CATHOMYCIN. I. ISOLATION AND CHARACTERIZATION

Sir:

We have isolated in crystalline form a new antibiotic from broths of a new actinomycete. This antibiotic, designated cathomycin, shows clinical promise.[1]

The first papers on cathomycin from these laboratories were presented before the Annual Symposium on Antibiotics.[2] The production[3] of cathomycin by *Streptomyces spheroides*, the antimicrobial properties,[3-5] and the absorption and distribution in mice[6] have been reported. Cathomycin is highly effective for staphylococci resistant to other antibiotics.[3,4]

The isolation of the antibiotic from the broth was accomplished by the following steps. A crude residue from the filtered and evaporated broth was dissolved in water, and the solution was acidified to *ca.* *p*H 2. A precipitate formed which was separated and dried. The precipitate was triturated with acetone and the insoluble material was removed. The acetone solution was evaporated *in vacuo* and the residue was triturated with methanol. The insoluble material was removed, and the methanol filtrate was evaporated *in vacuo*. The methanol-soluble residue was triturated with petroleum ether which dissolved most of the dark-colored substances. The remaining residue was dissolved in dilute sodium hydroxide and then hydrochloric acid was added to cause precipitation. The dried precipitate was triturated repeatedly with ether, and the ether extract was evaporated. The amorphous residue crystallized from aqueous acetone or ethanol or mixtures of petroleum ether and acetone or ethanol.

Cathomycin is a pale yellow compound which has been obtained in two crystalline forms, one melting at 152–154° (most common), the other at 170–172°. It is optically active; $[\alpha]^{25}D$ −27° (*c* 1 in 1 *N* sodium hydroxide) and $[\alpha]^{25}D$ −44° (*C* 1 in pyridine).

Potentiometric titration in a mixture of water and acetone (3–4) showed two acidic functional groups, $pH_1\ ^1/_2$ *ca.* 4.7, equivalent weight 653, and $pH_2\ ^1/_2$ *ca.* 10, equivalent weight 660–680. Determination of acidic groups by the ultraviolet absorption method, gave values of $pH_1\ ^1/_2$, 3 8 and $pH_2\ ^1/_2$ 9.2.

The principal maxima in the ultraviolet absorption spectra of solutions are as follows: 307 mμ, $E^{1\%}_{1\ cm}$ 600 in 0.1 *N* sodium hydroxide; 324 mμ, $E^{1\%}_{1\ cm}$ 390 in 0 1 *N* hydrochloric acid–methanol; 304 mμ, $E^{1\%}_{1\ cm}$ 350 in *p*H 7 phosphate buffer.

The infrared spectra of the two crystalline forms are different. However, when the two forms are dissolved in acetone, followed by rapid precipitation with petroleum ether, the spectra of the precipitates are identical. The principal bands in the infrared spectra of the precipitates, examined as a Nujol mull, expressed in microns are: 5.8–6.0 (broad), 6.10, 6.21, 6.30, 6.49, 6.63, 7.4–7.6, (broad-shoulder), 7.78, 7.96, 8.27 (weak), 8.60 (shoulder), 8.7 (shoulder), 9.13, 9.40, 10.0–10.1 (broad), 10.28, 10.60 (broad), 12.0–12.30 (broad), 12.60–12.75 (broad), 13.07 and 13.39.

(1) H. J. Robinson, E. Alpert and R. F. Sterner, manuscript in preparation.

(2) Third Annual Symposium on Antibiotics, November 2, 3 and 4, 1955, Washington, D. C.

(3) H. Wallick, D. A. Harris, M. A. Reagan, M. Ruger and H. B. Woodruff, "Antibiotics Annual, 1955–1956," Welch and Martí-Ibanez, Medical Encyclopedia, Inc., New York, N. Y., in press.

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

(5) W. S. Verwey, A. K. Miller and M. K. West, *ibid.*, in press.

(6) W. S. Verwey, M. K. West and A. K. Miller, *ibid.*, in press.

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An ebullioscopic determination of the molecular weight of cathomycin in isopropyl alcohol–water azeotrope gave a value of 592 ± 25. A solubility analysis of a sample showed a purity of 98.8%. Additional work on the solubility analysis is continuing. The composition of cathomycin is $C_{30}H_{36}N_2O_{11}$ or a very closely related formula.

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