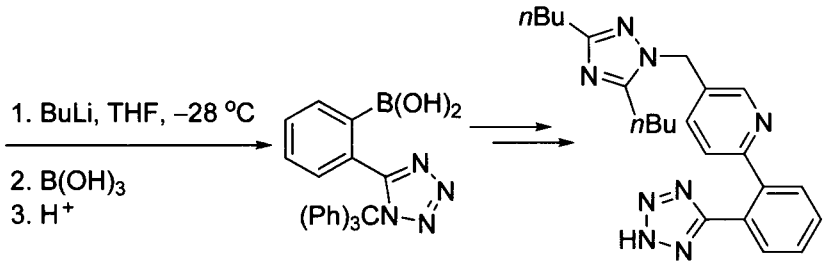
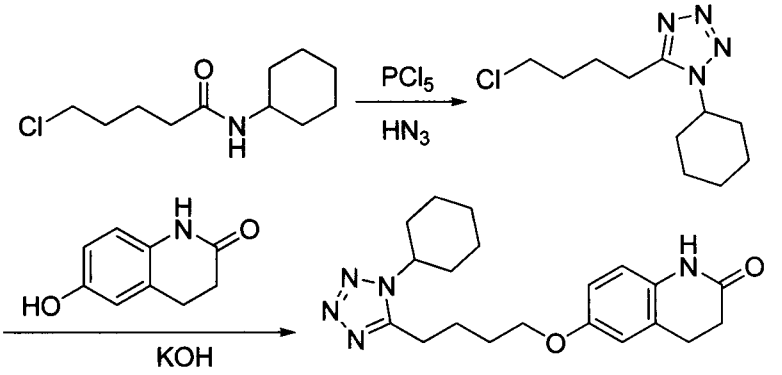


Cilostazol has been used to treat intermittent claudication in individuals with peripheral vascular disease. A similar molecule as cilostazol may have the risk of death in patients with congestive heart failure. The synthesis of cilostazol contains a 1,3-dipolar addition for the construction of the tetrazole ring, and the resulting tetrazole was coupled with 6-hydroxy-3,4-dihydroquinolin-2(1*H*)-one with the aide of potassium hydroxide.[45]



9.4 Possible Liabilities of Triazole-containing Drugs

Triazoles are known metal chelators, and triazoles have been associated with a number of adverse events and significant drug–drug interactions (DDIs). Triazoles are metabolized by the CYPP450 enzymes, and all triazoles exhibit some degree of drug–drug interactions. Triazoles can be substrates, inducers, and inhibitors of CYP enzymes, and, when administered with other agents that interfere with the CYP450 system, may result in significant alteration of plasma triazole levels. P-glycoprotein is a transporter protein involved in the absorption and distribution of triazoles. Triazoles can function as substrates for P-glycoprotein (Pgp) and/or inhibitors, thus, creating drug–drug interactions (DDI) with other agents that also interact with this protein.

All triazoles have been associated with some degree of hepatotoxicity, ranging from mild hepatitis to cholestasis and, rarely, fulminant hepatic failure.[46] Although not entirely clear, it seems that liver