STRUCTURE OF EVERNINOMICIN C

Sir:

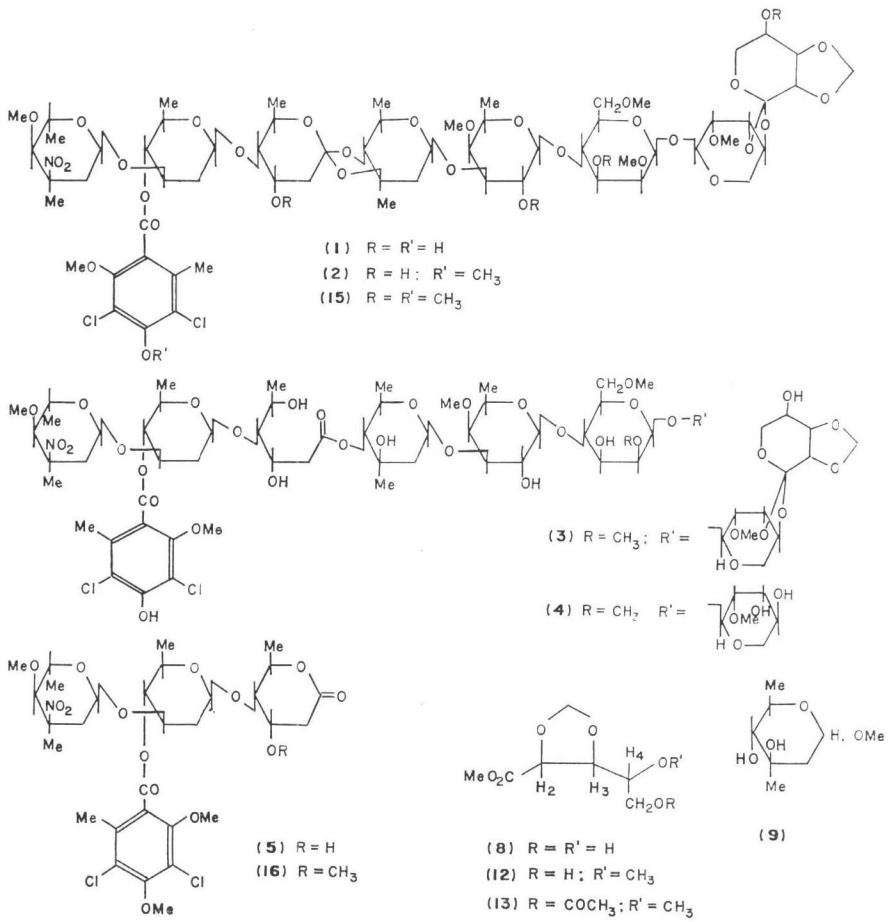
Everninomicin antibiotics are produced[1] by *Micromonospora carbonaceae*. We report here the structure of everninomicin C.

Everninomicin C (1) is a colourless crystalline solid, $C_{63}H_{93}NO_{34}Cl_2$,* m.p. 181~184°C, $[\alpha]_D$—33.7°, ν max 1538 (nitro), 1730 cm^{-1} (carbonyl); the nitro absorption was stronger than the carbonyl absorption. On methylation with diazomethane everninomicin C formed a monomethyl ether (2), $C_{64}H_{95}NO_{35}Cl_2$, m.p. 184~188°C, $[\alpha]_D$—30.8°. The molecular weight of 2 was determined to be 1493 (calc. for $C_{64}H_{95}NO_{35}Cl_2$ is 1528) by the application of the radioactive method described by us earlier.[2]

Everninomicin C on hydrolysis (two phase with aqueous acid) yielded everninomicin C_1 (**3**), $C_{63}H_{95}NO_{35}Cl_2$, $[\alpha]_D$—41.0, ν max 1538, 1730 cm^{-1}. As in everheptose[3] (**4**) the carbonyl absorption in **3** was stronger than the nitro absorption. On treatment with diazomethane **3** underwent smooth cleavage to **5**[3] and olgose C (**6**).

Olgose C (**6**) is a colourless crystalline solid, $C_{34}H_{56}O_{21}$, m.p. 196~198°C, $[\alpha]_D$—16.9°. It does not show absorption for carbonyl group in the ir. On solvolysis** with methanolic *p*-toluene sulphonic acid **6** yielded evertetrose[4] (**7**) and compound **8** which could not be obtained pure because it co-chromatographed with methyl glycoside of evermicose[5] (**9**).

Permethylated olgose-C (**10**) is a crystalline solid, $C_{39}H_{66}O_{21}$ (M^+ 870), m.p. 197~199°C,



* Satisfactory analyses were obtained for all new compounds.

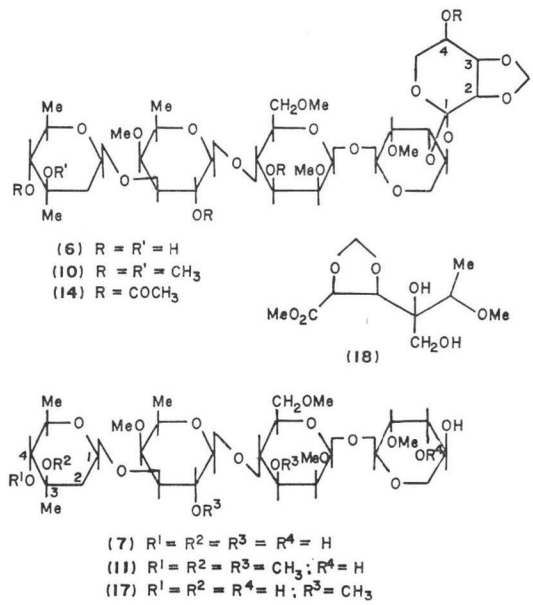
** Solvolysis in this communication refers to treatment of the compound with methanolic *p*-toluene sulphonic acid.

$[\alpha]_D$ −8.7°, no hydroxyl or carbonyl absorption in the ir. On solvolysis compound **10** yielded **11**[6] and **12**. Compound **12** distills at RT/0.5 mm Hg, $C_8H_{14}O_6$ (M^+ 206), ν max 3450 and 1754 cm^{-1}, δ 3.52, 3.81 (3H each, s; $-OCH_3$ and $-COOCH_3$), 3.49 (1H; m; H_3), 4.60 (1H, d, J 4.5 Hz, H_1), 4.25 (1H, t, J 4.5 Hz; H_2), 5.03, 5.20 (1H each, $-O-CH_2-O$)[6]. On acetylation compound **12** yielded a colourless liquid **13** $C_{10}H_{16}O_7$ (M^+ 248), no hydroxyl absorption in the ir. In the nmr spectrum, compound **13** besides showing all the features of **12** showed the presence of $-CH_2-OCOCH_3$ grouping, δ 2.1 (3H, s, $-OCOCH_3$), 4.12, 4.47 (1H each; dd; J 4 and 11.5 Hz).

Based on the aforementioned observations we propose structure **6** for olgose C and **10** for permethylated olgose C. The formation of **11** and **12** on solvolysis of **10** is then easily explained by the opening of the ortho ester function. The relative stereochemistry of H_1 and H_2 and H_3 in olgose C is deduced in the following way. Olgose C (**6**) yielded a tetra-acetyl derivative (**14**), $C_{42}H_{64}O_{25}$ (M^+ 968), $[\alpha]_D$ −4.7° which showed in the nmr signal for H_4 at δ 4.53 (d of t; J=2 and 9 Hz) thus indicating that H_3 and H_4 were axial protons. The trans geometry of H_2 and H_3 followed from their coupling constants in **12** and its derivatives which were similar in value when compared with the H_2 and H_3 couplings in **18**.[6]

The linkage of **5** to **6** to reconstitute the structure of the methyl ether of everninomicin C (**2**) was shown essentially the same way as outlined in the structure of everninomicin D.[6] Permethylated everninomicin C (**15**) is an amorphous solid, $[\alpha]_D$ −25.0°, which on hydrolysis yielded **16**,[5] **17**[6] and **12**. It has been shown already that the two hydroxyl groups of 2-O-methyl lyxose portion of the molecule is linked with **8** in olgose C; it follows, therefore, that the two hydroxyl groups in evermicose portion of **17** must be linked with the lactone carbonyl group of **16** in the structure of permethylated everninomicin C (**15**). Based on all the above observations, we propose structure **15** for permethylated everninomicin C and **1** for everninomicin C.

As in the formation[6] of everninomicin D_1 from everninomicin D, the conversion of everninomicin C (**1**) to everninomicin C_1 (**3**)



involves opening of one of the ortho ester linkages. On treatment with diazomethane everninomicin C_1 undergoes similar cleavage to **5** and **6** as has been described in everninomicin D_1[6] and everheptose.[3]

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