

Figure 12.6 Examples of nucleotide prodrug constructs developed to mask the charged nature of phosphate and phosphonate groups to enable diffusion across biological membranes and to stabilize the nature of a phosphate group. Several of these prodrug constructs have been designed to support tissue targeting.

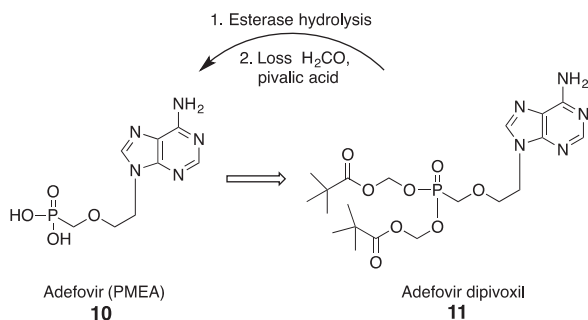


Figure 12.7 Adefovir dipivoxil [adefovir bis(POM)] (**11**) is the phosphonate prodrug of the antiviral adefovir (PMEA) (**10**) developed as an oral agent for the treatment of HBV infection.

nucleotides into cells *in vitro* and *in vivo* in animals, but only a few have translated into human clinical successes.

Adefovir (PMEA) (**10**, Figure 12.7) is an acyclic phosphonate nucleotide analog of adenine. Adefovir is an effective inhibitor of HBV replication *in vitro* following phosphorylation by cellular kinases. Adefovir diphosphate inhibits