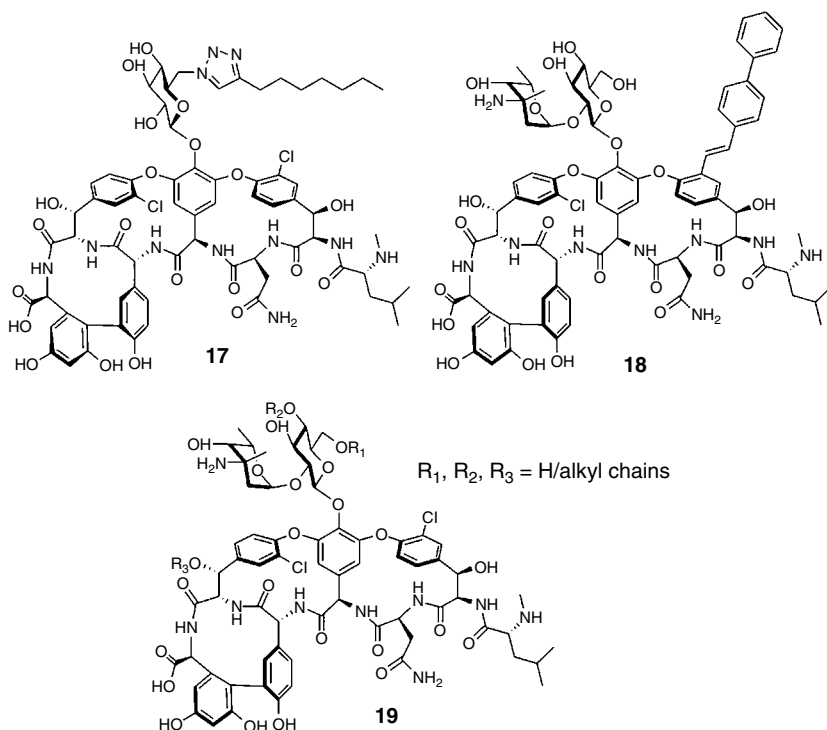


dimers with linkers varying in lipophilicity and charge were developed by Yarlagadda et al. (2015d). The vancomycin dimer that contained two positively charged centers in the octylene linker (**15**) exhibited a 15-fold (MIC = 48  $\mu$ M) and 130-fold (MIC = 0.1  $\mu$ M) increase in activity over vancomycin against VRE and VISA, respectively. In order to impart membrane-anchoring properties to vancomycin aglycon dimers, a pendant octyl lipophilic moiety was attached to the linker (**16**) (Yarlagadda et al. 2015d). This molecule showed a 300-fold higher activity than vancomycin against VRE (MIC = 2.5  $\mu$ M).

#### 4.6.2 Incorporation of Lipophilicity

Teicoplanin possesses a lipophilic chain that helps anchor the drug to the cell membrane. Thus, it was hypothesized that the membrane interaction properties could be imparted by the attachment of lipophilic moieties to vancomycin or other glycopeptides.

Thorson et al. incorporated a lipophilic 6-azido glucose onto the vancomycin aglycon (**17**, Figure 4.5) (Fu et al. 2005). This compound was found to be more



**Figure 4.5** Vancomycin derivatives with lipophilic moieties to enhance activity.