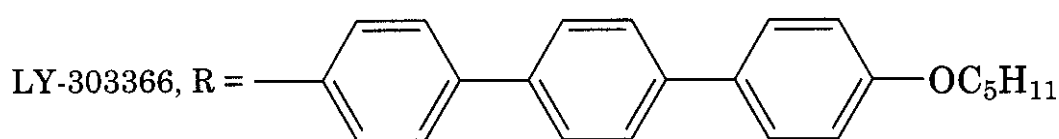


and the complex stereochemistry generated by the high degree of hydroxylation. However, echinocandin B can be produced efficiently by fermentation of a culture of *Aspergillus nidulans* and then deacylated by fermentation with *Actinoplanes utahensis* (151). The free amino group thus exposed can be derivatized with a number of active esters. Synthesis of the amide from 4-octylbenzoic acid gives **cilofungin (119)**, which has specifically high potency against *Candida albicans* and some other *Candida* species (151).

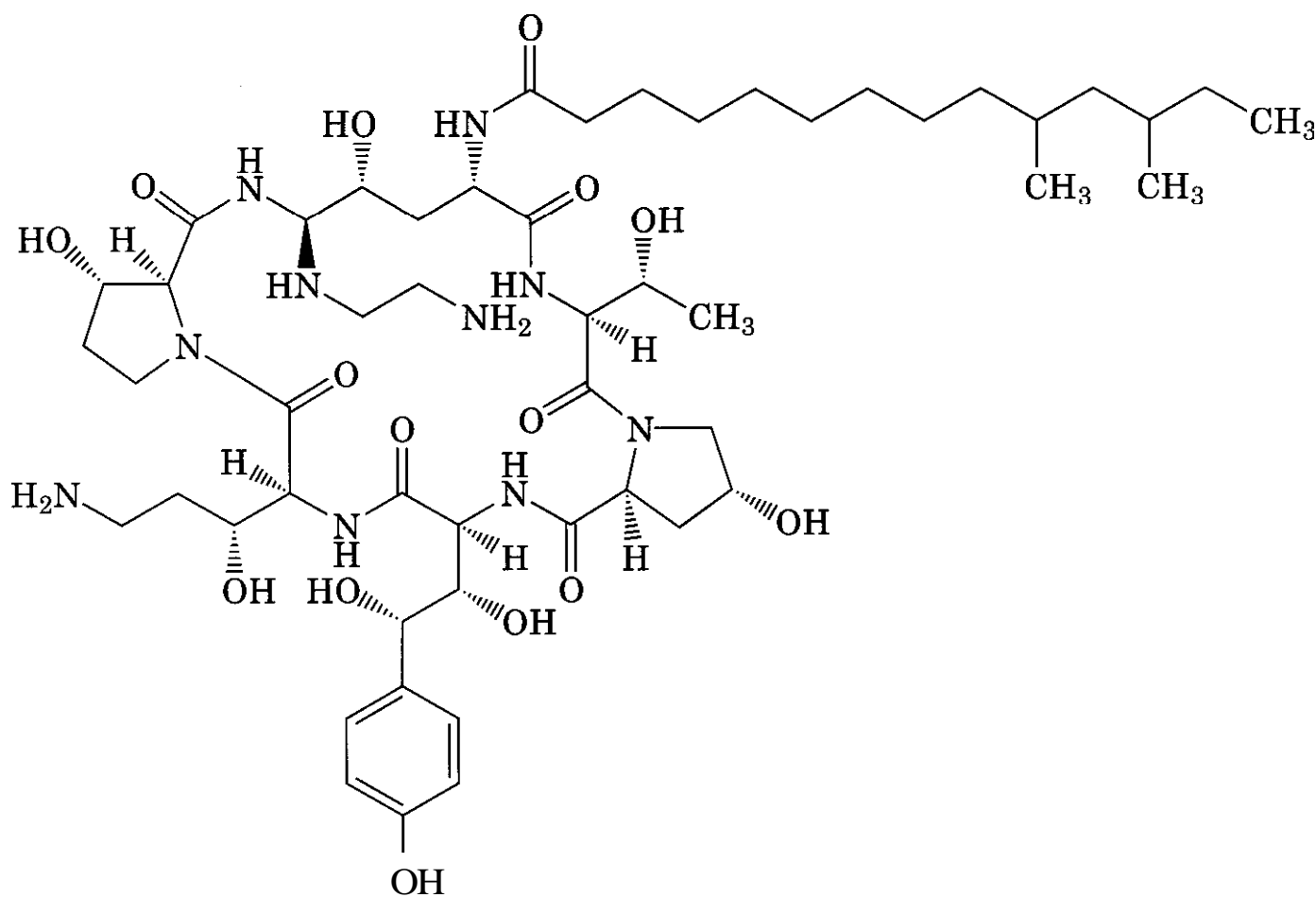


(119) cilofungin, R =

For systemic use cilofungin had to be given intravenously and unfortunately ran into problems associated with the cosolvent (PEG) (152). A better derivative, LY-303366 (**120**) is



(120)



(121) caspofungin

now in clinical trial and has the major advantage of oral bioavailability (153). Many other antifungal **peptides** are under investigation (152). The member of this series that is furthest advanced is caspofungin (MK-991, L-743,872) (**121**), following its approval by the FDA, early in 2001, for the treatment of aspergillosis. The two analogs, LY-303366 and caspofungin, have been compared against clinical fungal isolates *in vitro* (154) and the latter has been evaluated in immunosuppressed mice (155).

## 6 CARDIOVASCULAR DRUGS

### 6.1 Lovastatin, Simvastatin, and Pravastatin

One of the most significant natural product discoveries in the last 25 years has been a fungal secondary metabolite called lovastatin (122). Heralded as a major breakthrough in