Structure proof was provided by converting IV to 3,20-diketo-4-pregnen-18-oic acid (V) by hydrolysis in 60% sulfuric acid. A base-soluble product thus obtained was identical in melting point, paper-chromatographic migration rate and infrared spectrum with a genuine sample obtained from conessine.[4]

(4) R. Pappo, THIS JOURNAL, **81**, 1011 (1959). We wish to thank Dr. Pappo for his kindness in providing us with the comparison sample.

SCHERING CORPORATION
BLOOMFIELD, NEW JERSEY
A. L. NUSSBAUM
F. E. CARLON
E. P. OLIVETO
E. TOWNLEY
P. KABASAKALIAN

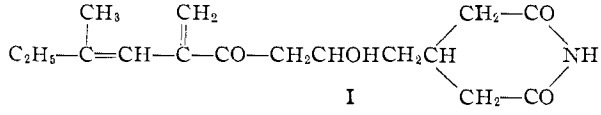
RESEARCH INSTITUTE FOR MEDICINE AND CHEMISTRY
49 AMHERST STREET
CAMBRIDGE, MASSACHUSETTS
D. H. R. BARTON

RECEIVED APRIL 29, 1960

STRUCTURE OF THE ANTIBIOTIC STREPTIMIDONE

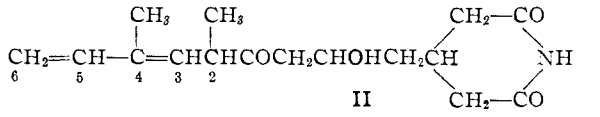
Sir:

Recently structure I was proposed for a new



I

Streptomyces antibiotic, streptimidone.[1] It appeared to us that certain of the recorded properties, in particular the base-catalyzed conversion of the existing chromophore to a 2,4-dienone system, could be better interpreted in terms of an alternative, II. We have now found that, by employing



II

nuclear magnetic resonance data, a clear decision in favor of the latter possibility can be made.

The n.m.r. spectrum[2] of O-acetylstreptimidone[3] displays the following major absorptions, due to hydrogens of the type indicated: (a) −106 (imide); (*b*) *ca.* −25 to +75 (olefinic, and acetoxyl methine); (c) *ca.* +100 to +175 (saturated methine and methylene); (d) +178 and +186 (4- and acetyl methyls), (e) +214 (2-methyl). The hydrogen peak ratio (1:5) of (a) to (b) supports formulation II, but not I. Furthermore, proposal I predicts essentially a simple three peak pattern in region (b), whereas that area features in fact an irregular quadruplet centered at about 0 (one hydrogen), and broadened doublets at about +45 and +62 (four hydrogens). This absorption character corresponds to a superimposition of an "AB" (2- and 3-hydrogens) upon an "ABX" (5- and 6-hydrogens) pattern,[4] and corresponds well to that exhibited by isoprene,[5] a close model for the unsaturated portion of II. Finally, the C-methyl group designated as (e) is split, as required, by the methine hydrogen at position 2; structure I, on the other hand, bears a methyl group in the ethyl unit, and would have given rise to a triplet in (e).

The ultraviolet spectrum (λ_{Max}^{MeOH} 232 and 291 mμ, ϵ 23,100 and 790)[1] and infrared absorption *in solution (inter alia,* 5.8 μ, ketone –CO–; 5.9 μ, imide –CO–; 6.0 (w) and 6.1 (w), diene)[1] are consistent with the revised structure, II. This formula is also compatible with the recorded chemical behavior,[1,6] and has been confirmed by additional chemical findings obtained more recently in the laboratories of the Research Division of Parke, Davis and Company.[7]

(5) Pople, Schneider and Bernstein, *ibid.*, p. 244.

(6) The positive *m*-phenylenediamine test for an α,β-unsaturated ketone is regarded as due to either prior isomerization of II to a conjugated ketone system, or to dehydration of the aldol moiety.

(7) Re-examination of the ozonolysis of streptimidone has revealed that formaldehyde and pyruvaldehyde are the end products, not formaldehyde and methyl ethyl ketone as reported previously (ref. 1). The latter ketone originated as an impurity in the reagent ethyl acetate (distilled from 2,4-dinitrophenylhydrazine) which was used as a solvent in the isolation procedure (personal communication from H. W. Dion, Parke, Davis and Company).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN
E. E. VAN TAMELEN
V. HAARSTAD

RECEIVED APRIL 8, 1960

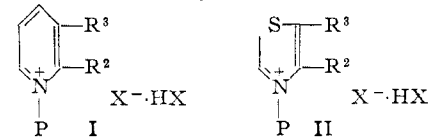
ANTIPARASITIC DRUGS. III. THIAMINE-REVERSIBLE COCCIDIOSTATS

Sir:

We have found that many 1-(2-alkyl-4-amino-5-pyrimidinylmethyl)-alkylpyridinium salts possess marked prophylactic activity in coccidiosis, a protozoan disease of importance in poultry production. Analogous 3-thiazolium compounds are also effective.

The new anticoccidial agents are related structurally to thiamine (II: R^1 and R^2, CH_3, R^3, CH_2CH_2OH) and function by a reversible thiamine inhibition mechanism. These quaternaries, administered in feed, are selectively effective against coccidia of the digestive tract and make possible adequate disease prevention without adverse effect upon the growth of chickens. Another relative of the new coccidiostats is the thiamine antagonist pyrithiamine (neopyrithiamine, I: R^1 and R^2, CH_3, R^3, CH_2CH_2OH).[1]

Compounds of types I and II are made by reaction of 2-alkyl-4-amino-5-pyrimidinylmethyl halide



P is 2-R′-4-amino-5-pyrimidinylmethyl

dihydrohalide with excess pyridine or thiazole base in acetonitrile or other solvents. The synthesis of the 2-methylpyrimidine intermediate has been described by Grewe.[2] Data on typical quaternaries are given in Table I.

(1) A. H. Tracy and R. C. Elderfield, *J. Org. Chem.*, **6**, 54 (1941); A. N. Wilson and S. A. Harris, THIS JOURNAL, **71**, 2231 (1949).

(2) R. Grewe, *Naturwiss.*, **24**, 657 (1936); *Z. physiol. Chem.*, **242**, 89 (1936).

(3) We wish to thank Dr. Q. R. Bartz (Parke, Davis and Company) for his coöperation, especially for his kindness in supplying a sample of the derivative used in this investigation.

(4) Pople, Schneider and Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., New York, N. Y., 1959, p. 132.

(5) Obtained in $CDCl_3$ solution with a Varian Associates instrument operating at 40 mc. Chemical shifts given in cps. relative to benzene = 0.

(6) R. P. Frohardt, H. W. Dion, Z. L. Jakubowski, A. Ryder, J. C. French and Q. R. Bartz, THIS JOURNAL, **81**, 5500 (1959).