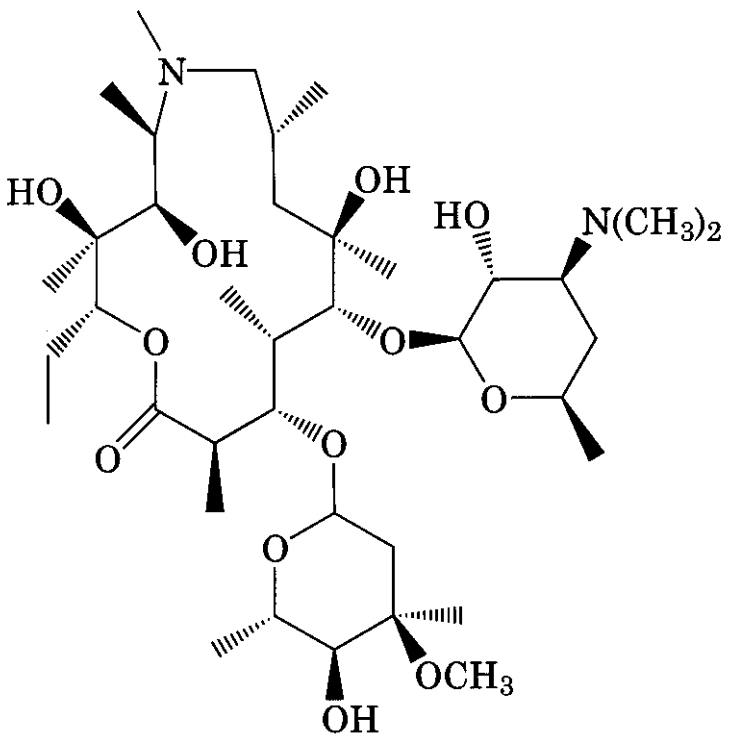
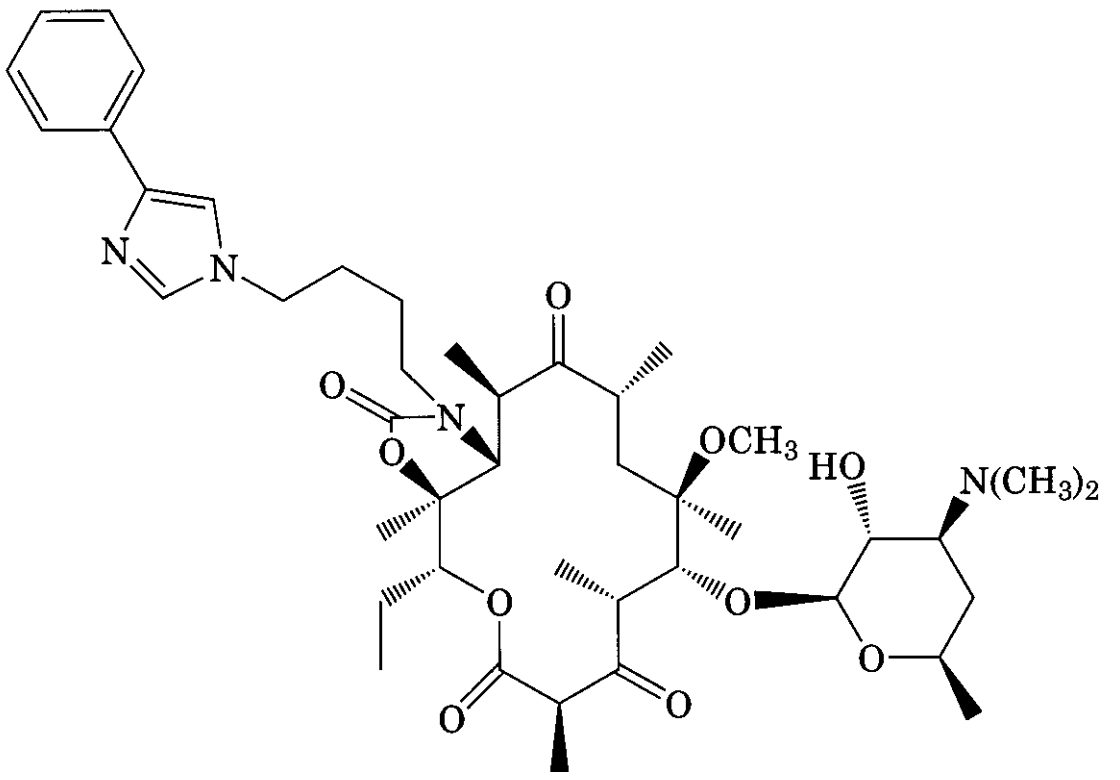


(113) Azithromycin

Both azithromycin and clarithromycin have been used for various bacterial infections for a number of years. Within the last decade, resistance has emerged to a range of antibacterials, including the macrolides, arising from methylation of an adenine in the 23S ribosomal RNA target site, which prevents binding (146). The invention of the ketolides [e.g., telithromycin (**115**)] overcomes MLS_B resistance by removing the L-cladinose moiety at position 3: the exposed hydroxyl is also oxidised to a ketone (147). The loss of potency that would ensue is compensated by two further modifications, which improve binding, formation of a carbamate at positions 11/12, and extension with a heterocycle-substituted side-chain. In ABT 773 a similar side-chain is placed at position 6, with comparable results (147).

5.3 Streptogramins

The streptogramins are produced by *Streptomyces* species and have been classified into two groups: Group A are polyunsaturated macrocyclic lactones and Group B are cyclic hexadepsipeptides. Both groups bind bacterial ribosomes and inhibit protein synthesis at the elongation step and they act synergistically against many Gram-positive microorganisms. However, the naturally occurring streptogramins are poorly soluble in water and this, until recently, has limited their use to treat bacterial infections. New, water-soluble derivatives have been developed and the semisynthetic dalfopristin (116) and quinupristin (117) mixture (Synercid) has been approved for the treatment of Gram-positive infections, including multidrug-resistant strains of *Enterococcus faecium, Staphylococcus aureus,* and *S. pneumoniae* (148).



(115) Telithromycin