Structure and Absolute Stereochemistry of Evermicose[1]

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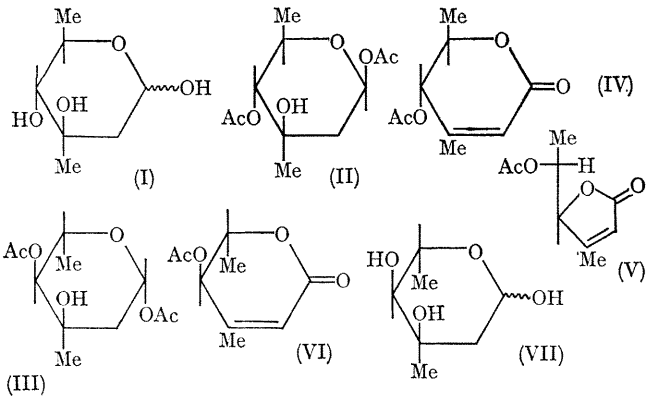
Summary Evermicose, an hydrolysis product of everninomicin B and D, has been shown to be 3-*C*-methyl-2,6-dideoxy-D-arabinohexose, or D-3-epimycarose.

EVERMICOSE was obtained from everninomicin B and D[2] on hydrolysis with aqueous acid, followed by chromatography of the resulting product mixture on silica gel. Evermicose (I), $C_7H_{14}O_4$,† crystallized from acetone as colourless needles, m.p. 108—112°, $[\alpha]_D$ + 20·7° (water, 24 hr.). It had no selective absorption in the u.v. above 210 nm, and in the infrared it did not show the presence of any carbonyl group. Evermicose formed a diacetate (II), $C_{11}H_{18}O_6$, which

† Satisfactory elementary analyses were obtained for all new compounds; i.r. spectra were recorded in $CHCl_3$ unless otherwise noted; n.m.r. spectra were taken at 60 Mc. sec. in $CDCl_3$ with internal Me_4Si standard; optical rotations were measured in $CHCl_3$ at 25° unless otherwise noted, and the u.v. spectra were in MeOH.

crystallized from ether–hexane as colourless needles m.p. 73°, $[\alpha]_D$ + 39·5°, ν_{max} 1740 cm.$^{-1}$; n.m.r. methyl δ 1·2 (secondary CH_3; J = 6 c./sec.), 1·3 (tertiary CH_3) 2·1 and 2·13 (2CO·CH_3), 4·6 (d, 1H, J = 10 c./sec.), (octet, 1H, J = 10 c./sec. and 6 c./sec.), 5·75 (quartet, 1H, J_{aa} = 9 c./sec.; J_{ae} = 3 c./sec.) and 2·6 p.p.m. (br s, O*H*, exchangeable). From this data, evermicose is 3-epimycarose. This was further substantiated when the n.m.r. spectrum of L-mycarose diacetate (III) was compared with that of the diacetate (II). As predicted by Lemieux and Stevens[3] 1-H and 5-H were deshielded in (III) by the axial hydroxy-group at C-3 and appeared at δ 6·07 and 4·01 p.p.m., respectively. Another feature of interest is the shift of the 3-CH_3 signal from δ 1·3 in (II) to 1·18 p.p.m. in (III).

To prove the gross structure of evermicose (I) and its absolute stereochemistry unequivocally, we have converted evermicose into (IV). Evermicose on oxidation with bromine water yielded a mixture of γ- and δ-lactones (i.r.) which was directly acetylated, and the acetate dehydrated[1] by refluxing in benzene solution in the presence of toluene-*p*-sulphonic acid to a mixture of (IV) and (V). This mixture was separated using preparative t.l.c. The α,β-unsaturated



δ-lactone (IV) sublimed at 60°/0·5 mm. as a colourless liquid $C_9H_{12}O_4$, ν_{max} 1720 cm.$^{-1}$, no hydroxy-group, λ_{max} 211 nm. (13150), $[\alpha]_D$ + 97·8°; n.m.r. δ 1·4 (secondary CH_3, J = 6·5 c./sec.), 1·95 (vinyl CH_3), 2·1 (CO·CH_3), 4·5 (quintet, 1H, J = 6·5 c./sec.), 5·31 (d, 1H, J = 6·5 c./sec.) and 5·91 p.p.m. (t,C=C-*H*). Compound (V) sublimed at 40°/0·5 mm. as a colourless liquid, $C_9H_{12}O_4$, ν_{max} 1760, 1730 cm.$^{-1}$, no hydroxy-group, λ_{max} 211 nm. (12000), $[\alpha]_D$ + 43·6°; n.m.r. ($CHCl_3$) δ 1·13 (d, 3H, J = 6·5 c./sec.), 2·08 (6H) δ 5—5·55 (m, 2H) and 5·88 p.p.m. (q, 1H): n.m.r. (C_6H_6) showed rather remarkable shifts, *e.g.*, δ 0·8 (d, 3H, J = 6·5 c./sec.; 5-CH_3), 1·2 (quartet, 3H, vinyl CH_3 at C-3), 1·66 (s, 3H, CO·CH_3), δ 4·47 (m, 1H, 4-H), 4·86 (octet, 1H, J = 6·5 c./sec. and 3 c./sec.), and 5·31 p.p.m. (quintet, 1H). The above spectrum revealed that 2-H, 4-H, and vinyl methyl protons were mutually coupled with small coupling constants. Formation of (IV) and (V) from evermicose (I) in contrast with the formation of only (VI) from L-mycarose confirms the previous suggestion[4] that in the furanoside derived from mycarose there exists serious repulsion between the *cis* disposed 3-methyl group and 4α-hydroxyethyl function whereas in the furanoside derived from evermicose the α-hydroxyethyl group is nicely positioned with the 3-OH for hydrogen bond formation.

Starting from L-myacrose (VII) and following the above series of reactions described previously for evermicose, *i.e.* (*a*) oxidation; (b) acetylation and (c) dehydration, we have prepared compound (VI) and shown it to be identical with compound (IV) [t.l.c., i.r., u.v., n.m.r.] excepting that it had $[\alpha]_D$ − 99·8°, *cf.* $[\alpha]_D$ + 97·8° for (IV), thus proving conclusively that evermicose (I) is 3-*C*-methyl-2,6-dideoxy-D-arabinohexose, or D-3-epimycarose.

(±)-3-Epimycarose has been obtained[4] as a by-product during the synthesis of L-mycarose. T.l.c. behaviour of evermicose and (±)-3-epimycarose was identical.

We thank Professor H. Grisebach, University of Freiburg, for a sample of (±)-3-epimycarose.

(*Received, August 14th*, 1969; *Com.* 1251.)

[1] Part of the series, The Chemistry of Everninomicin Antibiotics; for previous part, see A. K. Ganguly, Olga Z. Sarre, and Hans Reimann, *J. Amer. Chem. Soc.*, 1968, **90**, 7129.

[2] (a) H. L. Herzog, E. Meseck, S. DeLorenzo, A. Murawski, W. Charney, and J. P. Roselet, *Appl. Microbiol.*, 1965, **13**, 515; (b) M. Weinstein, G. M. Luedemann, E. M. Oden, and G. H. Wagman, "Antimicrobial Agents and Chemotherapy—1964", American Society for Microbiology, Ann Arbor, Michigan, 1965, p. 24.

[3] R. V. Lemieux and J. D. Stevens, *Canad. J. Chem.*, 1965, **43**, 2059.

[4] D. M. Lemal, P. D. Pacht, and R. B. Woodward, *Tetrahedron*, 1962, **18**, 1275.