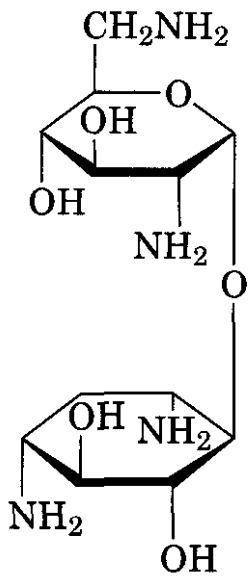
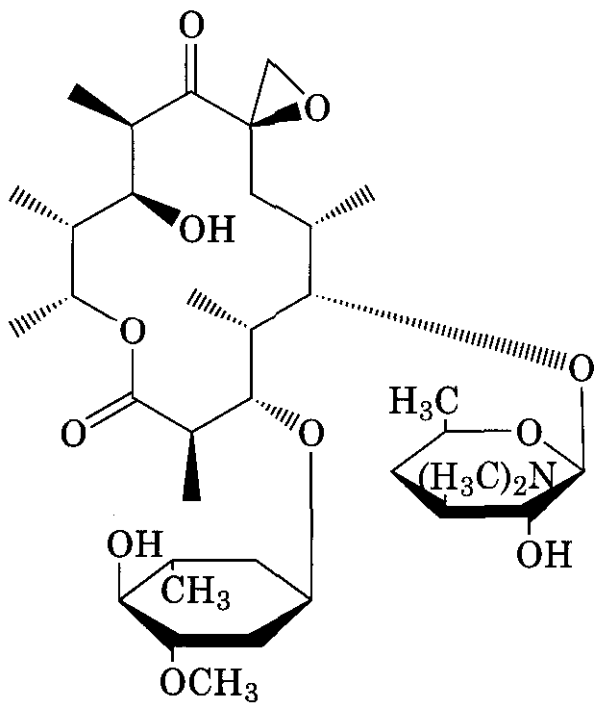


(84)



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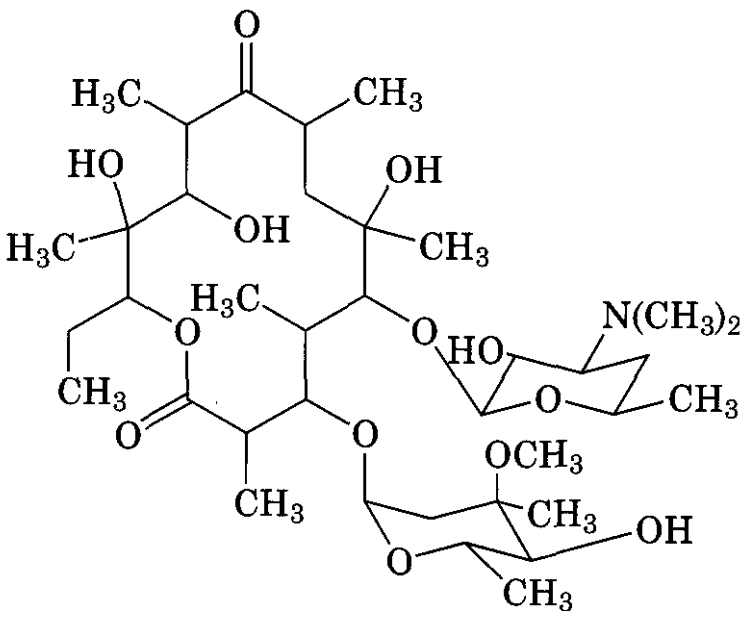
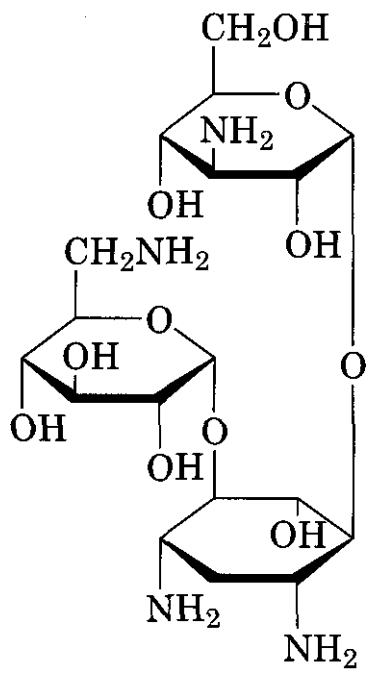


(86)



(88)

showed good resistance to β-lactamases and was less toxic than benzylpenicillin. However, plans to market the compound were terminated with the introduction of methicillin (see above).

The discovery that the basic structural building block of cephalosporin C, that is, 7-aminocephalosporanic acid (7-ACA) (**91**), could be synthesized led to the preparation of numerous cephalosporin derivatives in a similar way to the synthesis of penicillins from 6-aminopenicillanic acid (129, 130). Modification of the substituent at the 7-position, while retaining the 3-acetoxymethyl group, gave cephalothin (**92**), cephacetrile (**93**), and cephapirin (**94**), so-called first-generation cephalosporins with good activity against Gram-positive bacteria, although the acetyl ester was susceptible to degradation by esterases and thus limited the duration of action. Replacement of the acetoxy group by other substituents rendered the products less prone to esterase attack. For example, the pyridinium derivative, cephaloridine (**95**), has a longer duration of action than that of cephalothin.

The first orally active cephalosporin was cephaloglycin (**96**), which possessed a phenylglycine substituent in the C-7 side-chain, although the labile 3-acetoxymethyl group was retained. Replacing the acetoxy group with a proton or chlorine, for example, cephalexin