dto)_3]^{2-} \xrightarrow{+1e} [Fe(Dto)_3]^{3-}$$

is well defined on cycling over a 1-V range. With scan rates less than 10 V $sec^{-1}$, however, the height of the reduction wave diminishes.[19]

The above observations suggest that the oxidized form of I is depleted from the electrode surface by a reaction following the oxidation. A similar reaction[20] could also be responsible for the formation of V following the chemical oxidation of I. By comparison to the 1,2-dithiolates, the dithiooxalate and thioxanthate complexes are not subject to extensive electron delocalizations. The possibility that the reversible oxidation observed in the iron(III)–thioxanthate and –dithiooxalate complexes results in coordinated, labile, radical anion ligands is at present under study.

In conclusion we wish to emphasize the similarities of the iron–dithiooxalate complexes to the thioxanthates and dithiocarbamates and, in particular, the interesting cooccurrence of oxidation properties and spin-state equilibria in these complexes.

**Acknowledgments.** The authors wish to acknowledge Drs. R. E. McCarley and J. P. Fackler for assistance with some of the magnetic measurements, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a grant (No. PRF No. 1775-G3) that partially supported this research.

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*Received May 21, 1970*

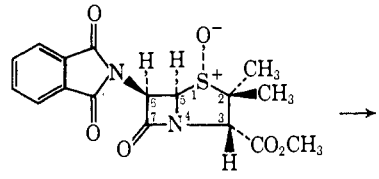
(13) The nature of this interesting nitrosyl abstraction reaction is presently under investigation.
(14) C. C. McDonald, W. D. Phillips, and H. F. Mower, *J. Amer. Chem. Soc.*, 87, 3319 (1965).
(15) In the presence of $SnCl_4$, IV reacts instantly, presumably forming the 2:1 adduct (see ref 1).
(16) (a) F. Rohrscheid, A. L. Balch, and R. H. Holm, *Inorg. Chem.*, 5, 1542 (1966). (b) The first oxidation wave of $Ni(MNT)_2^{2-}$ was observed at $+0.15$ V. The voltage scan rate was 0.5 V/sec.
(17) B. F. Hoskins, R. L. Martin, and A. H. White, *Nature (London)*, 211, 627 (1966).
(18) R. L. Martin and A. H. White, *Inorg. Chem.*, 6, 712 (1967).
(19) Cyclic voltammetry within the voltage ranges used in this work revealed no redox properties for V.
(20) Such a reaction perhaps could be a nucleophilic substitution of $Dto^-$ by $I^-$ or $Et_2NH$.

## Conversion of Penicillin to Cephalosporin *via* a Double Sulfoxide Rearrangement

*Sir:*

In 1963 Morin and coworkers[1a] reported the chemical conversion of penicillin to deacetoxycephalosporin *via* a cyclic sulfoxide rearrangement. I now wish to report the conversion of penicillin to cephalosporin *via* a *double sulfoxide rearrangement.*

Treatment of methyl phthalimidopenicillinate $\alpha$-sulfoxide (**1**)[2] with acetic anhydride[3,4] gave a mixture of 2-methylene-substituted penicillins and ring-expansion products. Oxidation of the mixture, followed by chromatography on silica, led to the isolation of the desired sulfoxides **2** and **3**, the stereochemistry being determined from nmr chemical shifts and internal nuclear Overhauser effects (NOE)[5] (see Table I).



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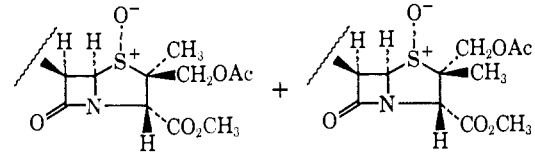


2 (30–40%) 3 (10%)

(1) (a) R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, and S. L. Andrews, *J. Amer. Chem. Soc.*, 85, 1896 (1963); (b) see also R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, and S. L. Andrews, *ibid.*, 91, 1401 (1969).
(2) R. D. G. Cooper, P. V. Demarco, and D. O. Spry, *ibid.*, 91, 1528 (1969).
(3) R. B. Morin, D. O. Spry, and R. A. Mueller, *Tetrahedron Lett.*, 849 (1969).
(4) R. B. Morin and D. O. Spry, *Chem. Commun.*, 335 (1970).

**Table I.** $CDCl_3$ Chemical Shift Values[a]

| Compd | 2-Me α | 2-Me β | $-OC(=O)CH_3$ | $CH_2OAc$ | $H_3$ | $H_5$ | $H_6$ | NOE |
|---|---|---|---|---|---|---|---|---|
| **1** | 1.33 | 1.83 | | | 4.61 | 4.86 d, $J$ = 4 | 5.89 d, $J$ = 4 | |
| **2** | 1.32 | | 2.23 | 4.41, 4.68 AB, $J$ = 12 | 4.88 | 4.87 d, $J$ = 4 | 5.89 d, $J$ = 4 | 6% αMe-$H_5$ |
| **3** | | 1.84 | 2.08 | 4.35, 4.48 AB, $J$ = 13 | 4.67 | 5.04 d, $J$ = 4 | 5.88 d, $J$ = 4 | 19% βMe-$H_3$ |

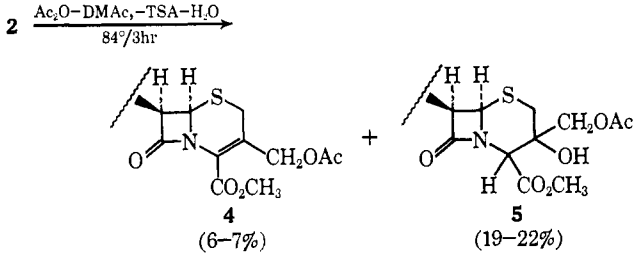
[a] Parts per million; $J$ values in hertz.

**Table II.** $CDCl_3$ (2.5%) Chemical Shift Values[a]

| Compd | 2-Me | $OC(=O)CH_3$ | $CH_2OAc$ | $H_3$ | $H_5$ | $H_6$ | NH | NOE |
|---|---|---|---|---|---|---|---|---|
| **11** | 1.51 | 2.18 | 3.80, 4.55 AB, $J$ = 12 | 4.67 | 5.64 d, $J$ = 4 | 5.78 q, $J$ = 4, 10 | 6.90 d, $J$ = 10 | |
| *b* | α β 1.25, 1.73 | | | 4.67 | 5.12 d, $J$ = 4 | 6.03 q, $J$ = 4, 10 | | |
| **12** | 1.25 | 2.13 | 4.57, 4.71 AB, $J$ = 12 | 4.68 | 5.06 d, $J$ = 4 | 6.13 q, $J$ = 4, 10 | 7.01 d, $J$ = 10 | αMe-$H_5$ 14% |
| **7** | 1.75 | 2.10 | 4.03, 4.59 AB, $J$ = 13 | 4.75 | 5.25 d, $J$ = 4 | 6.13 q, $J$ = 4, 10 | 7.02 d, $J$ = 10 | βMe-$H_3$ 18% |
| *c* | α β 1.32, 1.70 | | | 4.38 | 4.72 d, $J$ = 4 | 5.51 q, $J$ = 4, 10 | | |
| **13** | 1.38 | 2.17 | 4.50, 4.41 AB, $J$ = 13 | 4.67 | 4.89 d, $J$ = 4 | 5.63 q, $J$ = 4, 8 | 6.56 d, $J$ = 8 | αMe-$H_5$ 10% |
| **14** | 1.75 | 2.11 | 4.40, 4.50 AB, $J$ = 13 | 4.52 | 5.00 d, $J$ = 4 | 5.45 q, $J$ = 4, 8 | 6.58 d, $J$ = 8 | βMe-$H_3$ 12% |

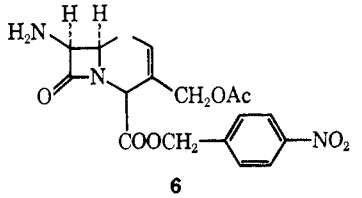
[a] Parts per million; $J$ values in hertz. [b] Methylpenicillin-β-sulfoxide methyl ester. [c] Methylpenicillin-α-sulfoxide methyl ester.[9]

A second sulfoxide rearrangement of **2** under conditions that cause predominant ring expansion resulted in the cephalosporin **4** and the 3-hydroxy compound **5**, mp 241–242°. Recyclizing compound **5** under the




conditions of the rearrangement causes partial dehydration to **4**, which is identical with authentic material prepared by acylation and esterification of 7-aminocephalosporanic acid.

Use of phthalimidopenicillin sulfoxide *p*-nitrobenzyl ester instead of the methyl ester results in the corresponding phthalimidocephalosporin *p*-nitrobenzyl ester which can be converted with strong base[1b] into the $\Delta^2$-cephalosporin and subsequently cleaved with hydrazine, giving nucleus **6** in a 30% yield (53% corrected for

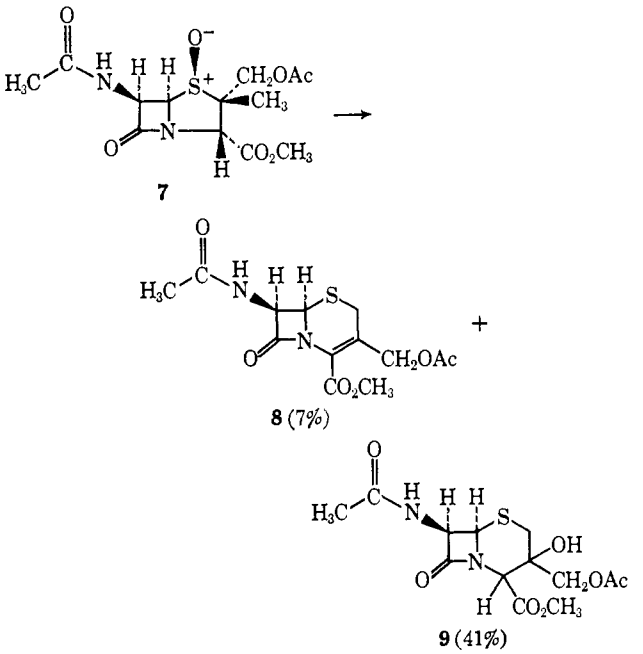



**6**

recovered starting material). Application of known methods to **6** thus allows conversion of 6-aminopenicillanic acid to 7-aminocephalosporanic acid.[6,7]

(5) R. D. G. Cooper, P. V. Demarco, J. C. Cheng, and N. D. Jones, *J. Amer. Chem. Soc.*, **91**, 1408 (1969).

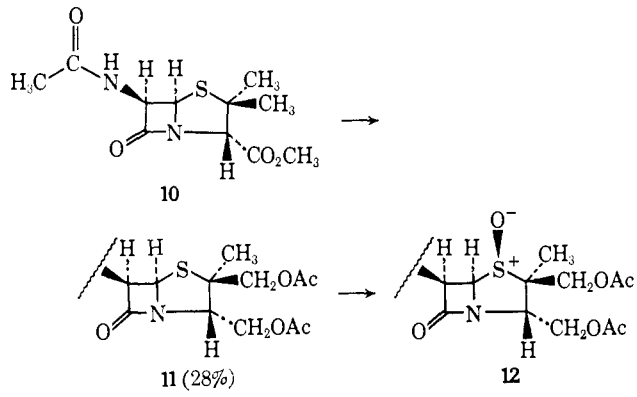
In order to determine whether the double rearrangement was applicable only to imide-type penicillins, **7** (mp 145–146°, $[\alpha]D$ +216° (dioxane)) was synthesized, and this also rearranges to give the corresponding cephalosporin **8** and the 3-hydroxy compound **9**,[8] mp 128–129°.




(6) J. A. Webber, E. M. Van Heyningen, and R. T. Vasileff, *ibid.*, **91**, 5674 (1969).

(7) G. V. Kaiser, I. G. Wright, C. F. Murphy, J. A. Webber, R. D. G. Cooper, and E. M. Van Heyningen, *J. Org. Chem.*, **35**, 2430 (1970).

(8) The second sulfoxide rearrangement of **3**, where the sulfoxide is cis to the methyleneacetoxy, does not yield cephalosporin-like products. This appears to be true of other penicillin sulfoxide methyleneacetoxy compounds.



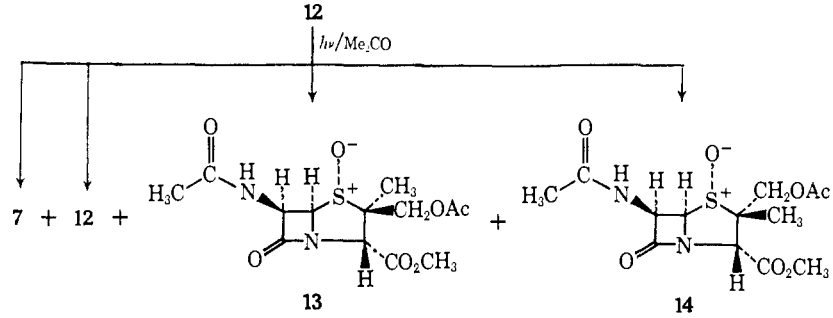
10



11 (28%) 12

mixture of sulfoxides. For example, phenoxymethylpenicillinic acid ($1.0 \times 10^{-2}$ *M*) in 1:1 water–acetone was treated with ozone (3.4 g/hr) for 2.5 hr. Evaporation of acetone gave crystalline, analytically pure β-sulfoxide acid in 49% yield; lyophilization of the aqueous solution gave analytically pure, noncrystalline α-sulfoxide acid in 51% yield. Treatment of sulfide **11** with ozone in 1:1 water–acetone gave **13** and **12** in a 2:1 ratio.

The selective oxidation of 2-methylene-substituted penicillins followed by ring-expansion rearrangement thus allows the conversion of penicillins to cephalosporins,



13 14

The synthesis of **7** is particularly interesting in that it establishes the $S_1$–$C_2$ cleavage mechanism for both the photochemical and thermal epimerization of penicillin sulfoxides.

Methylpenicillin methyl ester (**10**) was prepared in 97% yield from 6-aminopenicillanic acid and ketene, followed by esterification with diazomethane. Oxidation to the β-sulfoxide[9] with peracid, followed by acetic anhydride rearrangement, gave **11** which was then oxidized, again with peracid, to the crystalline β-sulfoxide β-methyleneacetoxy compound **12**, mp 184–185°, $[\alpha]_D$ +166° (dioxane).

Irradiation of **12** according to the procedure of Archer,[9] followed by chromatography on silica, led to the isolation of compounds **7**, **12**, **13**, and **14**.

The configurations were determined from nmr chemical shifts and internal NOE[5] (see Table II).

The thermal epimerization of **13** under refluxing benzene (30 min) gave **7** in good yield as the only lactam product.[10] A plausible mechanism to explain this involves $S_1$–$C_2$ cleavage to give the olefin–sulfenic acid, followed by $S_1$–$C_5$ and $C_2$–$C_3$ rotation and subsequent cyclization of the hydrogen-bonded sulfenic acid olefin.[11] The hydrogen bonding of the sulfenic acid with the amide apparently controls the stereochemistry.

To circumvent chromatographic problems associated with the photochemical preparation of the desired penicillin sulfoxide (cis to the methyl and trans to the methylene acetoxy), selective oxidation of the sulfide was investigated.

Ozone, under certain conditions, is an ideal reagent for converting various penicillin acids or esters into a

(9) R. A. Archer and P. V. Demarco, *J. Amer. Chem. Soc.*, **91**, 1530 (1969).

(10) Similar conditions on **14** do not result in **12**.

(11) I am indebted to Dr. B. B. Molloy of these laboratories for this explanation.

**Acknowledgment.** I wish to acknowledge the many helpful discussions with my colleagues, in particular Drs. B. B. Molloy, R. A. Archer, R. D. G. Cooper, R. B. Morin, and A. Pohland.

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## Azabicyclobutanes. Solvolytic Cleavage of 3-Phenyl-1-azabicyclo[1.1.0]butane

*Sir:*

Current conjecture concerning the role of 1-aza-, 1-oxa-, and 1-thiabicyclobutonium ions as intermediates in solvolytic reactions of 2-halomethyl and 2-arenesulfonyloxymethyl aziridines,[1] 3-substituted azetidines,[1] and related oxacyclic[2] and thiacyclic[3] systems prompts us to report our observations regarding the mechanism of acid-catalyzed reactions of 3-phenyl-substituted 1-azabicyclobutanes, **1a–c**.

It has previously been noted that **1a** is extremely sensitive to decomposition under acidic conditions,[4] and that other azabicyclobutanes can undergo facile addition of a variety of reagents to yield 3-substituted azetidines *via* cleavage of the 1,3 bond.[5]

Cleavage reactions of **1a–c** can be conveniently followed by measuring the decrease in uv absorption

(1) J. A. Deyrup and S. C. Clough, *J. Amer. Chem. Soc.*, **91**, 4590 (1969); J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1968); V. R. Gaertner, *ibid.*, 5919 (1968).

(2) H. G. Richey and D. V. Kinsman, *ibid.*, 2505 (1969).

(3) J. C. Martin and D. J. Anderson, Abstracts, 139th National Meeting of the American Chemical Society, St. Louis, Mo., March 1961, p 31-O.

(4) A. G. Hortmann and D. A. Robertson, *J. Amer. Chem. Soc.*, **89**, 5974 (1967); A. G. Hortmann and J. E. Martinelli, *Tetrahedron Lett.*, 6205 (1968).

(5) W. Funke, *Angew. Chem.*, **81**, 35 (1969); *Chem. Ber.*, 102, 3148 (1969).