salts showed only very strong basic groups. One very strongly basic function is the established guanidino group. The other is postulated to be an amidino group from its instability and strong basicity. The extreme instability of the amidine function suggests that the guanidinoacetamido group is the preferred location of this function. For these reasons structure I is postulated for the antibiotic T-1384.

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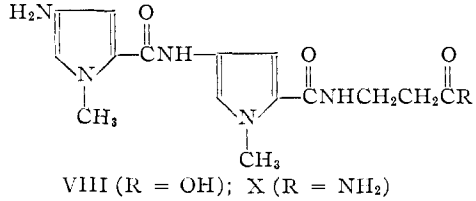
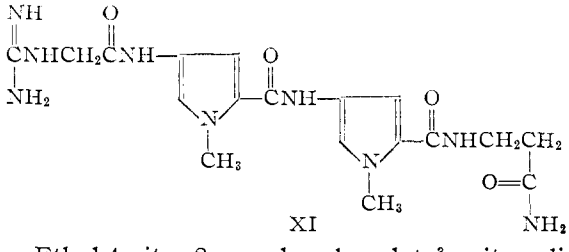
THE STRUCTURE OF ANTIBIOTIC T-1384. SYNTHESIS OF THE DEGRADATION FRAGMENTS

Sir:

Waller and co-workers[1] have reported that the stepwise degradation of the compound designated in these Laboratories as antibiotic T-1384 and identical with Netropsin[2] gives four new compounds. They postulated that these are 4-amino-1-methyl-2-pyrrolecarboxylic acid (III); the tripeptide derived from two moles of III plus β-alanine, β-[4-(4-amino-1-methyl-2-pyrrolecarboxamido)-1-methyl-2-pyrrolecarboxamido]-propionic acid (VIII); the amide of VIII (X) and the N-guanidinoacetyl derivative of X (XI). We wish to report the synthesis of these four compounds, all of which were found to be identical with the corresponding T-1384 degradation fragments by comparison of their infrared absorption spectra and other appropriate methods.



VIII (R = OH); X (R = NH_2)



XI

Ethyl 4-nitro-2-pyrrolecarboxylate[3] as its sodium salt was N-methylated with methyl iodide in ethanol to give 89% ethyl 1-methyl-4-nitro-2-pyrrolecarboxylate (I), m.p. 113–114°. *Anal.* C, 48.2; H, 5.06; N, 14.0. Catalytic reduction of I gave 90% ethyl 4-amino-1-methyl-2-pyrrolecarboxylate (II) isolated as a $^1/_2H_2SO_4 \cdot {}^3/_4H_2O$ salt, m.p. 185° dec. *Anal.* C, 41.6; H, 5.77; N, 12.1; S, 7.00; H_2O, 5.64. Hydrolysis of II with aqueous barium hydroxide gave 61% 4-amino-1-methyl-2-pyrrolecarboxylic acid (III) isolated as the $^1/_2H_2SO_4 \cdot {}^1/_2H_2O$ salt, m.p. 202° dec. *Anal.* C, 36.1; H, 5.53; N, 14.1; S, 8.22.

The tripeptide VIII was synthesized by the following sequence. Alkaline hydrolysis of I gave 82% of the corresponding acid (IV), m.p. 195–197°. *Anal.* C, 42.0; H, 3.38; N, 16.6. By heating with excess thionyl chloride IV was converted to the acid chloride (V) which, without purification, was treated with β-alanine in sodium bicarbonate solution to yield 78% β-(1-methyl-4-nitro-2-pyrrolecarboxamido)-propionic acid (VI), m.p. 180–183°. *Anal.* C, 45.3; H, 4.85; N, 17.2. Catalytic reduction of VI as the sodium salt in aqueous solution gave the corresponding 4-amino compound which without isolation was condensed with the acid chloride V to give 57% (based on VI) β-[1-methyl-4-(1-methyl-4-nitro-2-pyrrolecarboxamido)-2-pyrrolecarboxamido]-propionic acid (VII), m.p. 250.5–251.5° dec. *Anal.* C, 49.4; H, 4.48; N, 19.7. Catalytic reduction of VII gave in good yield β-[4-(4-amino-1-methyl-2-pyrrolecarboxamido)-1-methyl-2-pyrrolecarboxamido]-propionic acid (VIII), isolated as the sesquihydrate, m.p. 235° dec. *Anal.* C, 50.3; H, 6.07; N, 19.9.

The third degradation product (X) was synthesized by treating the mixed carbonic anhydride[4] of VII in dimethylformamide solution with ammonia to give 70% β-[1-methyl-4-(1-methyl-4-nitro-2-pyrrolecarboxamido)-2-pyrrolecarboxamido]-propionamide (IX), m.p. 259–260° dec. *Anal.* C, 49.4; H, 4.61; N, 22.9. Hydrogenation of IX in dimethylformamide solution with palladium on carbon catalyst gave 82% β-[4-(4-amino-1-methyl-2-pyrrolecarboxamido)-1-methyl-2-pyrrolecarboxamido]-propionamide (X), m.p. 247–248° dec. *Anal.* C, 54.3; H, 6.09; N, 25.1.

Finally, synthesis of XI was accomplished by condensing X with guanidinoacetic acid originally by the mixed carbonic anhydride procedure,[4] which gave XI in 10% yield and later by the dicyclohexylcarbodiimide method[5] which afforded a 30% yield of the same product.[6] In both cases the material isolated was the $^1/_2H_2SO_4 \cdot H_2O$ salt of β-[4-(4-guanidinoacetamido-1-methyl-2-pyrrolecarboxamido)-1-methyl-2-pyrrolecarboxamido]-propionamide (XI), m.p. 191–194° dec. *Anal.* C, 42.6; H, 5.41; N, 25.6; O, 22.4; S, 3.10.

We have just been informed that U. S. Patent 2,785,182 which covers compound XI above and was applied for on April 19, 1944, will be issued to C. W. Waller, M. J. Weiss and J. S. Webb on March 12, 1957.

(1) C. W. Waller, C. F. Wolf, W. J. Stein and B. L. Hutchings, THIS JOURNAL, **79**, 1265 (1957).

(2) Netropsin is the trademark of Chas. Pfizer and Co. for the antibiotic produced by *Streptomyces netropsis*. Structural studies on this antibiotic have been reported by Finlay and co-workers [*ibid.*, **73**, 341 (1951)] and by van Tamelen and co-workers [*ibid.*, **78**, 2157 (1956)]. Recently Watanabe [*J. Antibiotics* (A) **IX**, 102 (1956)] reported the antibiotic sinanomycin and Julia and Joseph [*Compt. rend.*, **243**, 961 (1956)] reported congocidine. Both these groups considered their antibiotics to be at least very similar to, if not identical with Netropsin.

(3) W. J. Hale and W. V. Hoyt, THIS JOURNAL, **37**, 2538 (1915).

(4) See J. R. Vaughan, Jr., *ibid.*, **73**, 3547 (1951).

(5) See J. C. Sheehan and G. P. Hess, *ibid.*, **77**, 1067 (1955).

(6) This latter preparation was carried out by Dr. A. S. Tomcufcik of these Laboratories.

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