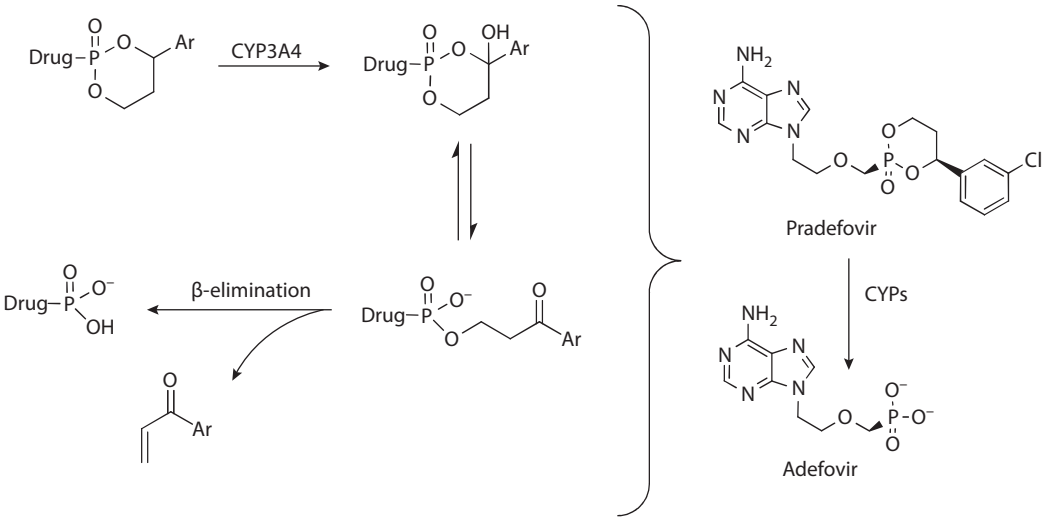

FIGURE 10.15 Bioconversion of HepDirect®-prodrugs to corresponding phosphates or phosphonates.

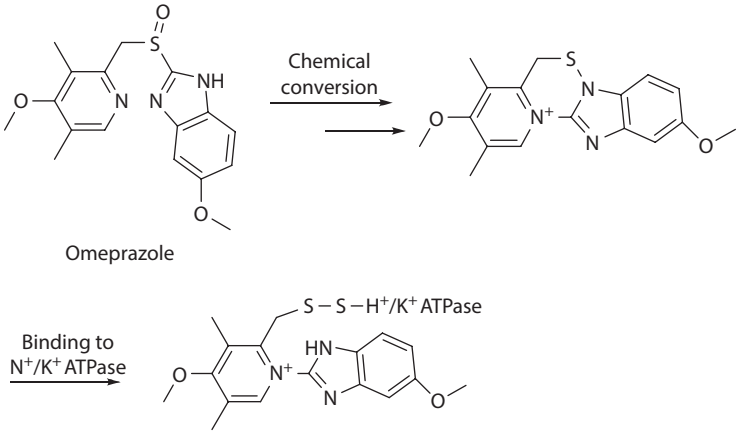

FIGURE 10.16 Bioconversion of omeprazole to its active sulfonamide and following irreversible binding to the cysteine group of H^+/K^+ ATPase.

10.5.5 Improved Metabolic Stability

The therapeutic activity of a drug can be prolonged either by slowing its enzymatic hydrolysis rate or by diminishing its rate of metabolism. Even though various pharmaceutical formulations or the synthesis of new drug analogs have most frequently been exploited to avoid rapid metabolism of a drug, a few examples of prodrugs also exist. In these prodrugs, the metabolically labile but pharmacologically essential functional group(s) of parent drug has generally been masked to avoid rapid elimination. In the case of bambuterol, which is a long-lasting bis-dimethylcarbamate prodrug of the bronchodilator and β_2-receptor agonist terbutaline, the metabolically susceptible phenolic hydroxyl groups have been protected to avoid rapid and extensive first-pass metabolism in the gut and the liver. After administration, bambuterol is slowly converted to terbutaline via its monocarbamate metabolite mainly outside the lungs by nonspecific butyrylcholinesterase, but other hydrolytic and oxidable enzymes may also be involved in the release of an active drug (Figure 10.17). As a result