COMMUNICATIONS TO THE EDITOR

THE PROBLEM OF THE CARBONATE APATITES

Sir:

Romo[1] recently has obtained some results that do not coincide with existing knowledge. Two major portions of his work are supported solely by infrared absorption spectrograms.

He states that an apatite from Durango, Mexico, (presumably from the well-known locality at Cerro Mercado) is hydroxyapatite. Hydroxyapatite, however, is not known from this locality, and a recent analysis by Ivan Barlow, of the U.S. Geological Survey, shows apatite from this locality to contain merely 0.13% water but 3.50% fluorine.[2]

Romo claims to have synthesized a carbonate apatite by wet methods, which (after drying) does not contain hydroxyl ions. He assigns to it the composition $Ca_{10}CO_3(PO_4)_6$. Again he decides the hydrous *vs.* anhydrous condition of the substance on the basis of the infrared absorption data, without other confirmatory tests.

Although the CO_3 group of such a substance would necessarily have its 3-fold axis parallel with the 6-fold screw axis of the structural arrangement, Romo assumes that the CO_3 group could replace OH groups without causing an increase in the size of the unit cell when measured perpendicular to the 3-fold axis. That this assumption has no validity was demonstrated in 1937 for the mineral francolite,[3] which likewise is a carbonate apatite for which considerable data have been presented.[4]

In recent years, the discussions concerning the true nature of carbonate apatites have involved consideration of such properties as the refractive index, the birefringence, the specific gravity, and the precise ratios of all of the different elementary constituents, including hydrogen. In light of the proposal in 1931[5] of the structural concepts presented by Romo, and a demonstration of their lack of validity in 1937,[3] the reiteration of these concepts, without any discussion of their interrelation to the extensive contrary data and conclusions, falls far short of a convincing presentation.

(1) L. A. Romo, This Journal, **76**, 3924 (1954).

(2) Z. S. Altschuler, personal communication, 1955.

(3) J. W. Gruner and D. McConnell, *Z. Krist.*, **97A**, 208 (1937).

(4) D. McConnell, *Bull. Soc. Franc. Mineral. Crist.*, **75**, 428 (1952).

(5) S. B. Hendricks, M. E. Jefferson and V. M. Mosley, *Z. Krist.*, **81A**, 352 (1932); see also *Ind. Eng. Chem.*, **23**, 1413 (1931).

College of Engineering
Ohio State University
Columbus, Ohio
Duncan McConnell

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D-4-AMINO-3-ISOXAZOLIDONE, A NEW ANTIBIOTIC*

Sir:

A new antibiotic has been isolated and determined to be D-4-amino-3-isoxazolidone (I). It was assigned the name "oxamycin." This compound is unique chemically, and the literature contains a paucity of isoxazolidones which are closely related to this 3-isoxazolidone.

This antibiotic was discovered as a metabolic product of a new species of *Streptomyces* and found to possess broad spectrum antibiotic activity.[1] It protects mice against a number of experimental infections.[2]

The crude fermentation broth was clarified with charcoal, adjusted to *p*H 3.0, and passed through a column of Amberlite IR-120.[3] Elution was accomplished by using 0.2 *N* ammonium hydroxide. The fraction collected between *p*H 5.5 and 10.5 was passed over a column of Amberlite XE98[4] on the hydroxide cycle, and 0.3 *N* acetic acid was used for elution. The eluate, adjusted to *p*H 10.5 and reduced to a concentration of 100 mg./ml., was treated with 5 volumes of isopropyl alcohol to precipitate impurities. Readjustment of the supernatant to *p*H 6 brought about crystallization of the antibiotic.

D-4-Amino-3-isoxazolidone is obtained as colorless crystals, m.p. 154–155°, $[\alpha]^{25}\text{D}$ +116° (*c*, 1.17 in water), $\lambda^{\text{water}}_{\text{max.}}$ 226 mμ ($E^{1\%}_{1\,\text{cm.}}$ 402). *Anal.* Calcd. for $C_3H_6N_2O_2$: C, 35.29; H, 5.96; N, 27.44; mol. wt., 102. Found: C, 35.75; H, 5.56; N, 27.19; mol. wt. (cryoscopic in water), 101. Titration with acid and base gave binding spans with *p*Ka values of 4.4 and 7.4, respectively, and equivalent weights of 101–102. The infrared absorption spectrum is characteristic of a zwitter-ion; there was no band in the region 2.5–3.4 μ, but broad hydrogen bonded NH–OH stretching frequencies in the region 3.6–4.7 μ, and maxima at 6.12, 6.20, 6.28, 6.43 and 6.52 μ. Crystalline sulfate, calcium, barium, and magnesium salts were prepared. The calcium salt (a tetrahydrate, m.p. 215–220° (dec.); $[\alpha]^{25}\text{D}$ 73.7° (*c*, 1 in water) was found to have stability properties superior to those of the zwitterionic form.

D-4-Amino-3-isoxazolidone was found to be relatively stable to alkali. Upon acid hydrolysis, it was readily degraded to hydroxylamine and serine as the major products. Catalytic hydrogenation of the antibiotic gave a quantitative yield of D-serine amide. Similar reduction of the N-acetyl derivative, m.p. 175–177°, yielded N-acetyl-D-serine amide. Upon treatment with methanolic hydrogen chloride, oxamycin was converted to β-aminoxy-D-alanine methyl ester (II), isolated as the dihydrochloride, m.p. 145–155° (dec.). *Anal.* Calcd. for $C_4H_{12}N_2O_3Cl_2$: C, 23.20; H, 5.84; N, 13.55; OCH_3, 14.97. Found: C, 23.21;

* A comparison of oxamycin with cycloserine, kindly furnished by Dr. Jerome Martin of Commercial Solvents Corporation, showed the two samples to be identical; *cf.* P. H. Hidy, *et al.* This Journal, **77**, 2345 (1955).

(1) D. A. Harris, H. Wallick, M. A. Reagan and H. B. Woodruff, *Antib. and Chemo.*, in press.

(2) A. C. Cuckler, B. M. Frost, L. McClelland and M. Solotorovsky, *ibid.*, in press.

(3) A sulfonic acid cation exchange resin, Rohm and Haas Co., Philadelphia, Pa.

(4) A strong basic anion resin, Rohm and Haas Co., Philadelphia, Pa.