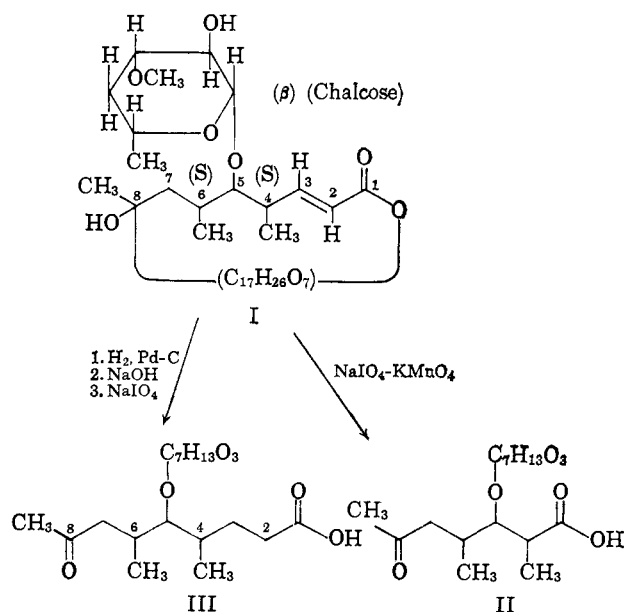


### Partial Structure of Chalcomycin. I. A C<sub>18</sub> Chalcosyloxy Moiety

Sir:

Previous communications have reported that acid degradation of the antibiotic chalcomycin<sup>1</sup> (I) yields chalcose<sup>2</sup> (4,6-dideoxy-3-*O*-methyl-*D*-glucose) and mycinose<sup>3</sup> (6-deoxy-2,3-di-*O*-methyl-*D*-allose), and that periodate-permanganate oxidation gives 2,4-dimethyl-3-chalcosyloxy-6-oxoheptanoic acid (II).<sup>4</sup> We now wish to present evidence which assigns the partial structure I to chalcomycin.



One of the possible formulas, C<sub>35</sub>H<sub>56</sub>O<sub>14</sub> (mol. wt. 700.8), is compatible with elemental analyses (*Anal.* Calcd.: C, 59.98; H, 8.06. Found: C, 59.84; H, 8.06) and molecular weight determinations (X-ray crystallography, mol. wt.<sup>5</sup> 701 ± 7; osmometric determinations, 725 ± 15 (butyl acetate) and 716 ± 14 (benzene); isothermal distillation (methanol), 575–592) of chalcomycin. This formula is also compatible with the elemental analyses of several derivatives and degradation products of chalcomycin.

The presence of an  $\alpha,\beta$ -unsaturated lactone (or ester) in chalcomycin (I) is indicated by its ultraviolet spectrum ( $\lambda_{\max}^{\text{EtOH}}$  218 m $\mu$  ( $\epsilon$  22,770)) and infrared absorption peaks (5.84, 6.03  $\mu$ ). The infrared peaks remained essentially unchanged by sodium borohydride reduction (5.84, 6.05  $\mu$ ), but were replaced by a single peak (5.80  $\mu$ ) upon hydrogenation (Pt, acetic acid). The n.m.r. spectrum of I in deuteriochloroform indicates the presence of a proton on C-2 coupled to a proton on C-3,  $J_{2,3} = 15.6$  c.p.s., typical of a *trans* olefinic function.<sup>6</sup>

(1) Parke, Davis & Company, Belgian Patent 587,213 (Aug. 2, 1960)

(2) (a) P. W. K. Woo, H. W. Dion, and Q. R. Bartz, *J. Am. Chem. Soc.*, **83**, 3352 (1961); (b) P. W. K. Woo, H. W. Dion, and L. F. Johnson, *ibid.*, **84**, 1066 (1962); (c) N. K. Kochetkov and A. I. Usov, *Tetrahedron Letters*, No. 8, 519 (1963).

(3) (a) H. W. Dion, P. W. K. Woo, and Q. R. Bartz, *J. Am. Chem. Soc.*, **84**, 880 (1962); (b) J. S. Brimacombe, M. Stacey, and L. C. N. Tucker, *Proc. Chem. Soc.*, 83 (1964).

(4) P. W. K. Woo, H. W. Dion, and Q. R. Bartz, *J. Am. Chem. Soc.*, **84**, 1512 (1962).

(5) We thank Mr. J. Krc and Mr. B. Scott, Parke, Davis & Company, for this determination.

(6) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 85.

The C-3 proton appears as a quartet, indicating the presence of a single proton on C-4,  $J_{3,4} = 9.8$  c.p.s. Spin-decoupling studies<sup>7,8</sup> verify these assignments and further indicate that the C-4 proton appears at  $\delta$  2.68, as expected from a methinyl proton. The C-2 proton doublet and the C-3 proton quartet are also shown by the sodium borohydride reduction product of I.

Hydrogenation of I (Pd-C, ethanol) followed by saponification and subsequent periodate oxidation yielded, as one of the major products, a C<sub>18</sub> acid (III). Acid III remained oily after purification by counter-current distribution (200 transfers,  $K = 1$  in chloroform-water system) but gave good analyses for C<sub>18</sub>H<sub>32</sub>O<sub>7</sub> (*Anal.* Calcd.: C, 59.97; H, 8.95. Found: C, 59.82; H, 9.26). The n.m.r. spectrum of III in deuteriochloroform indicates the presence of three C-methyl doublets, one methyl ketone singlet, and one O-methyl singlet. Oxidation of III with sodium hypiodite gave iodoform and a diacid IV (infrared peak at 5.85  $\mu$ ); acid hydrolysis of IV yielded chalcose and a  $\gamma$ -lactonic acid V (infrared peaks at 5.66, 5.83  $\mu$ ). On the other hand, acid hydrolysis of III did not give a  $\gamma$ -lactone (5.82  $\mu$ ). Hence chalcose is  $\gamma$ - to the methyl ketone group in III, and the established structure of II<sup>4</sup> allows assignment of partial structure from C-4 to C-9 of III.

Nitric acid oxidation of III yielded (+)-2-methylglutaric acid<sup>9</sup> (identified by comparison of infrared and n.m.r. spectra, melting point, and optical rotation with authentic (-)-2-methylglutaric acid and by elemental analyses), which established the partial structure of III from C-1 to C-4. The known absolute configuration of (+)-2-methylglutaric acid shows that the absolute configuration at C-4 in III is *S*.<sup>10</sup> The previously reported isolation of (+)-2,4-dimethylpentane-1,3,5-triol<sup>4</sup> from C-1 to C-5 of II reveals the relative configuration of the two asymmetric carbons corresponding to C-4 and C-6 of III, and thus establishes the configuration at C-6 in III as *S*.

The C-1 anomeric proton of chalcose shows large coupling with the C-2 proton ( $J = 7.4$  c.p.s. in II;  $J = 7.1$  c.p.s. in III), indicative of a diaxial coupling and hence a  $\beta$ -glycosidic configuration.<sup>2b</sup>

Thus, the structure of III is 4,6-dimethyl-5- $\beta$ -chalcosyloxy-8-oxononanoic acid and allows the structural assignment of C-1 to C-8 in chalcomycin.

(7) (a) W. A. Anderson and R. Freeman, *J. Chem. Phys.*, **37**, 85 (1962);

(b) J. D. Baldeschwieler and E. W. Randall, *Chem. Rev.*, **63**, 81 (1963).

(8) We thank Dr. L. Durham, Stanford University, for the spin-decoupling studies.

(9) (a) E. J. Eisenbraun and S. M. McElvain, *J. Am. Chem. Soc.*, **77**, 3383 (1955); (b) A. Fredga, *Arkiv. Kemi, Mineral. Geol.*, **24A**, No. 32 (1947); (c) K. Freudenberg and W. Hohmann, *Ann.*, **584**, 54 (1953); (d) J. F. Lane, *Science*, **113**, 577 (1951).

(10) R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

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### Partial Structure of Chalcomycin. II. A C<sub>17</sub> Mycinosyloxy Moiety

Sir:

In the preceding communication,<sup>1</sup> the structure and partial configuration of a C<sub>18</sub> chalcosyloxy moiety in

(1) P. W. K. Woo, H. W. Dion, and Q. R. Bartz, *J. Am. Chem. Soc.*, **86**, 2724 (1964).