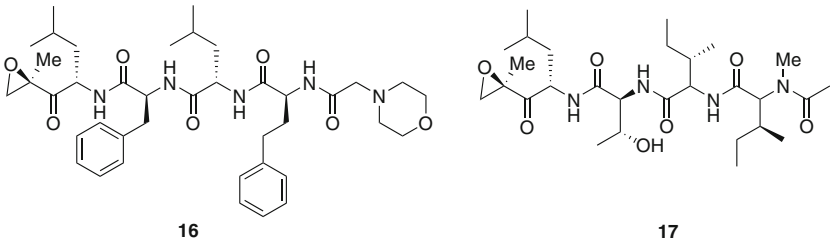

Fig. 7 Structures of the semisynthetic derivative carfilzomib (**16**) and the natural product epoxomicin (**17**)

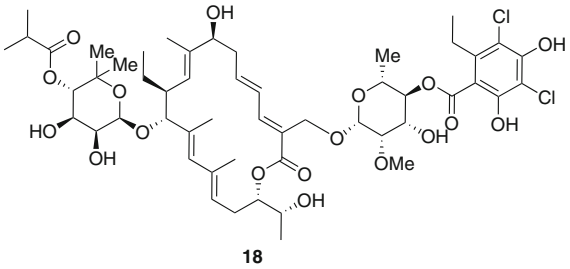

Fig. 8 Structure of the antibacterial natural product fidaxomicin (**18**)

proteasome inhibitors. Carfilzomib is based on epoxomicin (**17**), a natural product which was isolated from soil *actinomycete* No. Q996-17 and contains an unusual epoxide ring (Hanada et al. 1992). The compound's mechanism of action works through the irreversible inhibition of the proteasome, leading to apoptosis in tumor cells (Meng et al. 1999). The total synthesis was soon achieved (Sin et al. 1999), after which various analogues of epoxomicin were synthesized, creating variations on the amino acid residues, resulting in carfilzomib (Halford 2012).

Fidaxomicin (Dificid®)

Fidaxomicin (**18**, Fig. 8) is a new, first-in-class macrocyclic (1,072.1 Da) antibiotic which has been approved in 2011 for the treatment of *Clostridium difficile* bacterial infections in the gastrointestinal tract. It is one of the few unmodified natural products to be approved, and it belongs to a family of polyketide fermentation products of the soil actinomycete *Dactylosporangium aurantiacum*, known as the lipiarmycins/tiacumicins (Parenti et al. 1975). Although fidaxomicin shows high bactericidal activity against a wide range of Gram-positive bacteria (Coronelli et al. 1975), its size and polar surface area prevent it from being absorbed into the bloodstream in its current form. It was found however that naturally occurring gastrointestinal bacteria are relatively unaffected by fidaxomicin, which is why development of the drug has focused towards applications on the gastrointestinal tract.