

Figure 12.24 The specificity of imatinib.

(A) Structure of imatinib bound to the kinase domain of Abl. The drug penetrates deeply into the kinase domain and cannot bind tightly unless the kinase is in the specific inactive conformation shown here and also in (C). (B) Dasatinib, shown on the right, does not penetrate so much and binds to the active form of the kinase. (C) Conformation of Abl, as bound to imatinib, with the drug removed. (D) Conformation of inactive Src kinase. Differences in the structure of a centrally located "activation loop" prevent the binding of imatinib. (E) The conformation of the active kinase domain, to which imatinib also cannot bind. (PDB codes: 1IEP, 2GQG, 1QCF, 2G2I.)

