NOTE

FURTHER PROPOSALS FOR POLYETHER ANTIBIOTIC NOTATION

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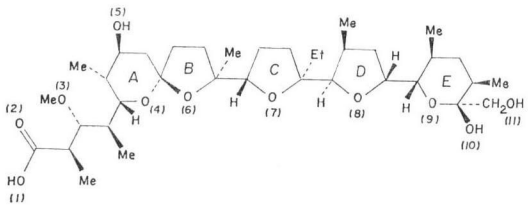
The polyether antibiotics reported by the year 1968 were nigericin[1] (X-464[2]), lasalocid (X-537A[2]), X-206[2], dianemycin[3] and monensin[4]. Monensin (**1**) was the only one whose structure was known at that time. In the following decade, the number of distinct polyethers increased from these five to forty-six, almost all of which were structurally assigned. As a result of this rapid growth, a number of different methods of numbering and drawing these compounds have arisen, which sometimes make structural comparisons difficult.

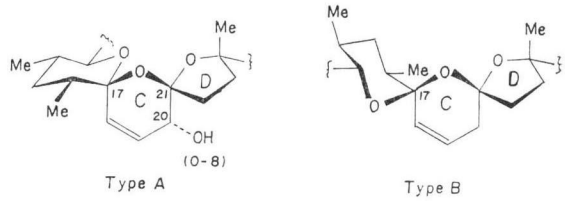


A universal numbering system for the polyethers has been proposed[5] and generally accepted. This system is illustrated for the oxygen atoms in **1**. Special attention is directed to the A ring of **1**, in which the ether (O-4) takes precedence over the hydroxyl (O-5) substituent on the ring, a circumstance not covered in the earlier note.

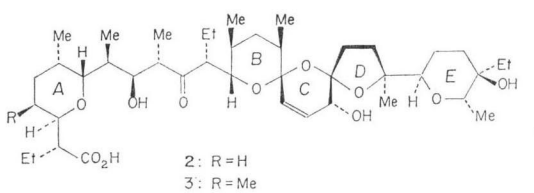
Another source of confusion has been the trispiroketal ring systems B, C and D in, for example, salinomycin (**2**)[6], narasin (**3**)[7] and *epi*-17-deoxy-(O-8)-salinomycin (**4**)[8]. The proposal for naming these moieties is the notation illustrated for **2**~**7**.

The notation used in the structures **2**, **3**, and **4** is based on DREIDING models constructed from X-ray crystallographic data (Fig. 1). There are, however, several other configurations theoretically possible for the trispiroketal system in addition to types A and B.

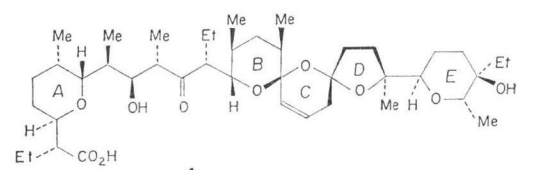
Fig. 1. Tri-spiroketal ring systems found in polyether antibiotics **2**, **3** and **4**.



Two further variations have recently been proposed for noboritomycins A and B[9], and antibiotic CP 44,161[10]. In the first two the type A structure was modified to give the opposite epimer at the C-D junction. However, as salinomycin is also assigned (incorrectly) this novel configuration in the noboritomycin structure paper, the correct representation of noboritomycins A and B should also probably be changed to the same type A system (**5** and **6**) as was found for salinomycin[6].* This same notational error has appeared in a recent review of the polyether antibiotics[11] and in both cases should be replaced by the correct salinomycin structure, **2**. Another error in the same review was the omission of a methyl substituent at the C-8 position of CP



2: R=H
3: R=Me



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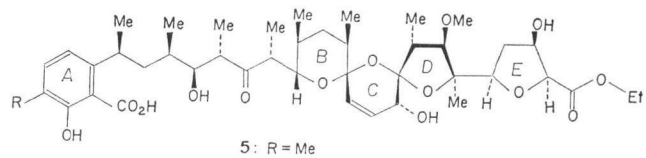
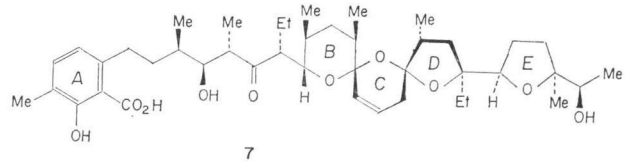
* This turned out to be true (M. KUHN private communication).

38,295 (etheromycin) from the structure as published in the patent literature[12]. For CP 44,161 an A type configuration has been proposed[10] which, however, lacks the allylic hydroxy (O-8) shown in Fig. 1. The stereoscopic diagram of the Cs^+ salt of CP 44,161* obtained by X-ray analysis was in complete agreement with the structure (7) as proposed. It is interesting to note that the antibiotic is the first ionophore reported to be produced by a genus other than *Streptomyces*, *i.e. Dactylosporangium salmoneum*.



5: R = Me
6: R = Et



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From the above observations, the more complex polyether antibiotics clearly represent unusual notational problems due to the multiplicity of asymmetric centers and fused cyclic ether functions in their structures. A number of other possible errors in notation of published polyether antibiotics are under active investigation.

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* The stereoscopic diagram was kindly provided by Drs. R. C. KOCH and C. E. MOPPETT, whose cooperation we wish to acknowledge.