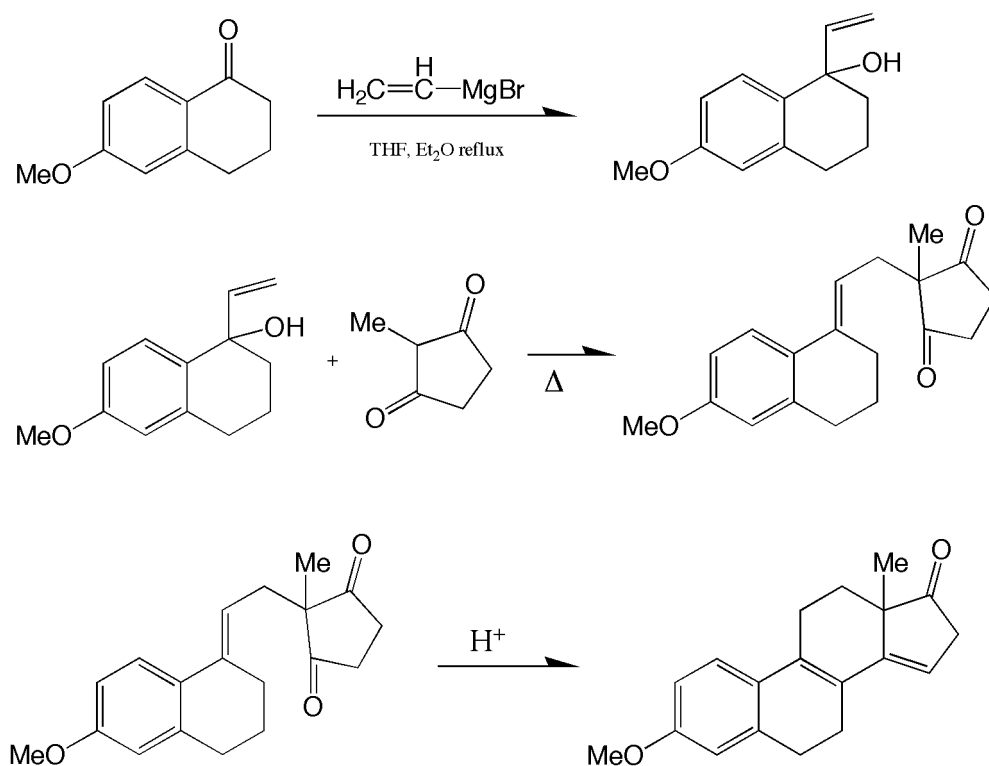
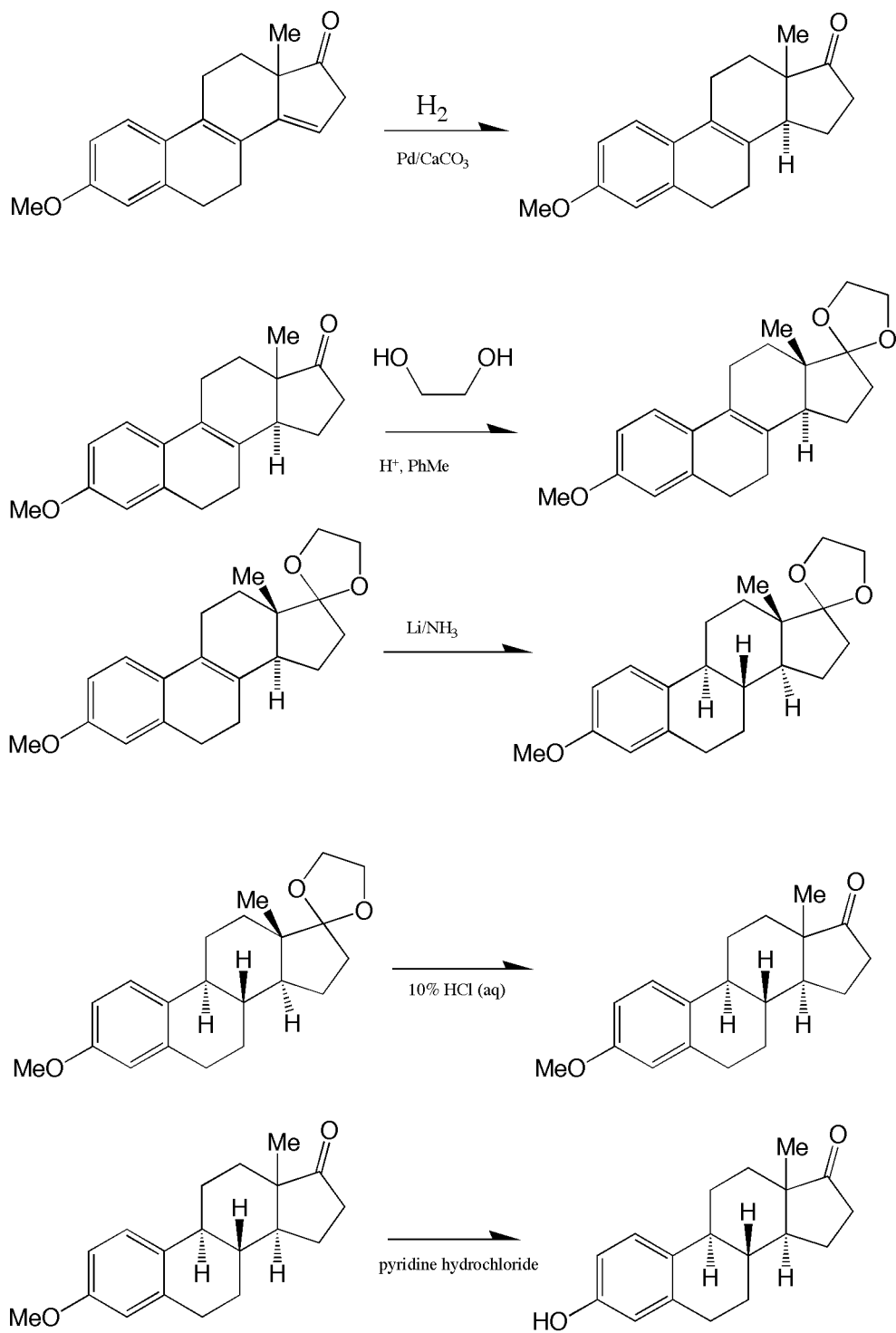


Exercise 3: The total synthesis of estrone

Estrone is a member of a large class of organic compounds, both naturally-occurring and synthetic, called steroids. Following the synthesis of a stereoisomer of estrone by W.E. Bachmann in 1942, Anner and Mischer synthesized natural estrone in 1948. The following reaction scheme is the Torgov estrone synthesis (Torgov and Ananchenko, *Tetrahedron Letters*, 1553 (1963)) which is carried out on an industrial scale to make the quantities needed for pharmaceuticals such as birth control pills.





Number the reactions 1 through 8 in sequence.

A. Classify the eight reactions according to reaction type. For instance, the last reaction is a nucleophilic substitution.

B. Write a reasonable mechanism for each of the reactions

C. The product of the final reaction is, of course, estrone. How many possible stereoisomers of the product are theoretically possible? Be careful to find all chiral centers!

D. In the fifth reaction, explain the "anti" stereochemistry of the added hydrogens. You may wish to redraw a portion of the mechanism to show how that particular stereochemistry is achieved.

E. What is the purpose of the fifth and seventh reactions? Hint: It's one of the non-assigned parts of chapter 18.

F. In the fourth reaction, explain why the hydrogen shown adds "anti" to the methyl group.