therapeutic window. Except incorporating with traditional antibiotics, photoswitching units also could be modified on new-type antibiotic–antimicrobial peptide. As the published work by Komarov's group, the diarylethene was inserted into the backbone of cyclic antimicrobial peptide Gramicidin S to construct a diarylethene-based amino acid analogue (Babii et al. 2014). Attributed to the different conformations of diarylethene under UV and visible light irradiation, the resultant products could form the "open" or "closed" status, resulting in a remarkable change in biological activity. Antibacterial regulation under light irradiation is an innovative route to explore using methods for antibiotics without the environment pressure. To develop these light-trigged antibiotics, all the photo-responsible units showed the great potential to be applied in the field of antibiotic modification. We believe that there must be some more exciting progress in the near future.

## 16.4 Antibiotic Modification by Supramolecular Chemistry

Supramolecular chemistry, which focuses on chemical systems beyond single molecule, is also a valuable route to modifying common antibiotics for dealing with pathogenic resistance. The self-assembly process driven by noncovalent force may endow classical drugs with some progressive properties. A promising strategy against drug-resistant bacteria is to reverse the drug resistance mechanisms, with the potential to rejuvenate large classes of previously powerful antibiotics (Zhang et al. 2008). As shown in Scheme 16.11, Structure (**32**), Patirick Couvreur and co-workers linked the penicillin G (PNG) with the hydrophobic squalene, which could form nanoparticles in aqueous environment by spontaneous assembly (Semiramoth et al. 2012). In neutral physiological environment, the synthesized SqPNG could enter cells by clathrin-dependent endocytosis. Because of the different membrane diffusion process, the new supramolecular complex could efficiently improve the concentration of PNG upon intracellular pathogens. Similarly, utilizing the unique self-assembly property of aggregation-induced emission (AIE) agents, Olof Ramstrom and co-workers synthesized a series of neoteric ciprofloxacin-based nanodrugs (Xie et al. 2017). As shown in Scheme 16.11, all these molecules (**33**)–(**36**) that ciprofloxacin bears with a perfluoroaryl ring (AIE agent) could form a propeller-shaped structure. More importantly, they are all endowed with higher bactericidal capability against both sensitive and resistant *E. coli*.

Host–guest chemistry, an important branch in supramolecular chemistry, also can be employed for improving the bactericidal activity. Utilizing the beta-cyclodextrin (β-CD) as host molecule and the antibacterial doxycycline (DOX) as guest molecule, Sinisterra et al. cleverly constructed the β-CD/DOX complex and successfully enhanced the drug activity of DOX (Suarez et al. 2014). Harshita