NOTES

A PROPOSED NUMBERING SYSTEM FOR POLYETHER ANTIBIOTICS

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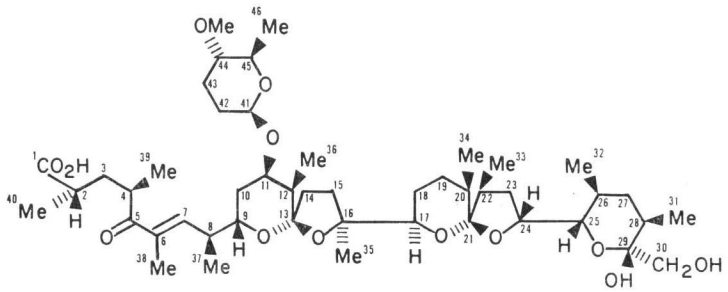
The structure, activity and biosynthesis of the streptomycetes-produced polyether antibiotics were recently reviewed[1]. Since that publication, more of these naturally occurring ionophores have been reported[2,3,4] and because of the rapidly increasing number of compounds being added to the polyether class, a consistent system of numbering is needed as an aid in comparing the chemistry and biological action of these versatile antibiotics.

A common feature of the polyether antibiotics is the presence of a single carboxylic acid function at one end of the molecule which represents the last carbon added during the biosynthesis of the antibiotics' polyketide precursors[5]. In the proposed system, this carbon is designated C-1 and the carbon backbone of the molecule is numbered consecutively to the terminal carbon. In the case of lasalocid, this terminal carbon (C-24) is derived from the methyl of the acetate unit involved in initiation of the compound's biosynthesis. By analogy with lasalocid, the starting point in the biosynthesis of nigericin[6], grisorixin[7], salinomycin,[8] antibiotic A204A[9] and septamycin[10] is C-30 (Fig. 1) suggesting that fifteen is the preferred number of sub-units in the biosynthesis of the carbon skeleton of the polyether antibiotics. An exception to the even numbered polyether backbones is lysocellin[11] (C-23) indicating propionic acid as initiator and eleven sub-units involved in the biosynthesis of that particular antibiotic.

Another characteristic of the polyether antibiotics is the prevalence of C-alkyl groups. In the case of lasalocid, the four branched methyls present (in contrast to C-24) are propionate derived and the three ethyls are derived from the C-3, 4 carbons of butyric acid. The system proposed for numbering these branched alkyl groups follows the steroid model as illustrated for Ro 21-6150[4] (**1**). The presence of a sugar-like function in **1** necessitates continuing the carbon numbering into the 2, 3, 6-trideoxy-4-*O*-methyl-D-erythrohexapyranose moiety (also present in salinomycin, septamycin and antibiotic A204A).

Oxygen and carbon atoms are differentiated in the proposed system with the oxygen numbers in parentheses as illustrated for antibiotic X-206[12] (**2**). This will simplify assign-

1



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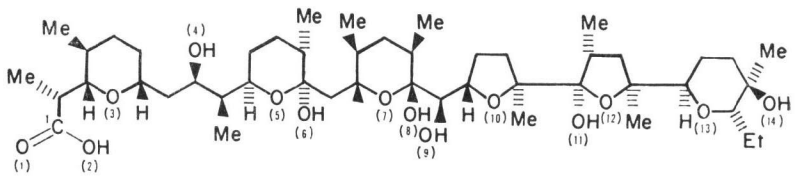
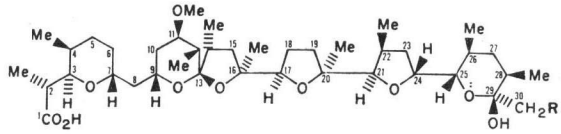
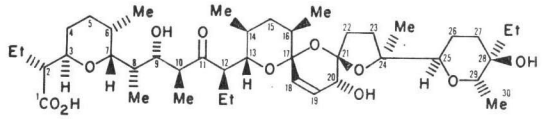


Fig. 1. Structures of typical polyether antibiotics

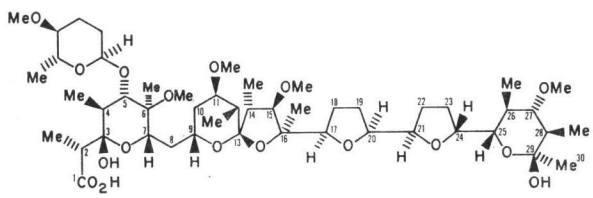


Nigericin R=OH $C_{40}H_{68}O_{11}$

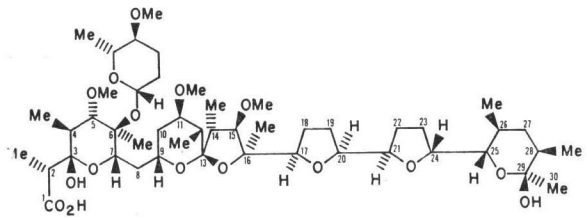
Grisorixin R=H $C_{40}H_{68}O_{10}$



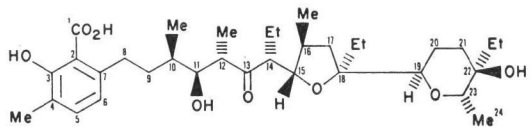
Salinomycin $C_{42}H_{70}O_{11}$



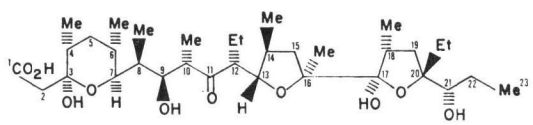
Antibiotic A204A $C_{49}H_{84}O_{17}$



Septamycin $C_{48}H_{82}O_{16}$



Lasalocid $C_{34}H_{54}O_8$



Lysocellin $C_{34}H_{60}O_{10}$

ment of trivial names for *O*-alkyl and desoxy analogues and can be used to distinguish methoxyls in those polyether antibiotics containing four or five -OMe groups such as septamycin and antibiotic A204A (Fig. 1). As proposed for the carbon system, the oxygen numbering would be continued in antibiotics having the hexapyranose moiety such as **1** in which the glycoside ether between C-41 and C-45 is O-12 and the methoxyl group is at O-13.

The system proposed in this communication (**1** and **2**) is easily applied to all the known antibiotics of the polyether class and the advantages of a universal method of numbering are self-evident.

References

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