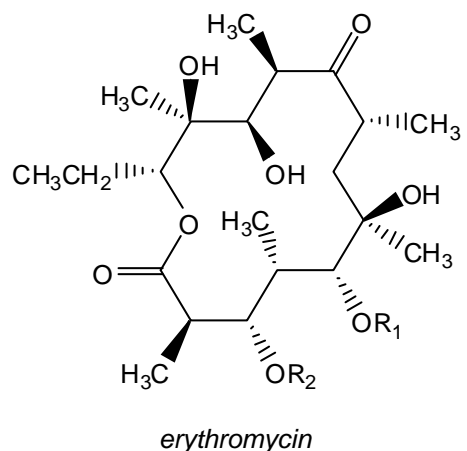


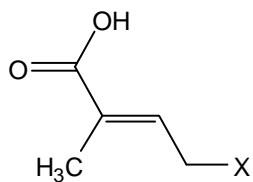
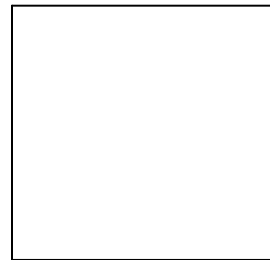
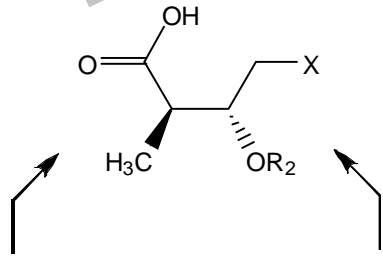
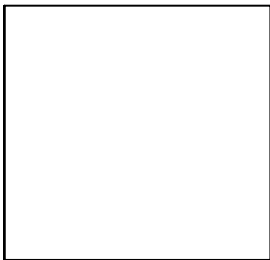
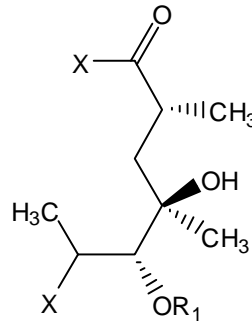
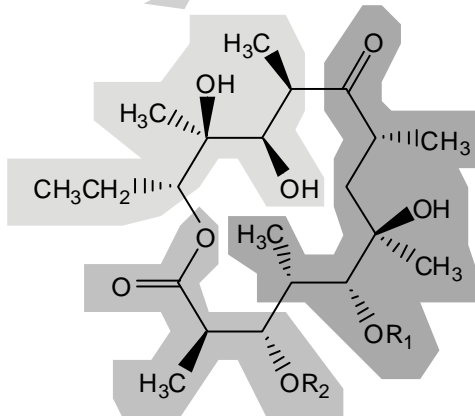
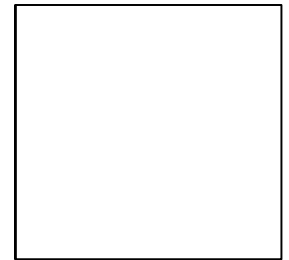
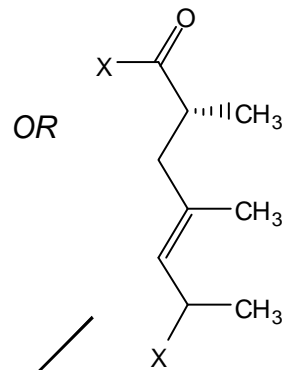
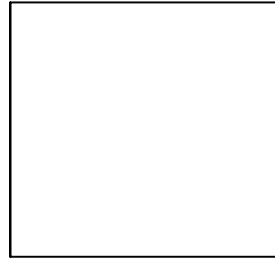
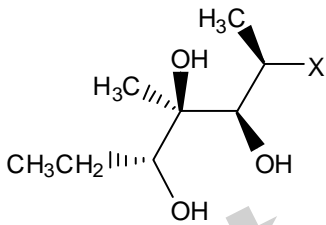
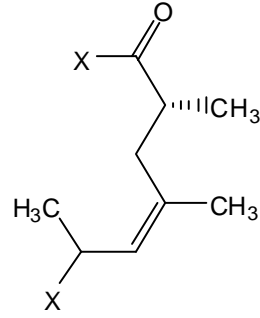
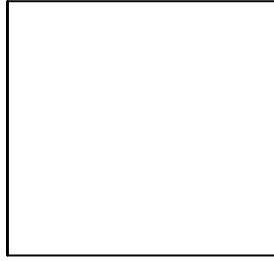
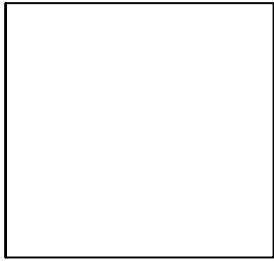
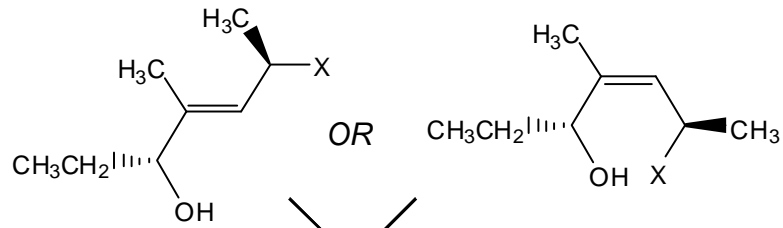
Workshop 20 Diastereoselectivity in Organic Syntheses

Many pharmaceutically active substances have lots of stereocenters, and as we discussed in Chapter 5 (Stereochemistry), the correct placement of these stereocenters is often critical to the therapeutic activity of these substances. This creates a challenge for medicinal chemists, in that functional groups often have to be installed in molecules with regio- and diastereo-selectivity. Erythromycin, an antibiotic, is a good example of this problem: 10 of the 13 carbons in the central ring are stereocenters, and synthetic chemists have not yet developed a chemical synthesis that both creates all of those stereocenters and is cost-competitive with biosynthetic methods for making the drug. (Currently, producers extract erythromycin from vats of cultured *Streptomyces erythraea* bacteria.) Most of the stereocenters are alcohol or ether groups, and over the last week we've learned of a number of methods to transform alkenes into alcohols and ethers with diastereoselectivity. So in this Workshop, we'll pretend that we are synthetic chemists designing a synthesis of erythromycin from alkene starting materials.



In order to simplify the problem of synthesizing a complex molecule like erythromycin, chemists will sometimes synthesize simpler fragments of the molecule and then zip the pieces together at the end. The diagram on the next page illustrates one way that a chemist might do this, and shows that a number of diastereoselective reactions would be required to achieve the total synthesis. (In the diagram, "X" signifies parts of molecules that would be connected at the end—ignore these.) It also suggests that there are multiple ways, from different starting materials, one might make this happen. In each empty box, propose a set of reagents that would achieve each transformation selectively. If you think there is no way to do a particular reaction in the way shown, write "no way" in the box.

(Don't worry about making the specific *enantiomer* shown; just make sure your steps are diastereo-selective—i.e., that they produce the correct *syn* or *anti* addition of groups to the alkene starting materials.)



OR

