COMMUNICATIONS TO THE EDITOR

TETRACYCLINE[1]

Sir:

During catalytic reduction studies on chlorotetracycline (Aureomycin) using a platinum catalyst it was noted that the mixture of compounds obtained showed a low chlorine content. Since dechlorination was occurring under these conditions, chlorotetracycline was then subjected to catalytic reductions more favorable to selective removal of an aromatic halogen.

Chlorotetracycline was found to be reductively dehalogenated at room temperature and atmospheric pressure in the presence of 10% palladium on charcoal catalyst and one mole of triethylamine. Slightly over one mole of hydrogen was absorbed in 15–20 minutes using about 100 mg. of chlorotetracycline/cc. in methyl cellosolve. Some heat is produced during this rapid hydrogenolysis and the uptake of hydrogen practically stops after one mole is absorbed.

After the catalyst is removed the filtrate is poured into 5 volumes of water and the free base of tetracycline crystallizes. This product which occurs as a trihydrate can be recrystallized from methanol and water. The anhydrous form can be obtained by drying at 60° *in vacuo* for 8 hours. Either form begins to swell at 165–170° melting with decomposition at 170–173°.

Anal. Calcd. for $C_{22}H_{24}O_8N_2 \cdot 3H_2O$: C, 53.0; H, 6.0; N, 5.6; H_2O, 10.8. Found: C, 52.9; H, 6.2; N, 5.5; H_2O, 10.9.

Tetracycline base dissolved in *n*-butanol by adding hydrochloric acid crystallizes from this solution as a hydrochloride; m.p., darkens gradually and melts with gas at about 214°; $[\alpha]^{25}D$ − 257.9° (0.5% in 0.1 *N* hydrochloric acid).

Anal. Calcd. for $C_{22}H_{24}O_8N_2 \cdot HCl$: C, 55.0; H, 5.2; N, 5.8; Cl, 7.4. Found: C, 54.9; H, 5.3; N, 5.8; Cl, 7.3.

The ultraviolet absorption spectrum in 0.1 *N* hydrochloric acid shows maxima at 220 mμ (ε, 13,000), 268 mμ (ε, 18,040), and 355 mμ (ε, 13,320).

Treatment of tetracycline with hydrochloric acid gives anhydrotetracycline completely identical with that prepared from chlorotetracycline by treatment with hydriodic acid.[2] This would indicate that no structural changes other than removal of the halogen took place during the reduction.

Tetracycline is a potent antibiotic having an antibiotic spectrum very similar to chlorotetracycline. The former compound exhibits increased stability in neutral or alkaline solution.

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Received August 6, 1953

(1) The use of this name as a generic term is discussed in This Journal, **74**, 4976 (1952).

(2) C. W. Waller, *et al.*, *ibid.*, **74**, 4981 (1952).

IDENTIFICATION OF AN ANTIBIOTIC POLYACETYLENE FROM *CLITOCYBE DIATRETA* AS A SUBERAMIC ACID ENE-DIYNE*

Sir:

The presence of two antibiotic polyacetylenes in culture liquids of the Basidiomycete *Clitocybe diatreta* was reported recently.[1] For one of these, which was obtained crystalline, the tentative formula $C_{17}H_{12}N_2O_6$ was suggested. Analysis of a fresh sample, however, indicates the formula $C_8H_5NO_3$ rather than that above. The compound can be purified by recrystallization from methanol. It does not melt, but explodes at 198° (uncor.). Found: C, 59.01; H, 3.15; O, 29.34; N, 8.42; mol. wt. (ebullioscopic), 159 (neut. eq., 170, from the previous analysis). Calcd. for $C_8H_8NO_3$ (163.13): C, 58.90; H, 3.09; O, 29.42; N, 8.59; mol. wt., 163. The new formula was further supported by analysis of the catalytic reduction product, the values for which agreed with the formula $C_8H_{15}NO_3$. This compound is a colorless crystalline solid, m.p. 144–145° (uncor). Found: C, 55.51; H, 8.77; N, 8.05. Calcd. for $C_8H_{15}NO_3$ (173.21): C, 55.48; H, 8.73; N, 8.09.

The above data, taken in conjunction with the ultraviolet absorption spectrum (Fig. 1) point to an octadioic acid monoamide containing an ene-diyne grouping, as the probable structure of the polyacetylene. Thus, the ultraviolet absorption maxima are close to those exhibited by the lachnophyllum esters,[2,3,4] compounds of known structure containing an ene-diyne system conjugated to an (esterified) carboxyl group. The remaining CH_2-NO indicated by the analysis is most readily accounted for as an amide group.

The reduction product of the antibiotic compound was identified as suberamic acid, the product to be expected on reduction of a polyacetylene of the proposed structure. To establish identity it was necessary to prepare an authentic sample of suberamic acid, since the only literature reference found to the compound is in a paper by Étaix,[5] who reports a melting point of 125–127°. Monomethyl suberate, obtained by the method of Hunsdiecker and Hunsdiecker[6] for the partial esterification of some dibasic acids, was converted to the amide by the method used by Jeffery and Vogel[7] for the preparation of some -amic acids (not including suberamic). The amide melted at 144–145° (uncor.) and gave no depression with the reduction product of the polyacetylene. Found: C, 55.57; H, 8.80; N, 8.02. Calcd. for suberamic acid, $C_8H_{15}NO_3$ (173.21): C, 55.48, H, 8.73; N, 8.09. Further proof of identity of the reduction product

(1) M. Anchel, This Journal, **74**, 1588 (1952).

(2) N. A. Sörensen and K. Stavholt, *Acta. Chem. Scand.*, **4**, 1575 (1950).

(3) T. Bruun, C. M. Haug and N. A. Sörensen, *ibid.*, **4**, 850 (1950).

(4) W. W. Wiljams, V. S. Smirnov and V. P. Goljmov, *J. Gen. Chem. (U.S.S.R.)*, **5**, 1195 (1935).

(5) L. Étaix, *Ann. chim. phys.*, [7] **9**, 356 (1896).

(6) H. Hunsdiecker and C. Hunsdiecker, *Ber.*, **75**, 291 (1942).

(7) G. H. Jeffery and A. I. Vogel, *J. Chem. Soc.*, 1101 (1934).