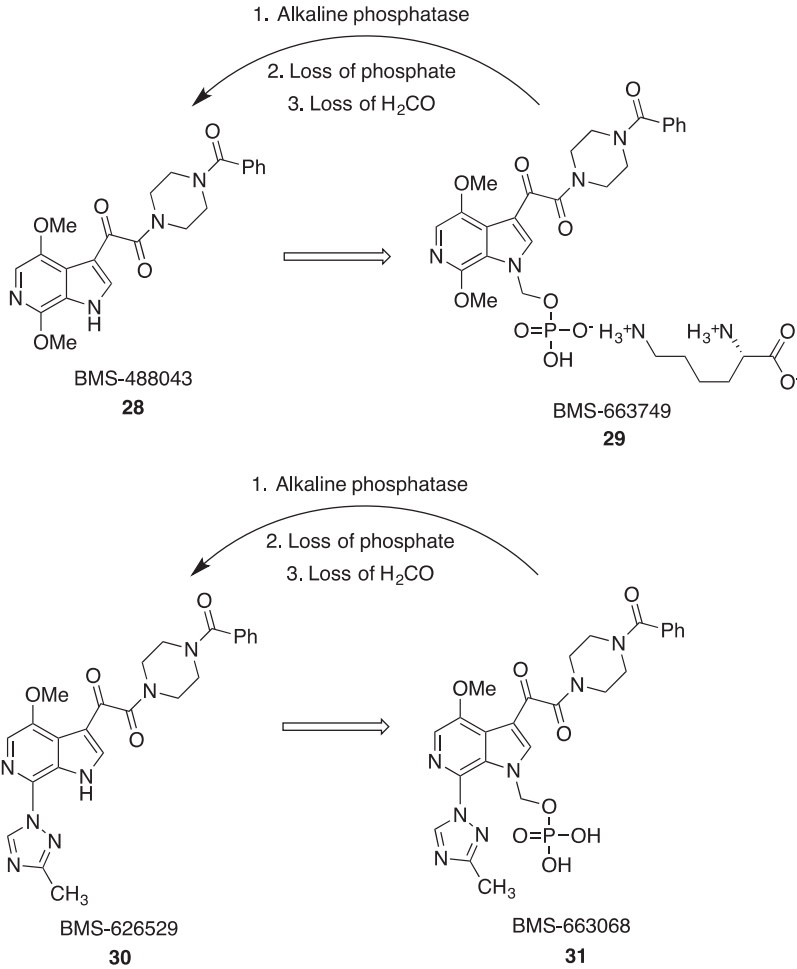

Figure 12.15 BMS-663749 (**29**) and BMS-663068 (**31**) are methylene phosphonate prodrugs of the HIV attachment inhibitors BMS-488043 (**28**) and BMS-626529 (**30**), respectively. They were developed to address the problem of solubility-limiting absorption.

PK characteristics of the parent did not meet a desired twice-daily dosing profile. Consequently, BMS-663749 was not taken further in development. Nevertheless, this prodrug strategy demonstrated its utility in addressing the problem of dissolution and solubility-limited absorption and was subsequently applied to the attachment inhibitor BMS-626529 (**30**, Figure 12.15) that possessed a more favorable intrinsic potency relative to BMS-488043. When administered to healthy volunteers, the phosphonooxymethyl prodrug BMS-663068 (**31**, Figure 12.15)[86] demonstrated rapid conversion to and absorption of the parent drug BMS-626529. An extended-release formulation was subsequently developed to decrease the maximum plasma concentration and