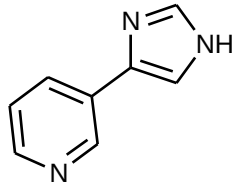
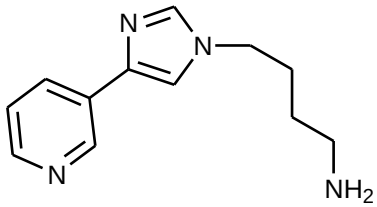
Chapter 13: Erythromycin and macrolide antibacterial agents

Question 13.1
Suggest a method of synthesising the primary amine (II) used in the synthesis of telithromycin (Fig. 13.8), starting from compound (I).

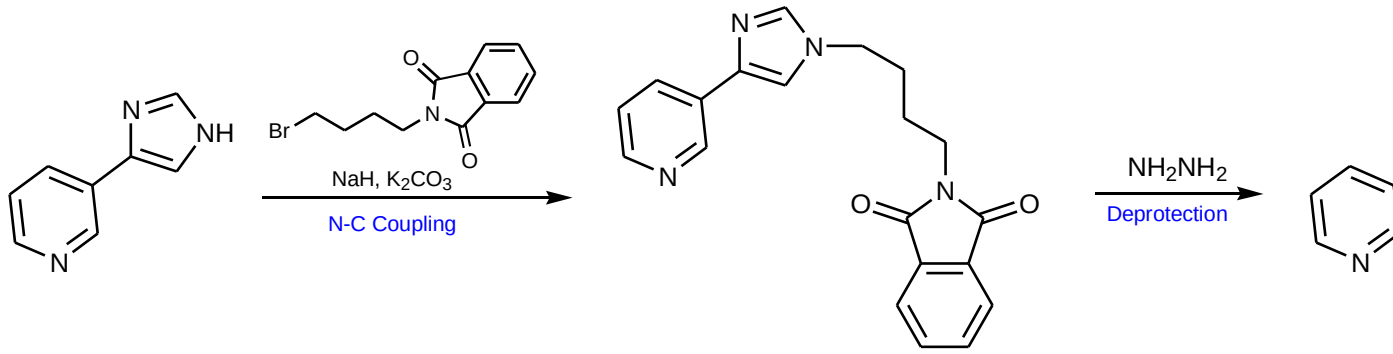


I



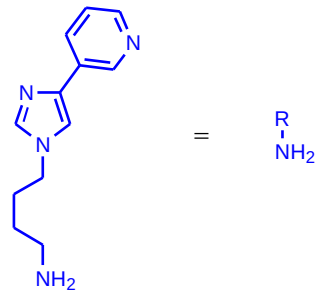
II

Answer
The synthesis could be carried out as follows. Note that it would be necessary to protect the primary amine group to prevent it reacting with the alkyl bromide. In this case, a phthalimide group has been used as the protecting group, but other protecting groups are equally possible.



Question 13.2
Propose a mechanism by which telithromycin is formed in the reaction shown in Figure 13.8.

Answer
We shall simplify the primary amine as follows.



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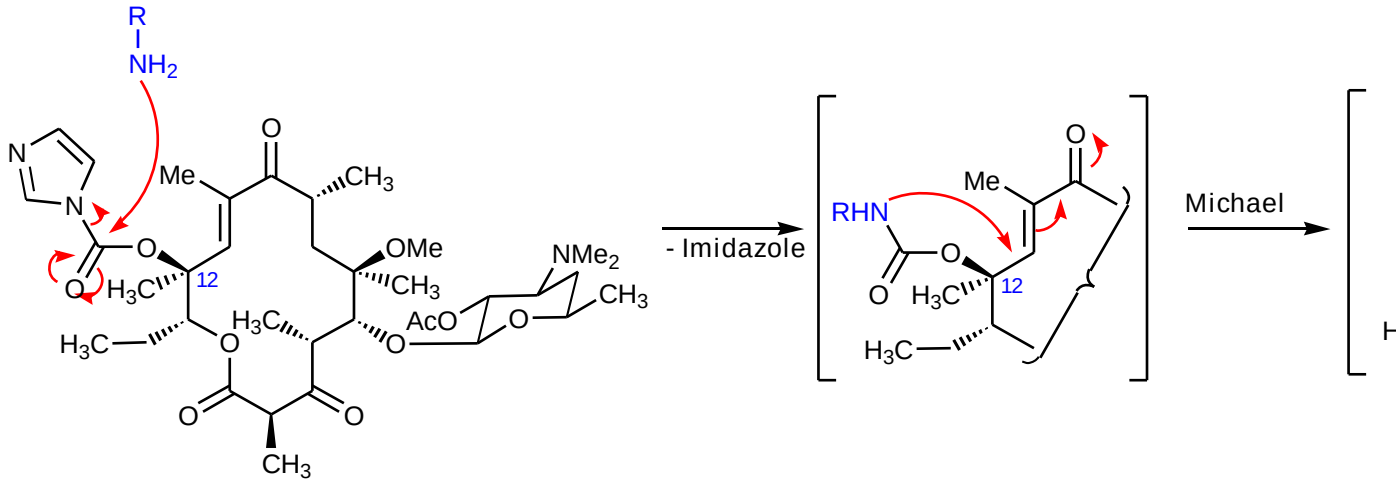
The mechanism could involve the primary amine reacting with the urethane group of the macrolide in a nucleophilic substitution reaction, with the imidazole ring acting as a leaving group. A cyclisation reaction then take place involving nitrogen atom of the inermediate urethane undergoing a Michael addition with the α,β-unsaturated ketone.



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