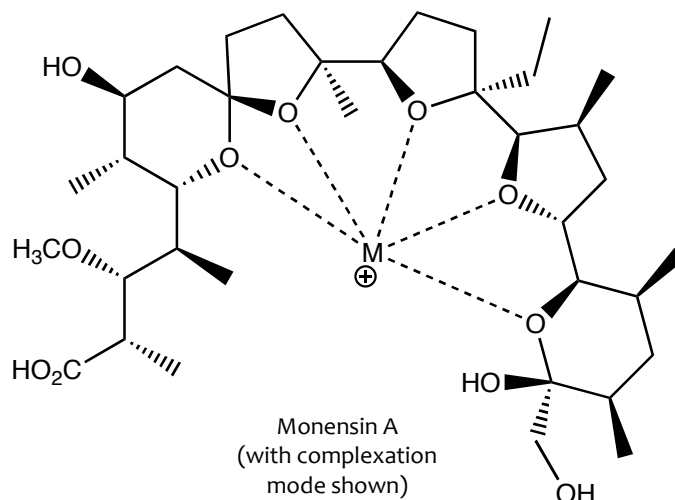


Study Question 4

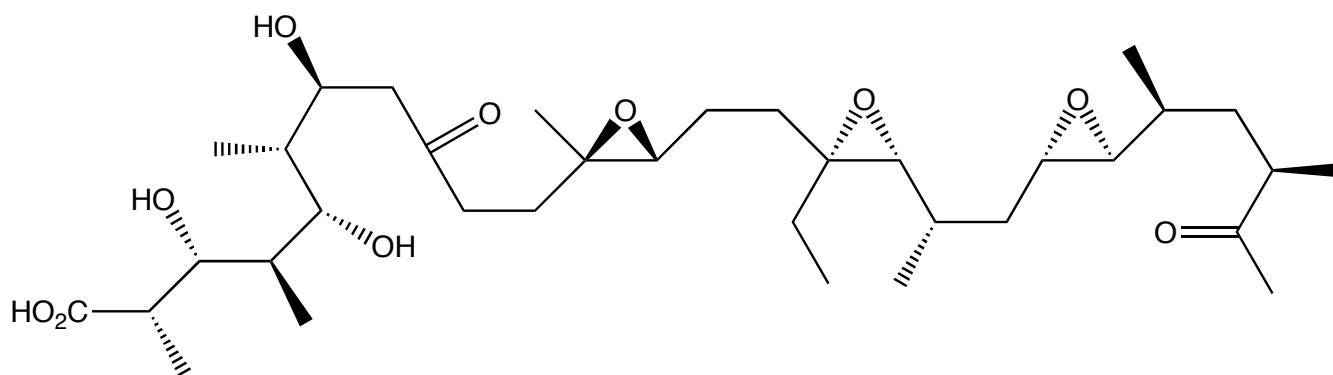
Monensin A is a complex molecule produced by bacteria in the genus *Streptomyces*. It acts as a defensive compound against other bacteria. It works by complexing ions (as shown), then transporting them across the bacterial membranes and destroying the functioning of the membrane in the process.

The bacteria make monensin by an elaborate cyclization of more or less linear intermediates in a process that is reminiscent of the biosynthesis of lanosterol (recall that the entire steroid ring system is made in one step from 2,3-oxidosqualene).



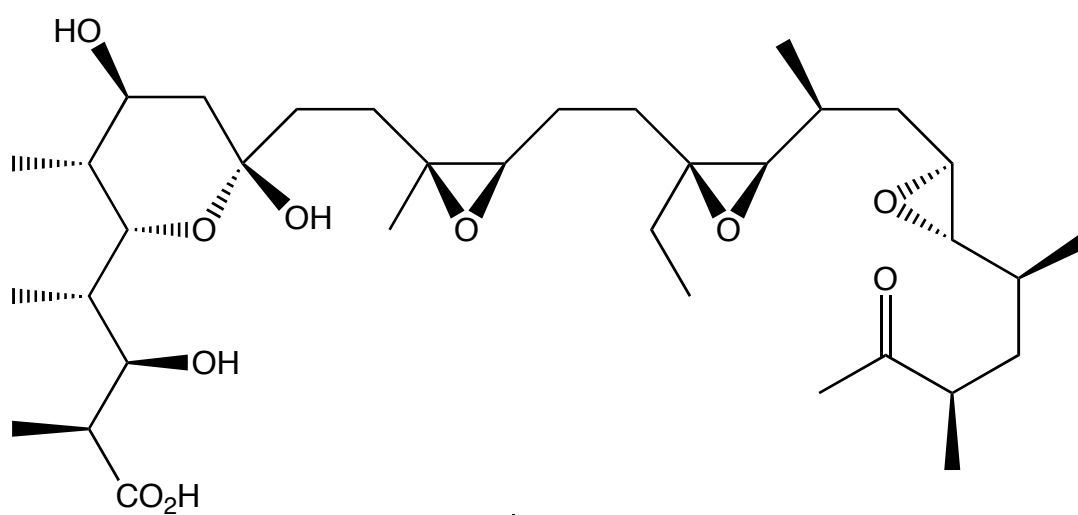
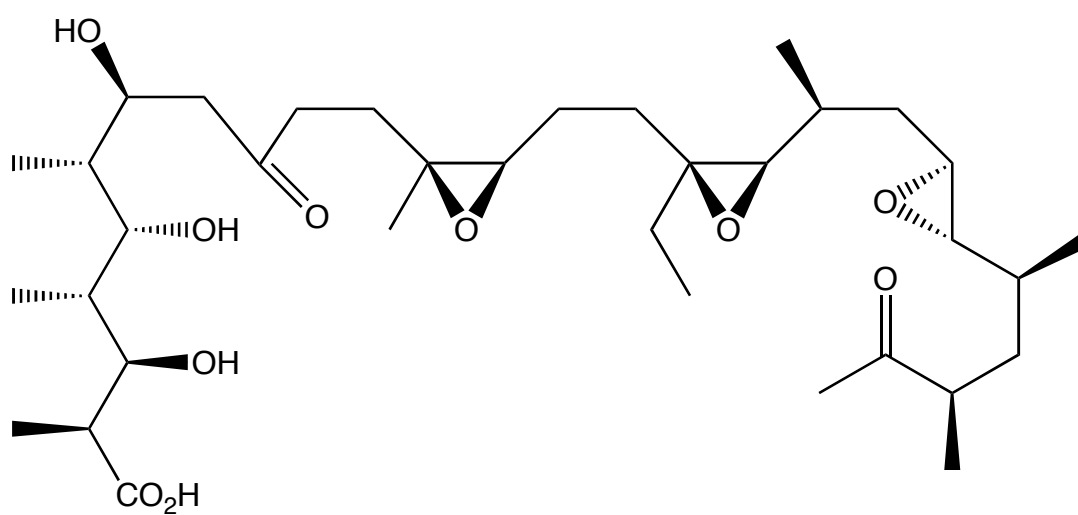
There are two competing hypotheses about how this cyclization takes place on the enzyme. Each starts from a slightly different precursor. A framework for each mechanistic hypothesis is shown below. Add mechanistic arrows to each framework showing the bond breaking/making that is needed to create the monensin structure. You may use $B^+ - H$ to represent an acidic amino acid side chain, and $-B:$ to represent a basic amino acid side chain (to handle your proton transfers).

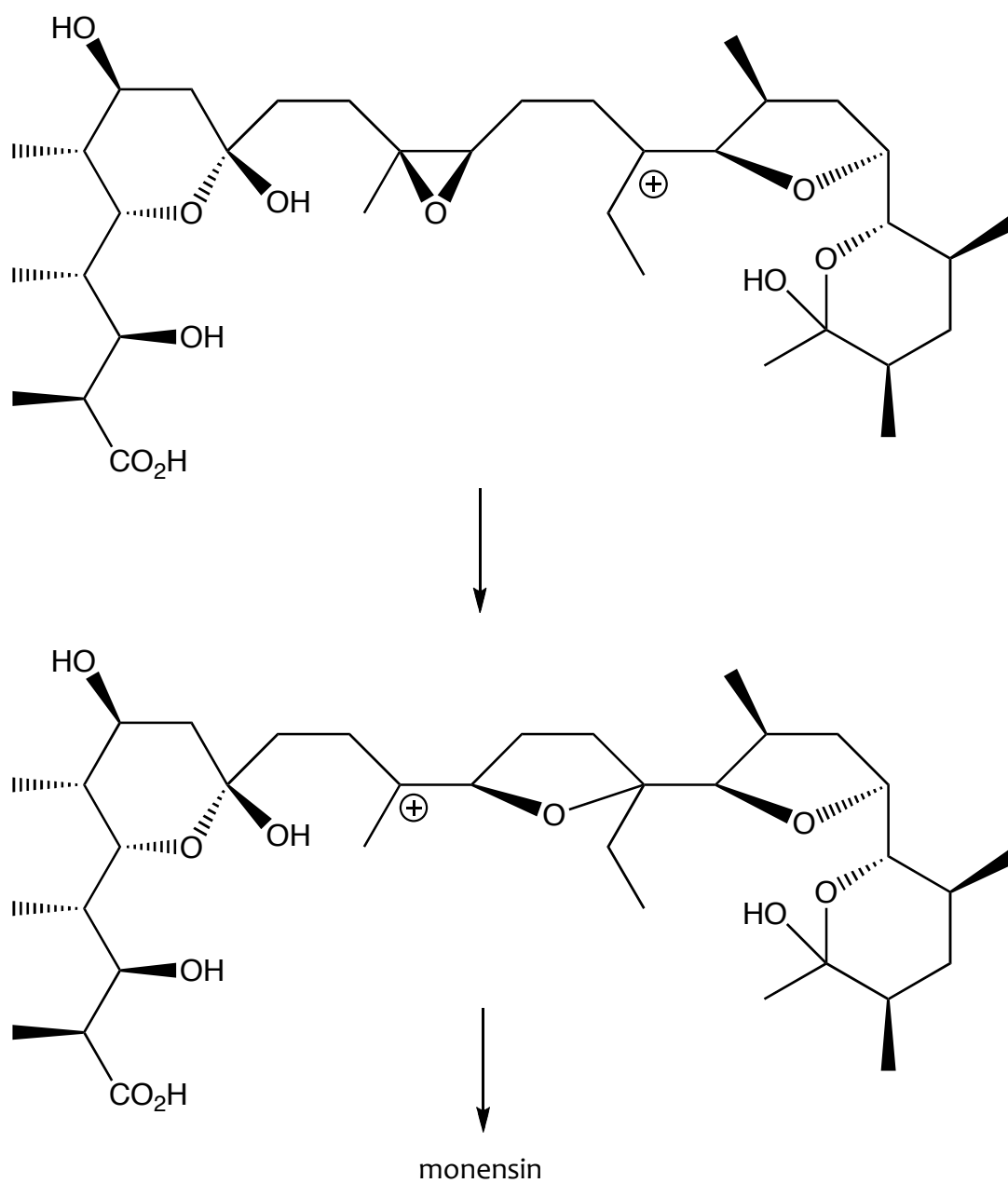
Mechanistic Hypothesis #1 (gives monensin in 1 step, not counting proton transfers)



What kind of mechanism is operating here?

Mechanistic Hypothesis #2





Reference: PF Leadley *et al* "Engineering of complex polyketide biosynthesis – insights from sequencing of the monensin biosynthetic gene cluster" *J. Ind. Micro. Biotech.* (2001) 27:360-367.