against the same panel of *E. coli* strains (Oh et al. 2010; Lidor et al. 2015). At similar concentrations of SPR741, strong RIF potentiation was also described against a panel of MDR *A. baumannii* (Zabawa et al. 2016; Corbett et al. 2017). The *in vivo* efficacy of SPR741 and RIF combination was shown in murine thigh and lung infection models (Warn et al. 2016a, b). Interestingly, the characteristic nephrotoxic concerns usually associated with polymyxins (Pogue et al. 2016; Zavascki and Nation 2017) were not observed with SPR741 at a dose of 60 mg kg^{-1} day^{-1} in cynomolgus monkeys after 7 days of a 1-hour infusion thrice daily (Coleman et al. 2016b). Other polymyxin-based adjuvants include the polymyxin dilipid (**5**) with two short C-4 lipid tails but not larger lipid tails as in polymyxin analogues (**6**)–(**9**) (Domalaon et al. 2018a). Compound (**5**) is a potent synergizer of RIF against various clinical *P. aeruginosa* isolates and other GNB (Domalaon et al. 2018a).

Our research group has demonstrated that amphiphilic tobramycin (TOB)-based hybrids (**10**)–(**15**) (Gorityala et al. 2016a, b; Lyu et al. 2017; Yang et al. 2017a) are potent synergizer of RIF against wild-type and MDR *P. aeruginosa* isolates (Figure 18.5). For instance, the TOB–ciprofloxacin hybrid at 3.5 μMol reduces the MIC of RIF below 1 mg l^{-1} against a panel of MDR *P. aeruginosa* isolates (Gorityala et al. 2016a). In addition, to RIF many other non-pseudomonal agents are potentiated against *P. aeruginosa* including fluoroquinolones

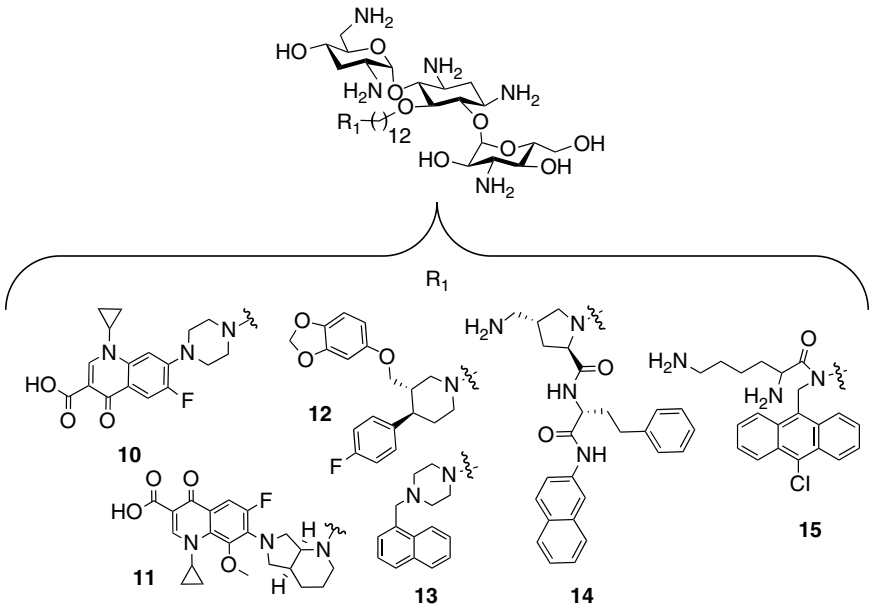

Figure 18.5 Structure of tobramycin-based antibiotic adjuvants that potentiate antibiotics against GNB.