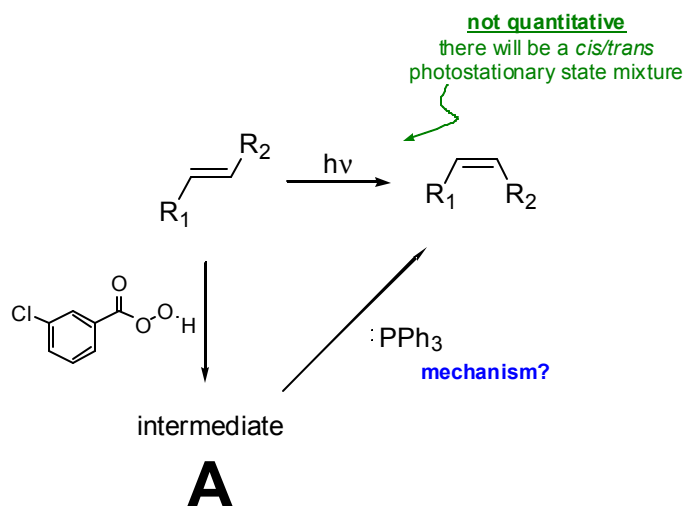


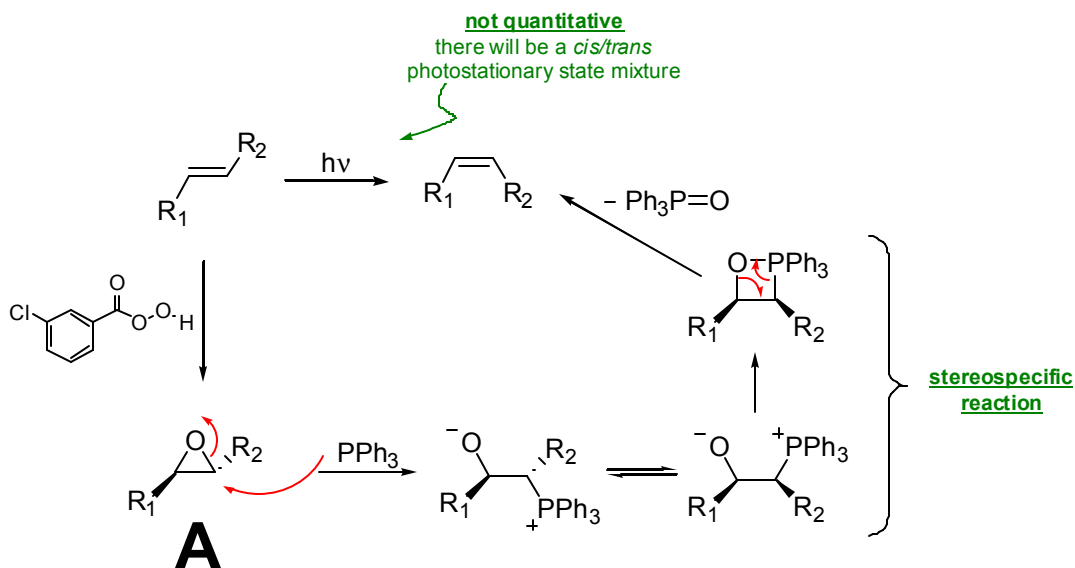
Section Solution Set

Carbonyl Chemistry and Carboxylic Acid Derivatives

Problem 1 An alternative to using UV irradiation to effect *cis/trans* isomerization of an olefin is treatment with *m*-chloroperbenzoic acid followed by triphenylphosphine. Provide a structure for the intermediate **A** and a mechanism for the second step.



Solution

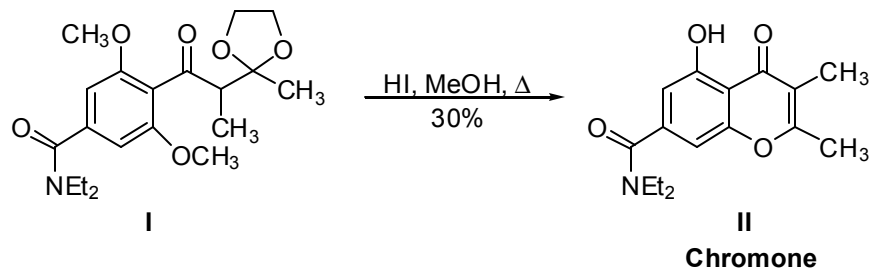


- The first reaction is a simple epoxidation
- Triphenylphosphine is an excellent nucleophile. After it opens the epoxide, rotation around the central bond axis leads to formation of an oxaphosphetane that subsequently fragments. Recall from the Wittig reaction that this is a very energetically favorable process.

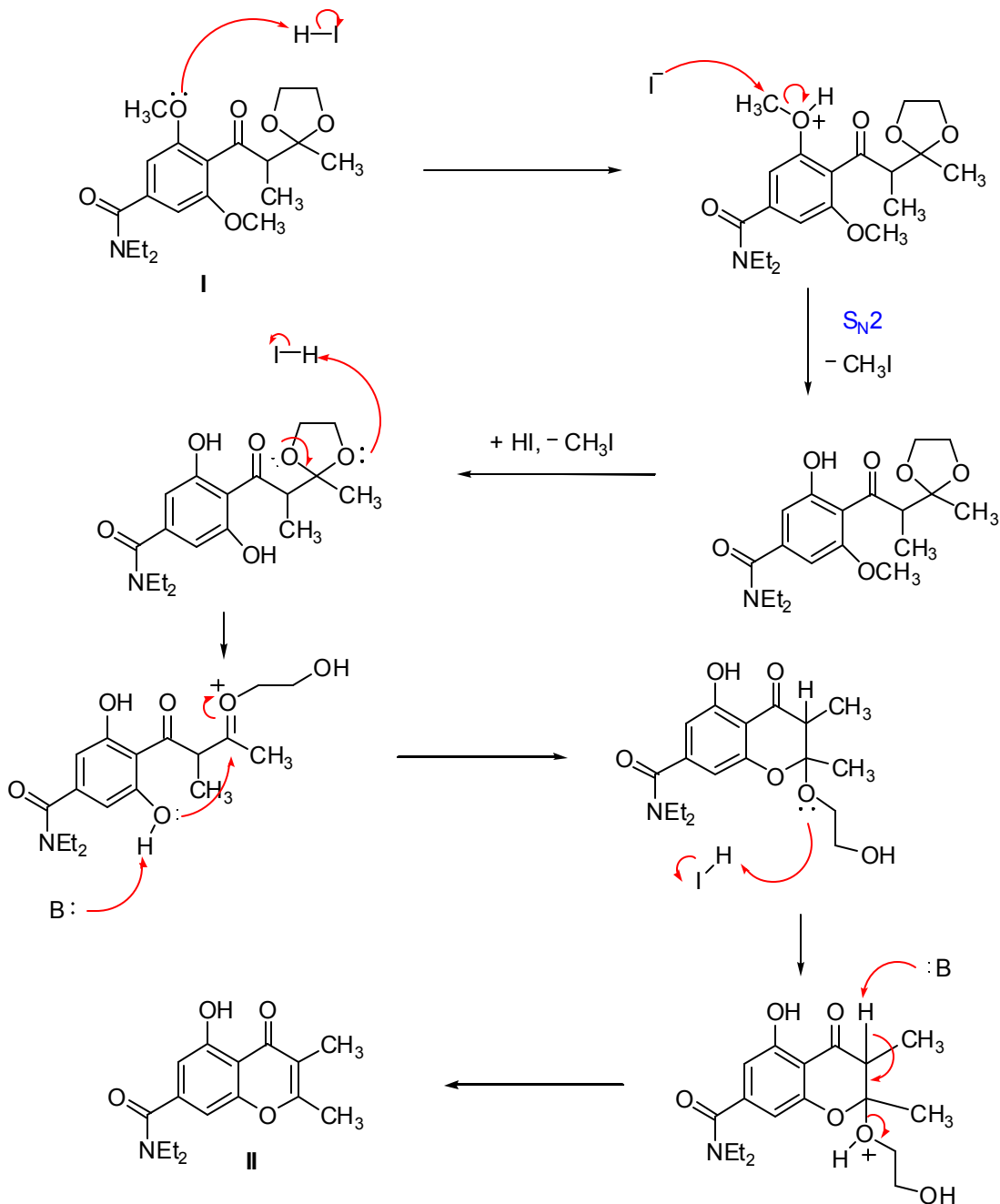
Key Lessons

- Mechanisms you learn in one context (here the Wittig olefination) are often applicable to ostensibly very different reactions. These reactions make good exam problems.

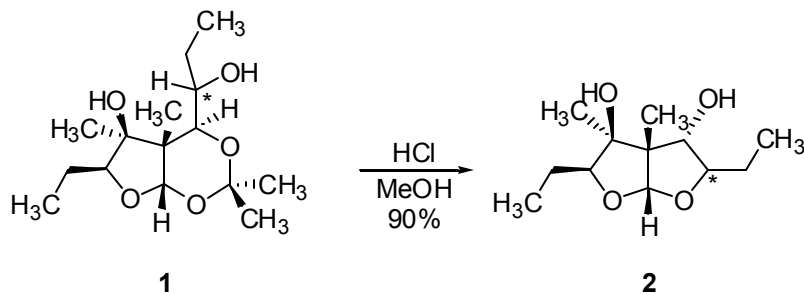
Problem 2 (from Fall 2003 Chem 30 Problem Set #2). Recently, Evans and coworkers developed a concise synthesis of chromone (compound II), an intermediate on their synthetic route to the natural product stachyflin A. In a single-pot process that provides a lot of bang for the buck, compound I is transformed into chromone when heated at reflux in methanolic hydroiodic acid. Provide a mechanism for this transformation.



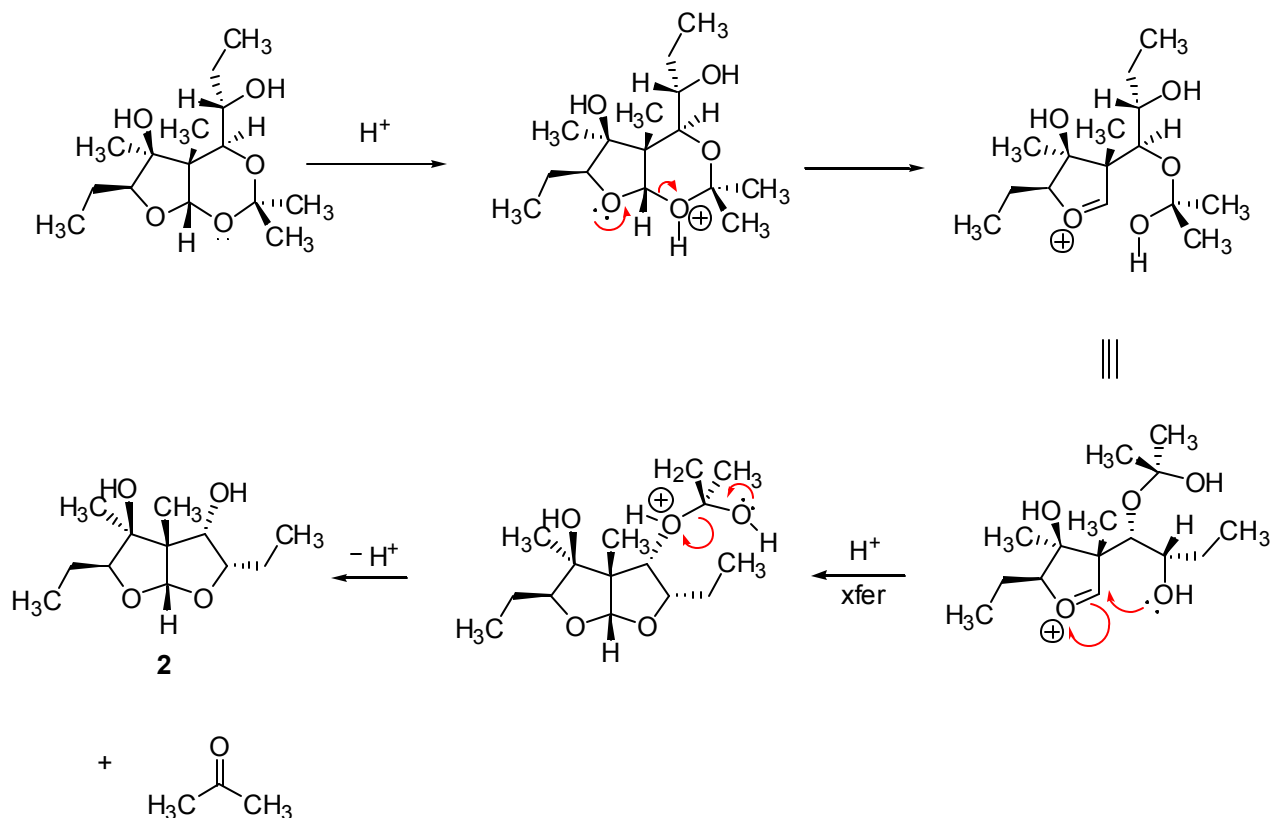
Solution



Problem 3 (also from Fall 2003 Chem 30 Problem Set #2). In a total synthesis project conducted in the lab of Prof. Stuart Schreiber at Harvard, compound **1** was converted to the bis(tetrahydrofuran) derivative **2** upon treatment with acid. Provide a mechanism for this transformation.



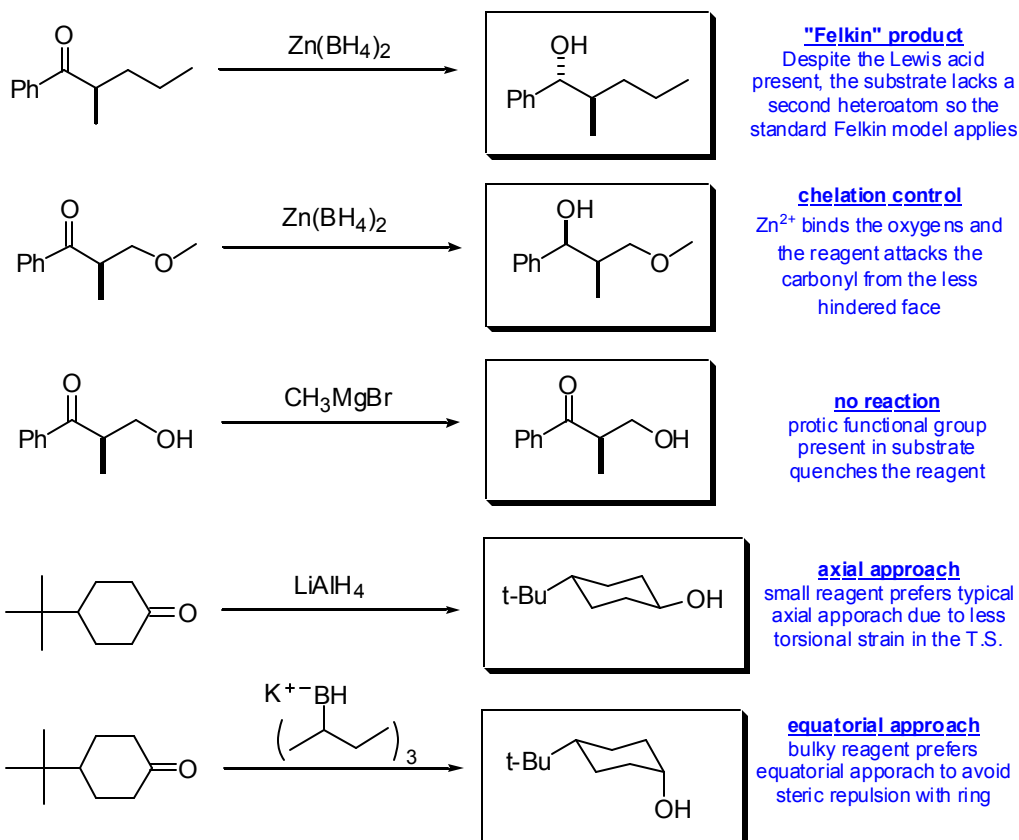
Solution



- Note: In this mechanism and the last, non-concerted processes have been combined in some steps to save time and space.

Problem 5 Given the substrates and reagents, predict the major product in the following reactions. Assume that one equivalent of the reagent is used and that acidic workups are performed in each case. Be sure to indicate stereochemistry in your products—that's the whole point of this problem!

Solution



Key Lessons

- The first pair is meant to demonstrate the different results of Felkin and chelate control.
- The last pair of reactions is meant to demonstrate that unless a nucleophile is bulky, attack from an axial approach will be faster when adding nucleophiles to cyclohexanones.
- Practice these sorts of problems and refer to the section five handout if you are having difficulty understanding these important models.
- The third reaction is a trick question. When a protic substrate is treated with a Grignard reagent, the acid-base reaction is fast, so no carbonyl addition occurs. You must use one more equivalent of reagent than the number of acidic hydrogens present. Another common trick question is to leave out the acidic workup and ask for the product, which will be an alkoxide salt. Always stay on your toes; don't lose dumb points.