THE CHEMISTRY OF THE EVERNINOMICIN ANTIBIOTICS. II.

THE STRUCTURE OF EVERNINOCIN AND ITS IDENTIFICATION WITH CURACIN

HANS REIMANN, ROBERT S. JARET and OLGA Z. SARRE

Natural Products Research Department
Schering Corporation, Bloomfield,
New Jersey 07003, U. S. A.

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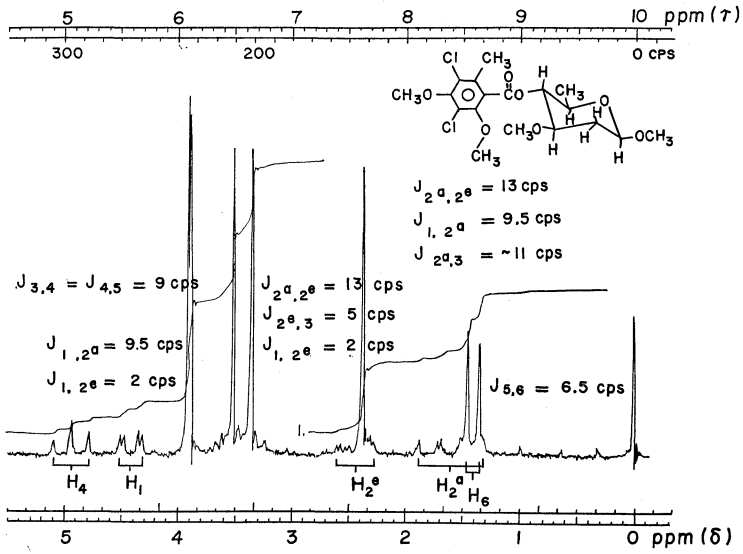
The production, isolation and preliminary chemical characterization of two new closely related antibiotics, everninomicins B and D, was described in earlier publications from these laboratories[1,2]. We now report the complete structure of everninocin, I, the carbohydrate ester end group isolated from both of these antibiotics by acid hydrolysis[2] and its identification with curacin[3b,6,7].

Methylation of everninocin with methyl iodide and silver oxide in dimethylformamide afforded tri-O-methyleverninocin as an oily anomeric mixture. Chromatography of the mixture on silica gel gave a pure crystalline anomer*, II, mp 105~106°C; $[\alpha]_D$ −22° (pyridine); λ_{max}^{MeOH} 283 mμ (ε 560); $\lambda\lambda^{Nujol}$ 5.72, 6.33, 7.9 μ. The nmr spectrum** of II (Fig. 1) showed bands at 1.41 (d., $C^6\underline{H}_3$), ~1.60 (oct., $C^2\underline{H}^a$), 2.37 (s., $ArC\underline{H}_3$), ~2.44 (oct., $C^2\underline{H}^e$), 3.35 (s., $C^1OC\underline{H}_3$), 3.51 (s., $C^3OC\underline{H}_3$), 3.89 (s., $ArOC\underline{H}_3$), 3.90 (s., $ArOC\underline{H}_3$), 4.40 (q., $C^1\underline{H}$) and 4.94 (t., $C^4\underline{H}$). The multiplets for the protons at C^3 and C^5 were superimposed on the aliphatic methoxyl groups, but the axial positions of these protons were evident from their couplings with adjacent protons.

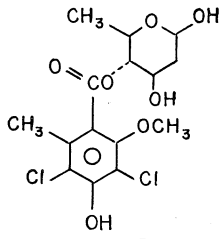
Compound II was subjected to vigorous hydrolysis with potassium hydroxide in aqueous ethanol; affording O-methyldichloroisoeverninic acid[3], mp 136~137°C and methyl β-D-oleandroside, III, mp 79~80°C; $[\alpha]_D$ −82° (EtOH); nmr 1.35 (d., $C^6\underline{H}_3$, J= 5.5 cps), ~1.41 (mult., $C^2\underline{H}^a$), ~2.34 (mult., $C^2\underline{H}^e$), 3.40 (s., $C^1OC\underline{H}_3$), 3.50 (s., $C^3OC\underline{H}_3$) and 4.39 (q., $C^1\underline{H}$, Jaa=9.5, Jae=2 cps). Mild acid hydrolysis of III yielded D-oleandrose, IV, as an oil which did not crystallize in our hands, $[\alpha]_D$ −9.3→−9.5° (H_2O, 24 hrs); reported[4] $[\alpha]_D$ −12° (H_2O). For comparison purposes, L-oleandrose was prepared by hydrolysis of a sample of oleando-

Fig. 1.

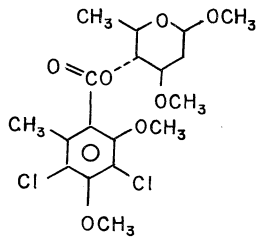


* Satisfactory elemental analyses were obtained for new compounds.

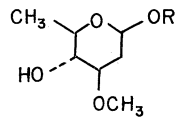
** NMR spectra were recorded on a Varian A-60 A instrument in $CDCl_3$ solution under the direction of Mr. M. YUDIS. Chemical shifts are recorded in ppm downfield from TMS as internal standard. We thank Mr. Yudis for helpful advise in the interpretation of the spectra.



I



II



III R = CH_3

IV R = H

mycin[5]. The sugar, which was also obtained as an oil, showed $[\alpha]_D$ +9.2→+8.7° (H_2O, 24 hrs).

The above sequence of reactions establishes the full structure of everninocin, I, as 4-O-dichloroisoeverninyl-2,6-dideoxy-D-arabino-hexose, Very recently the structure of curacin, a hydrolysis product of curamycin[3b] and avilamycin[6], was determined[6,7]. The structure of curacin is identical to that of everninocin as reported here. Avilamycin, curamycin and the everninomicins thus belong to a distinctive group of polysaccharide antibiotics bearing a curacin end group. A significant difference in the everninomicins, however, is the presence of a nitrogen containing fragment in the molecule[8].

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