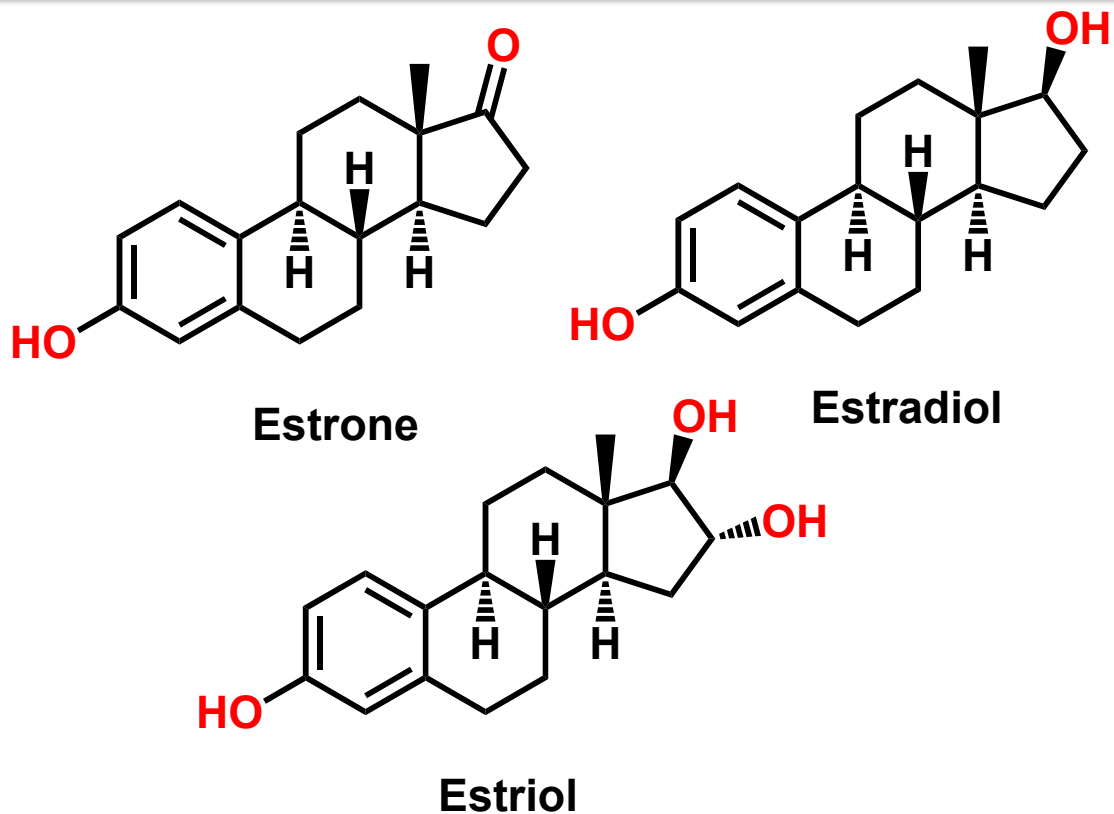


Total Synthesis of Estrone



Krishna P Kaliappan
Professor of Chemistry, IIT Bombay

CH-845 Course on Organic Synthesis



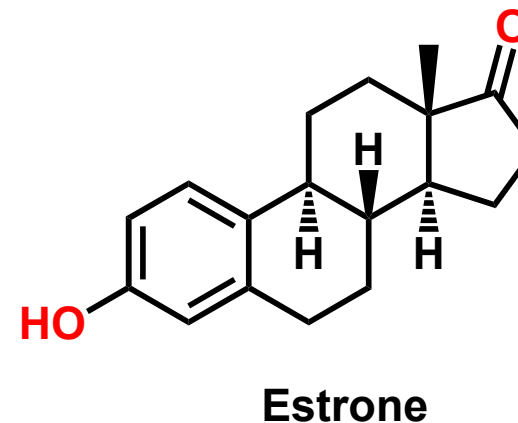
Estrone is a weak estrogen and a female sex hormone

Estrone is one of the three estrogens (the other two are estradiol and estriol)

Estrone is excreted in the form of estrone sulfate in urine

Estrone is the first steroid hormone to be discovered in 1929

Synthetic Challenges



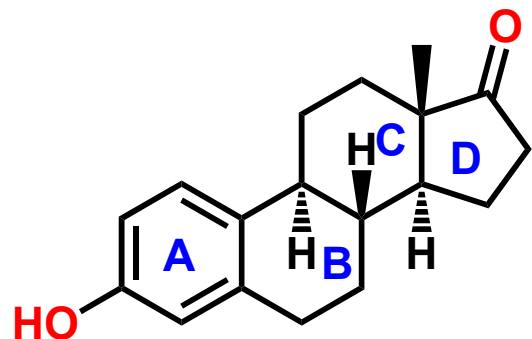
Four contiguous chiral centers

Angular methyl group

Trans-Anti-Trans ring junctions

Trans hydrindanone system

Torgov's Synthesis of Estrone



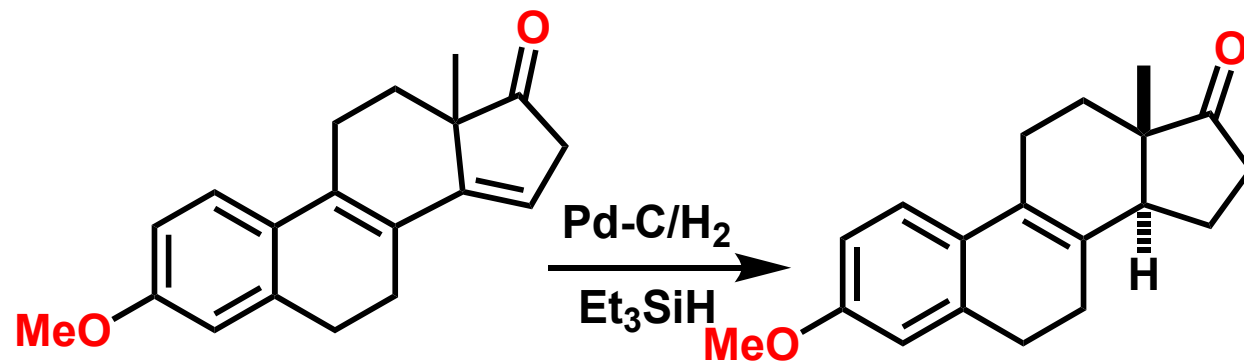
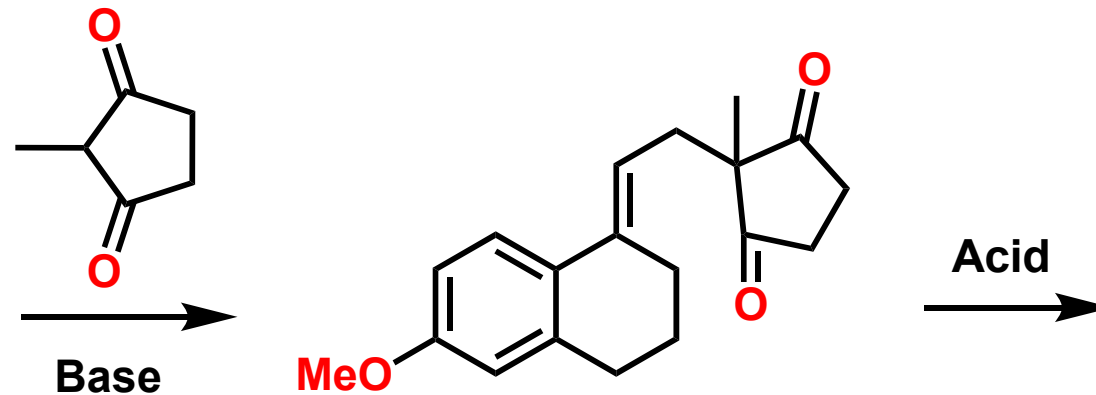
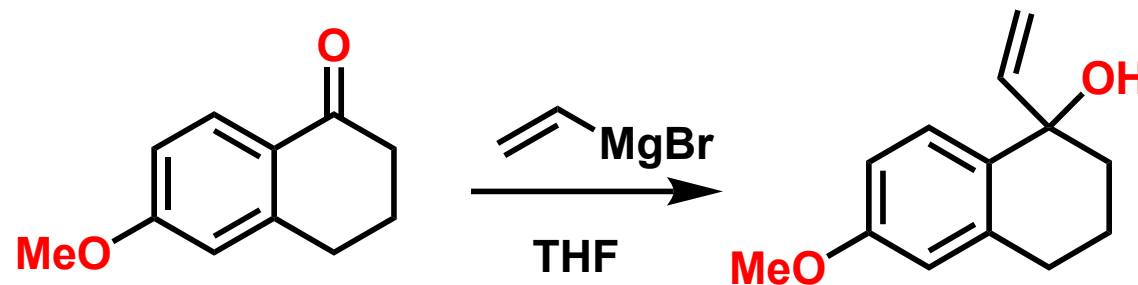
Estrone

Strategy used is $AB \longrightarrow ABD \longrightarrow ABCD$

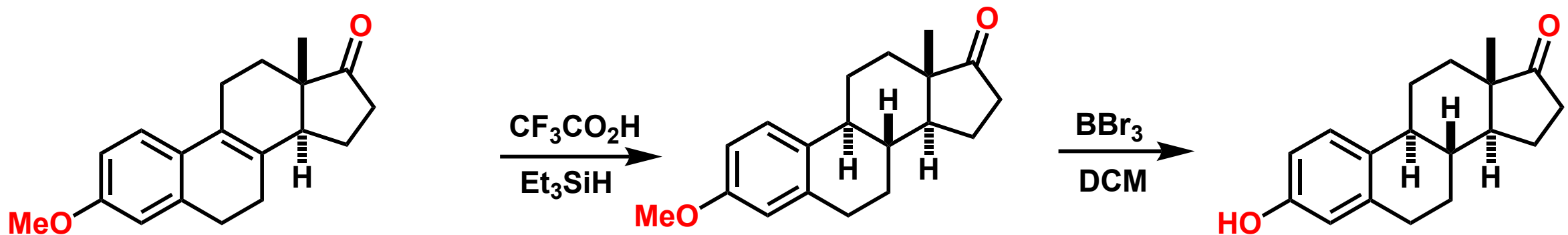
6-Steps Total Synthesis

Key reactions are: Acid catalyzed cyclization & Stereoselective reduction

Torgov., *Tetrahedron Lett.*, 1963, 4, 1553.

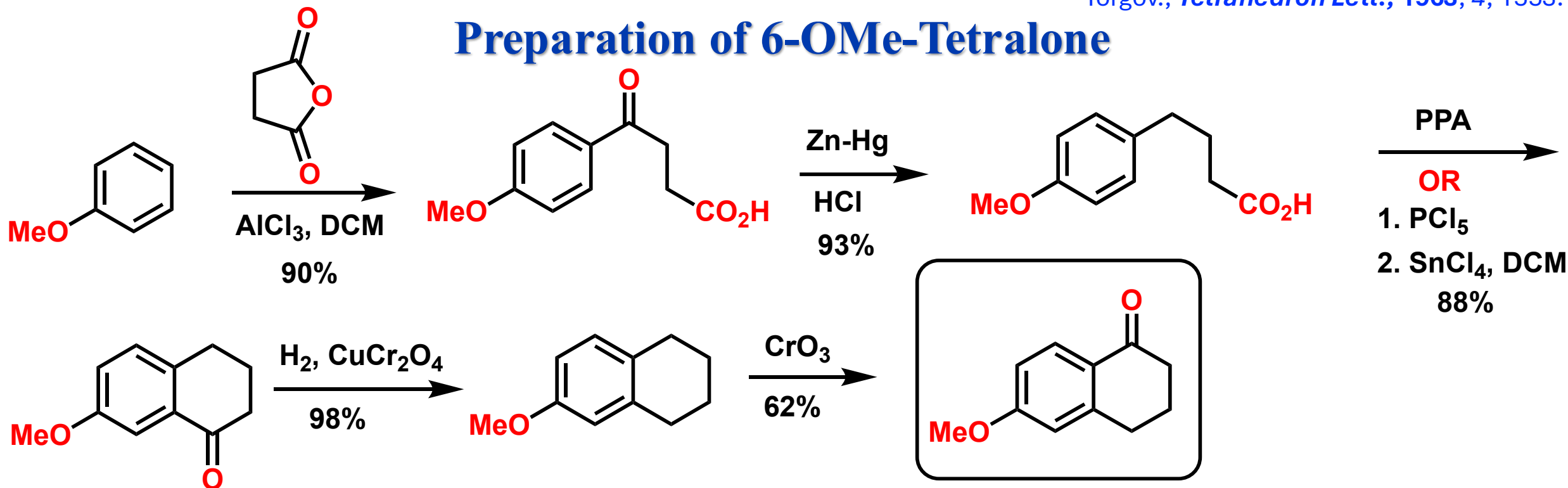


Torgov's Synthesis of Estrone

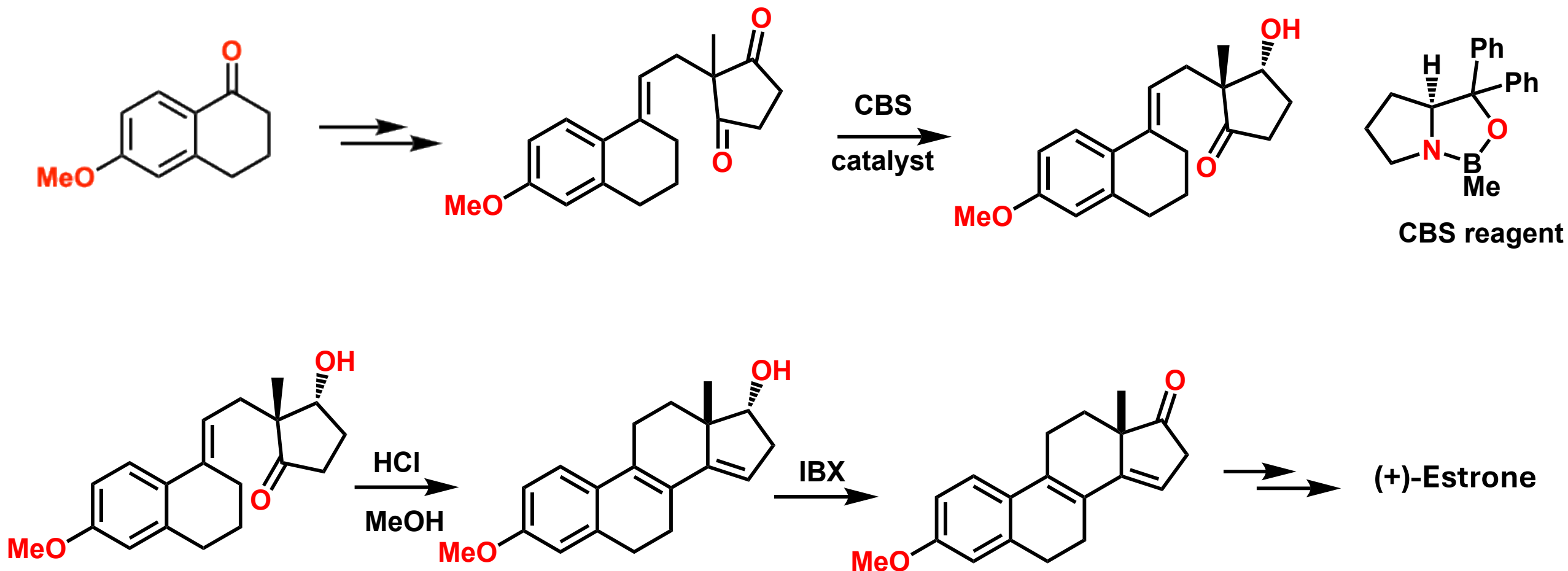


Torgov., *Tetrahedron Lett.*, 1963, 4, 1553.

Preparation of 6-OMe-Tetralone

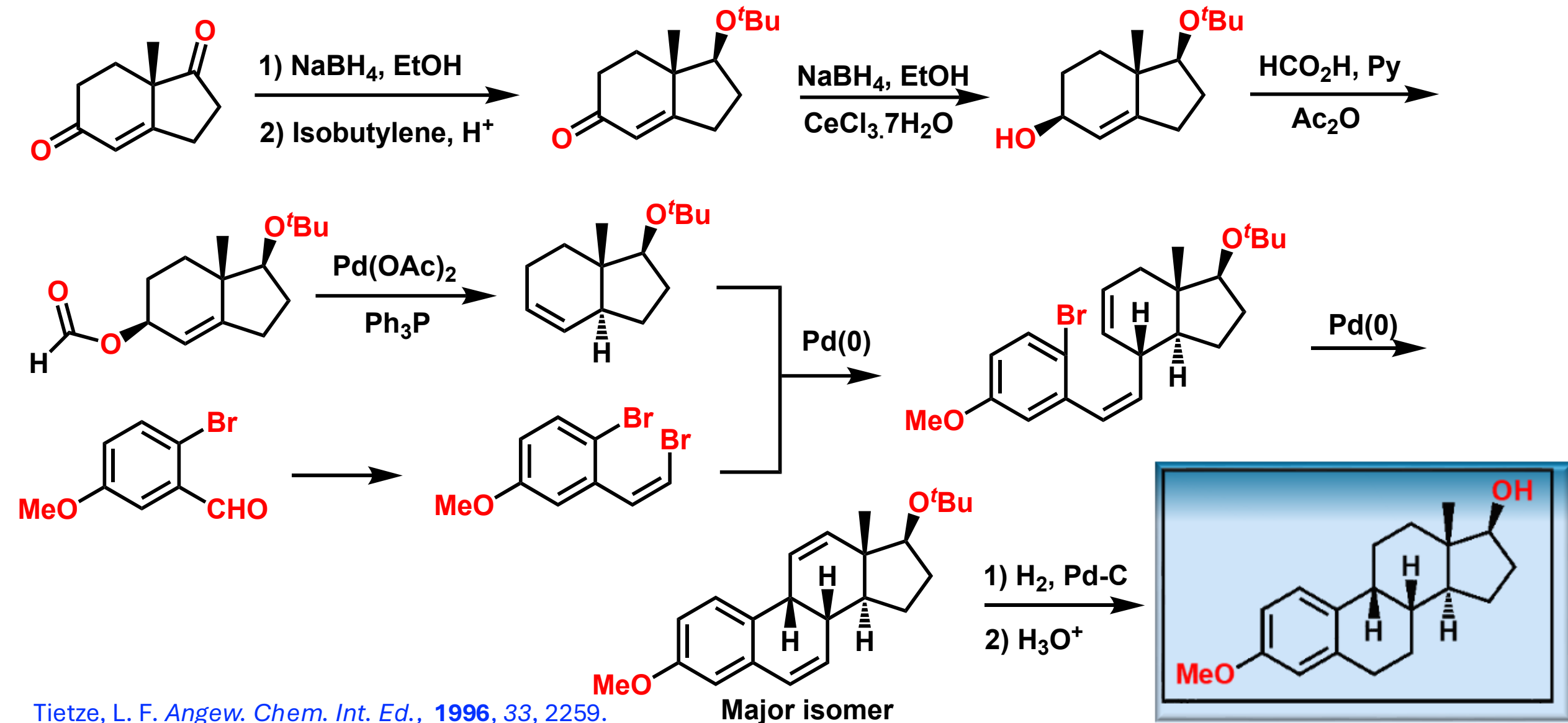


Corey's Asymmetric Synthesis of Estrone



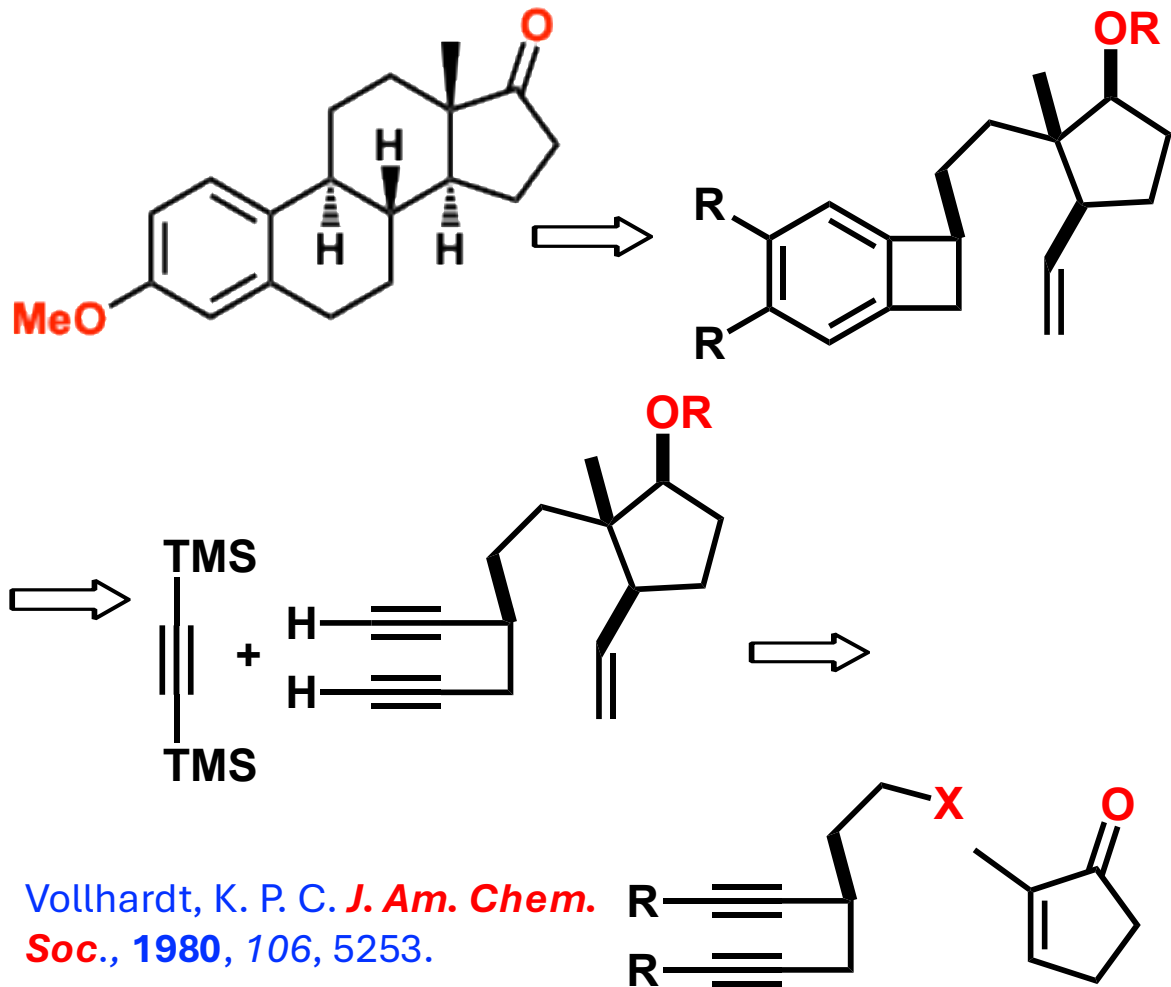
Corey, E.J. *J. Am. Chem. Soc.*, 2007, 129, 10346.

Tietze's Synthesis of Estradiol Methyl Ether

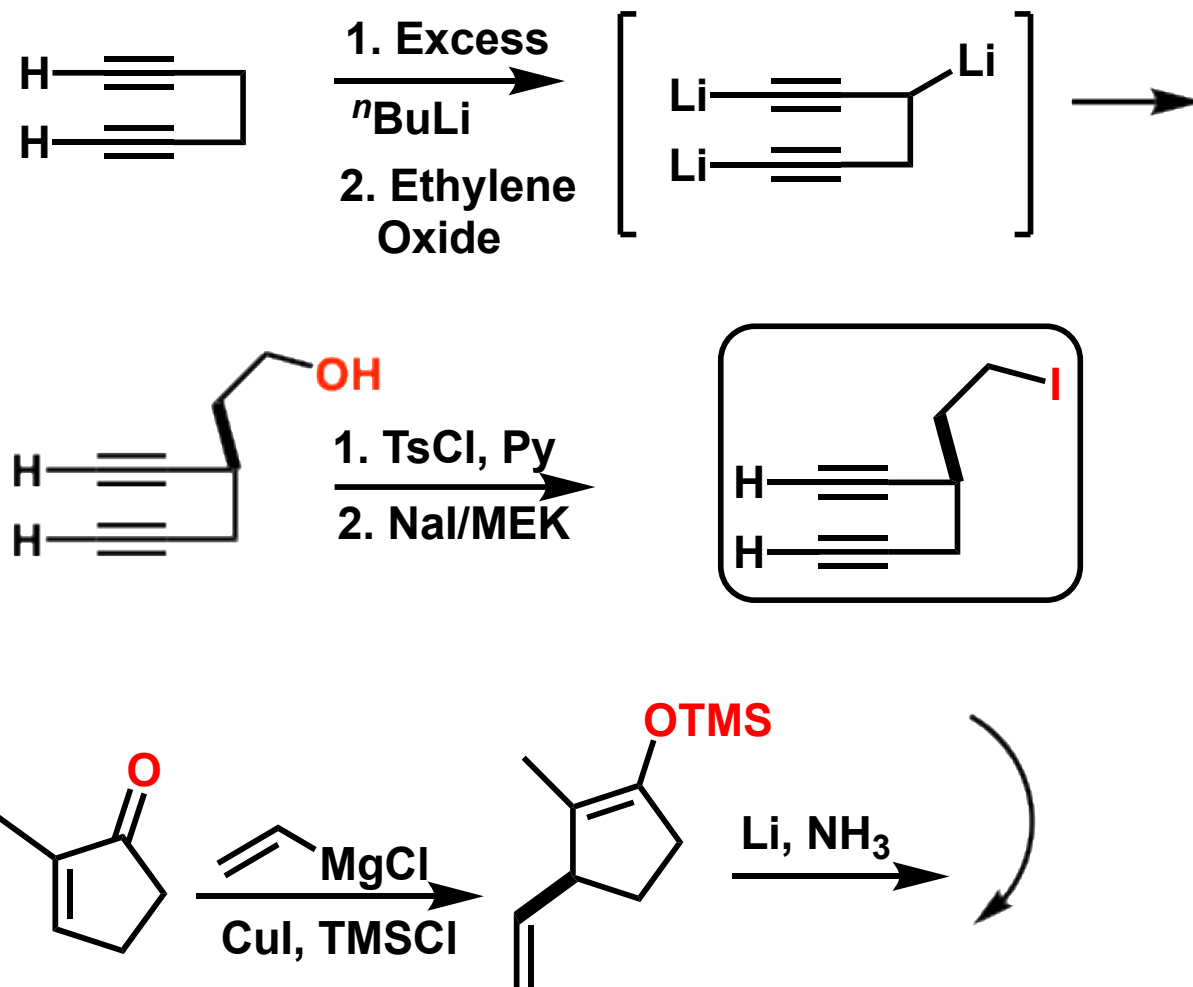


Vollhardt's Synthesis of Estrone

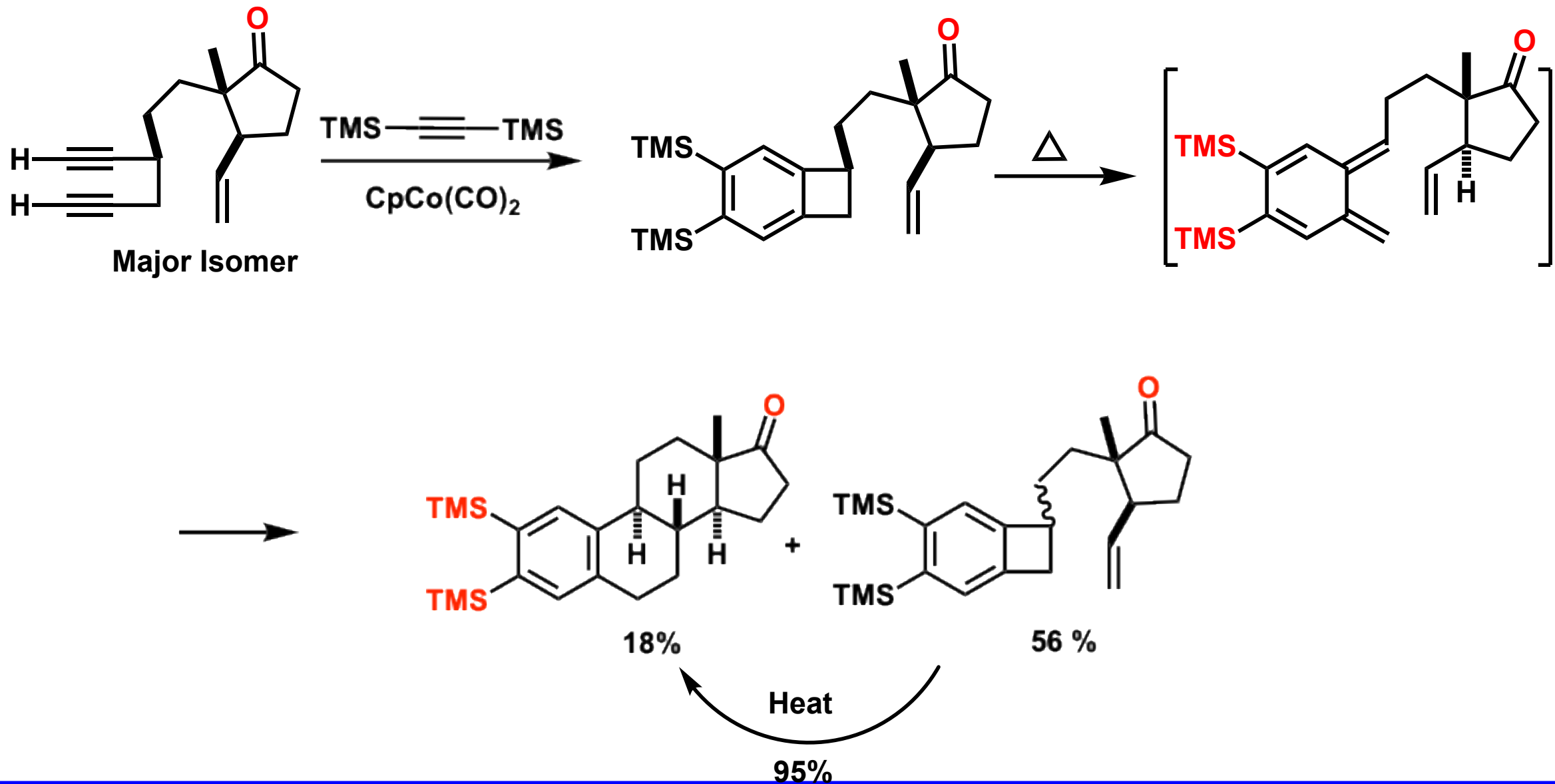
[2+2+2]-Cycloaddition Reaction



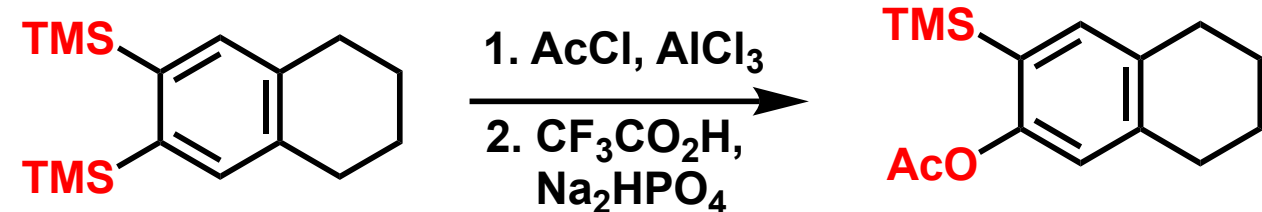
Synthesis of Estrone



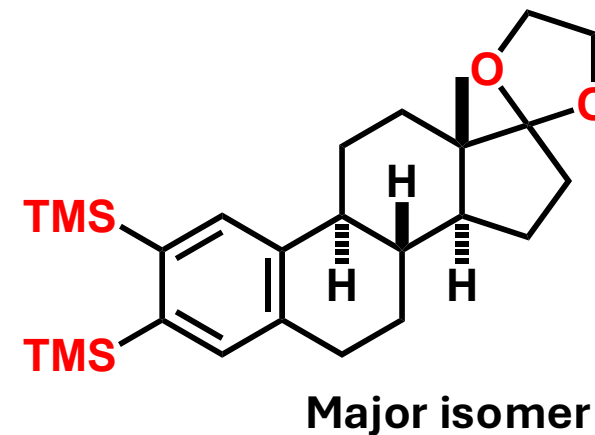
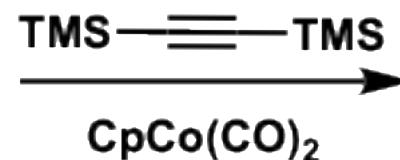
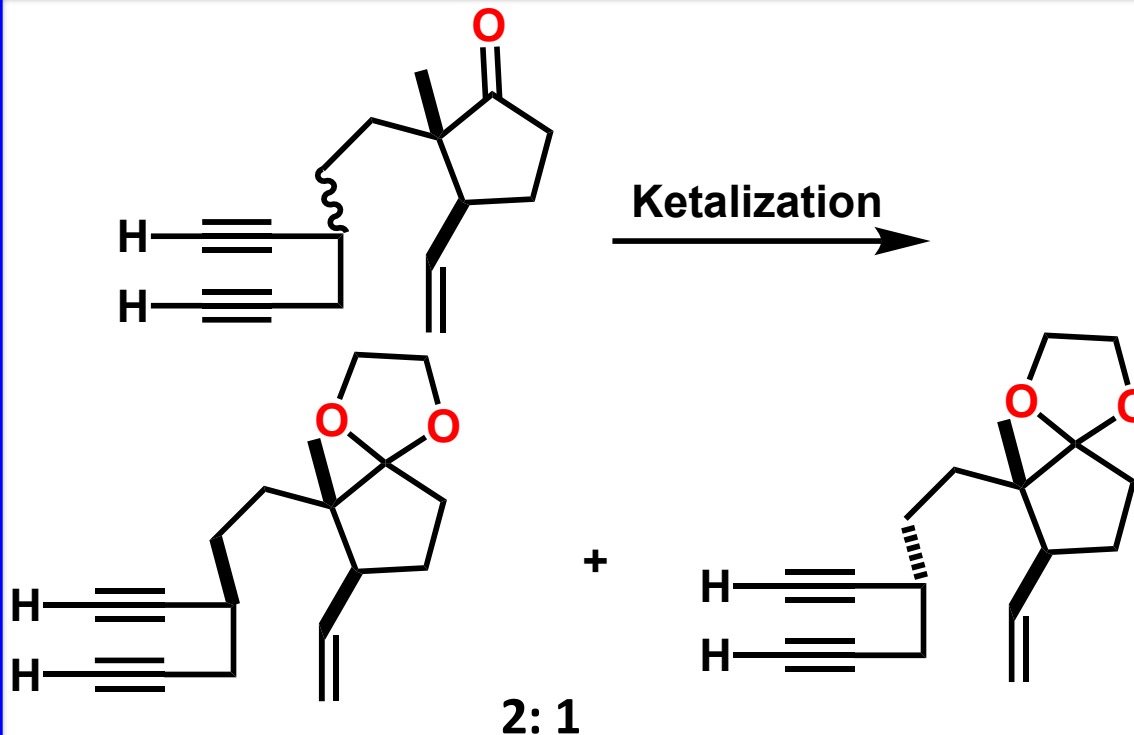
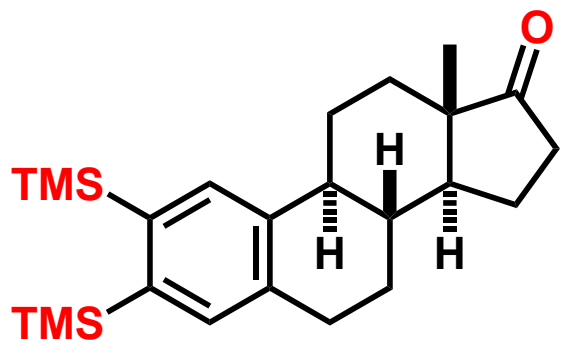
Vollhardt's Synthesis of Estrone



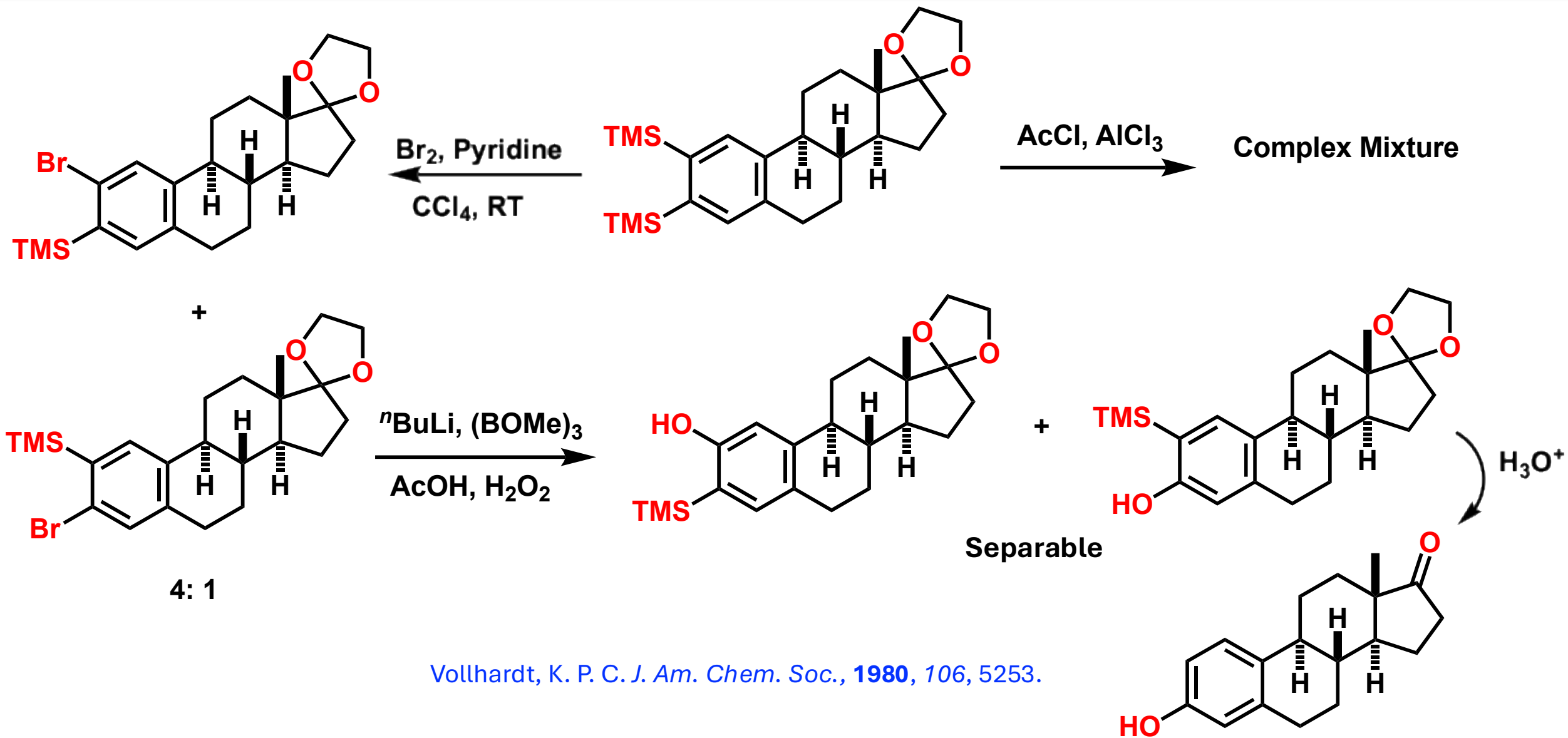
Model Studies



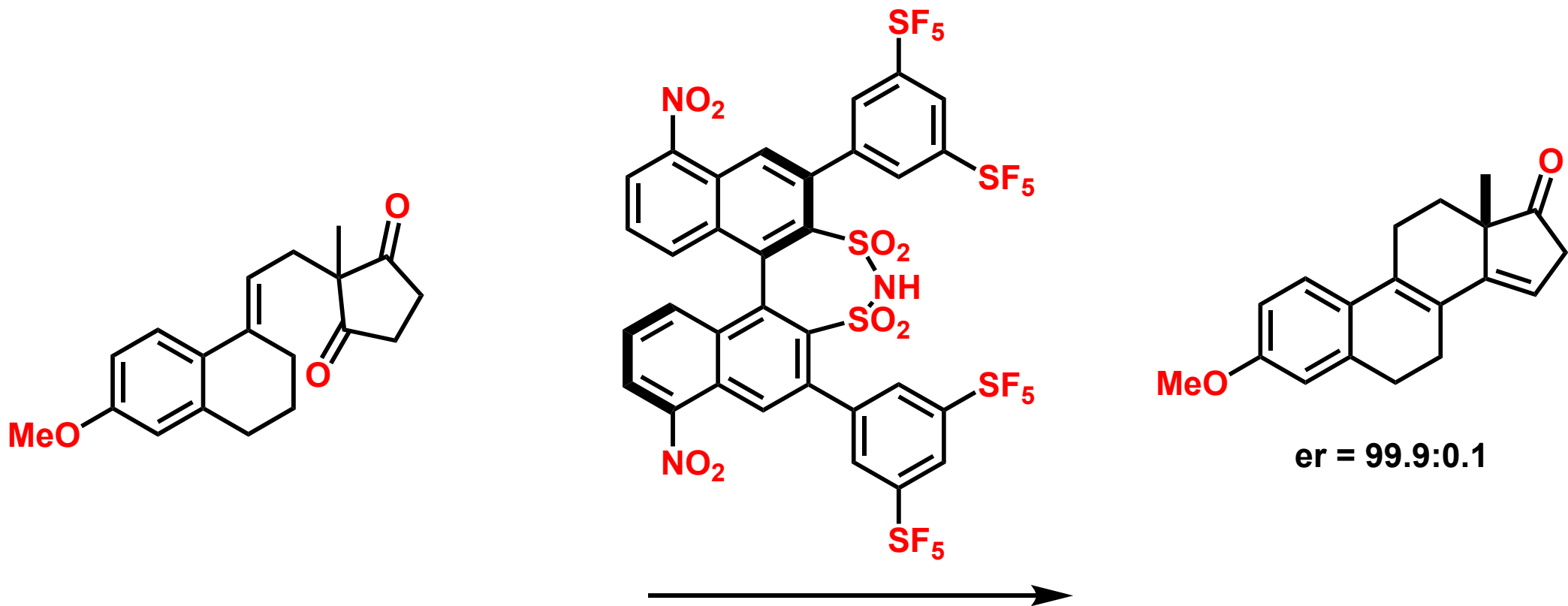
Extending this successful strategy to the below tetracyclic compound requires protection of the keto group to **avoid** Baeyer-Villiger oxidation



Vollhardt's Synthesis of Estrone

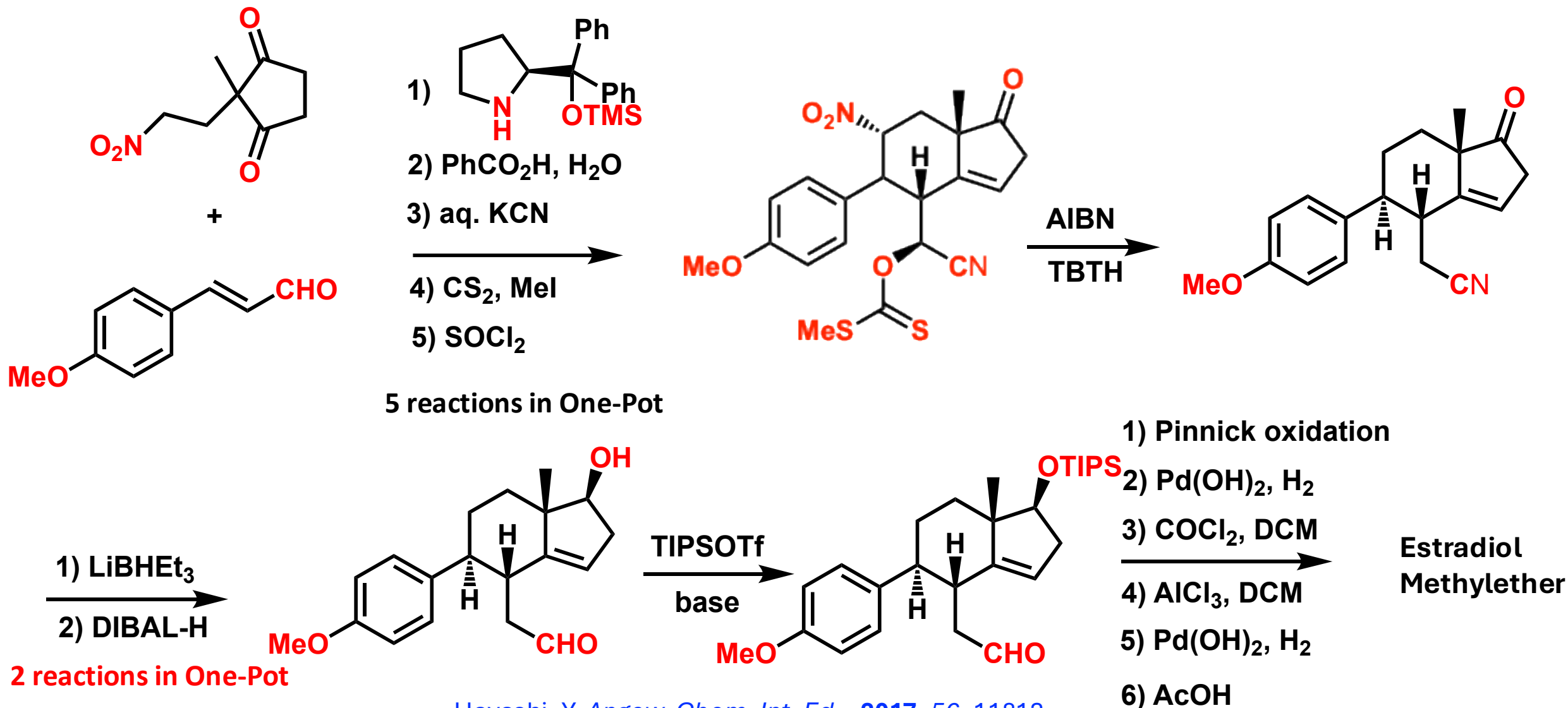


List's Synthesis of Estrone



List, B. *Angew. Chem. Int. Ed.*, 2014, 53, 8770.

Hayashi's Synthesis of Estrone



Hayashi, Y. *Angew. Chem. Int. Ed.*, 2017, 56, 11812.

Bruno's Synthesis of Estrone

