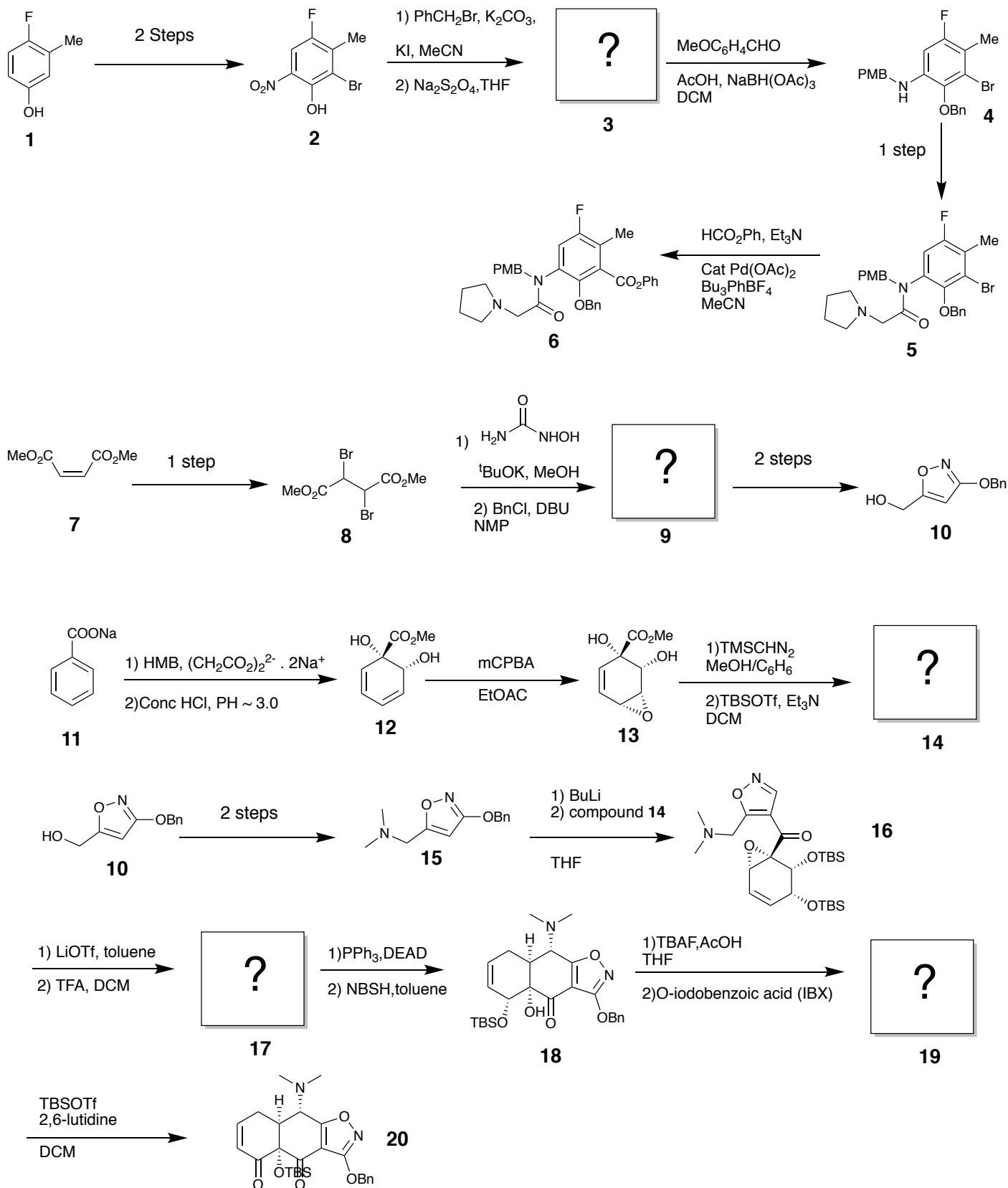
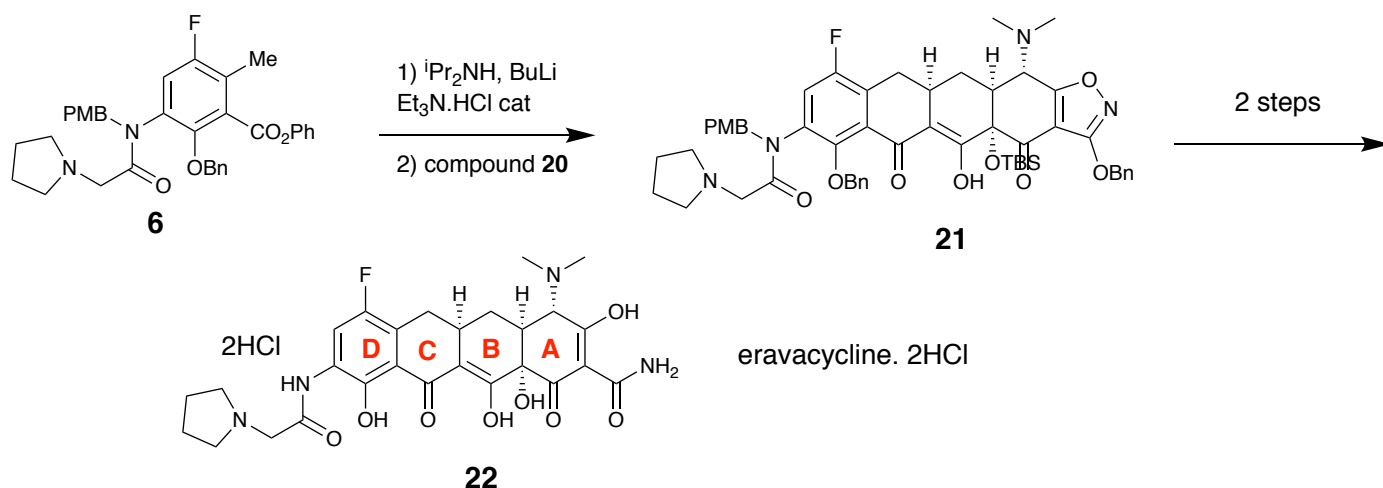


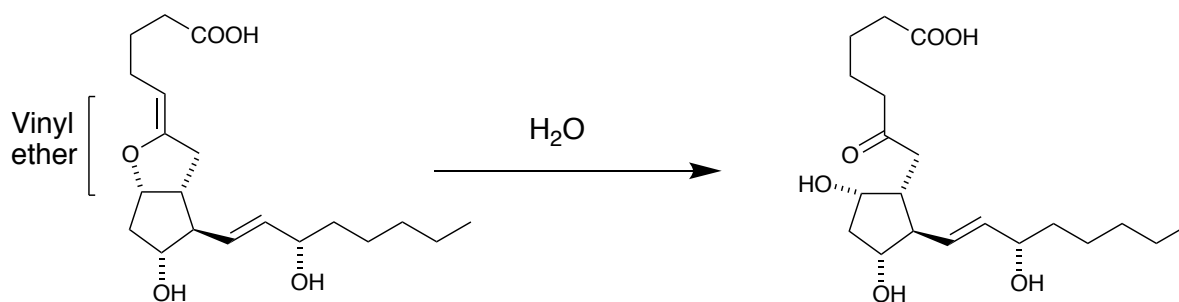
Problem Session Questions

1. Eravacycline, is the first fully synthetic fluorocycline eravacycline (Xerava) consisting of the tetracyclic scaffold with unique modifications in the tetracyclic D ring. Below is the scheme for its total synthesis. Please fill in the gaps for any intermediate compounds and propose mechanisms for each individual step.





2. Prostacyclin, discovered in 1976, is a naturally occurring of blood-clot formation, which has tremendous therapeutic potential. Unfortunately, the drug has a half-life of about 3 minutes at physiological pH. This was proposed to be due to the hydrolysis of vinyl ether group to ketone, as illustrated in the scheme below:



The pH-rate profiles of prostacyclin and its methyl ester analogue are shown below. Please derive rate equations for each section of the profile (regions 1 and 2). What atoms/groups would you introduce to prostacyclin, in order to increase the half-life at physiological pH?

