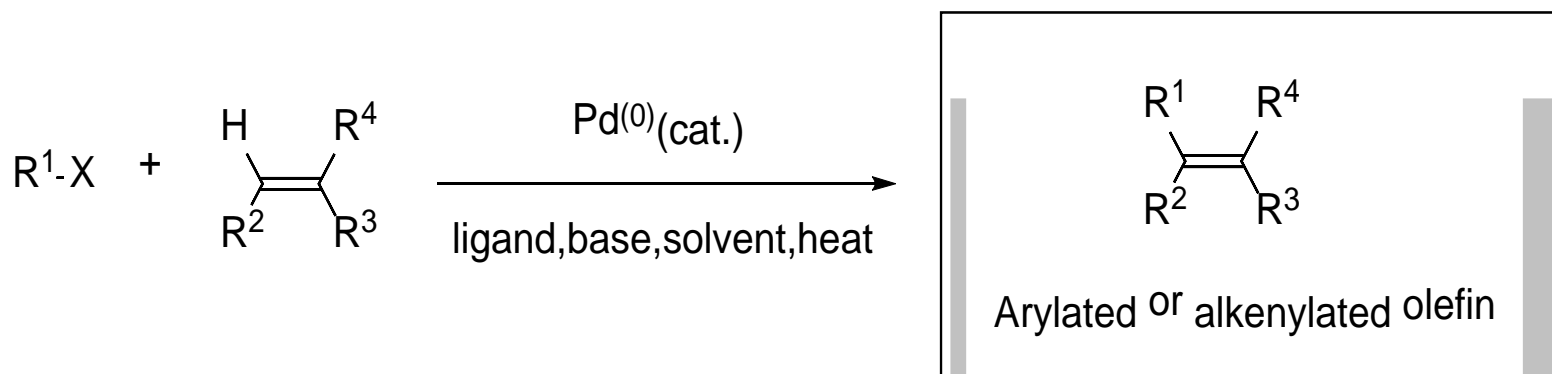


Heck Reaction

In the early 1970s, T. Mizoroki and R.F. Heck independently discovered that aryl, benzyl and styryl halides react with olefinic compounds at elevated temperatures in the presence of a hindered amine base and catalytic amount of Pd⁽⁰⁾ to form aryl-, benzyl-, and styryl-substituted olefins. The palladium-catalyzed arylation or alkenylation of olefins is referred to as the Heck reaction



R¹=aryl, benzyl, vinyl(alkenyl), alkyl (no β hydrogen); R², R³, R⁴=alkyl, aryl, alkenyl; X=Cl, Br, I, OTf, OTs, N₂⁺;
 ligand=trialkylphosphines, triarylphosphines, chiral phosphines; base=2 or 3 amine, KOAc, NaOAc, NaHCO₃

The general features:

- 1) it is best applied for the preparation of disubstituted olefins from monosubstituted ones;
- 2) the electronic nature of the substituents on the olefin only has limited influence on the outcome of the reaction; it can be either electron-donating or electron-withdrawing but usually the electron poor olefins give higher yields;
- 3) the reaction conditions tolerate a wide range of functional groups on the olefin component: esters, ethers, carboxylic acids, nitriles, phenols, dienes, etc., are all well-suited for the coupling, but allylic alcohols tend to rearrange;
- 4) the reaction rate is strongly influenced by the degree of substitution of the olefin and usually the more substituted olefin undergoes a slower Heck reaction;
- 5) unsymmetrical olefins (e.g., terminal alkenes) predominantly undergo substitution at the least substituted olefinic carbon;

6) the nature of the X group on the aryl or vinyl component is very important and the reaction rates change in the following order: I > Br ~ OTf >> Cl;

7) the R1 group in most cases is aryl, heteroaryl, alkenyl, benzyl, and rarely alkyl (provided that the alkyl group possesses no hydrogen atoms in the β -position), and these groups can be either electron-donating or electron-withdrawing;

8) the active palladium catalyst is generated in situ from suitable precatalysts (e.g., Pd(OAc)₂, Pd(PPh₃)₄) and the reaction is usually conducted in the presence of monodentate or bidentate phosphine ligands and a base;

9) the reaction is not sensitive to water, and the solvents need not be thoroughly deoxygenated;

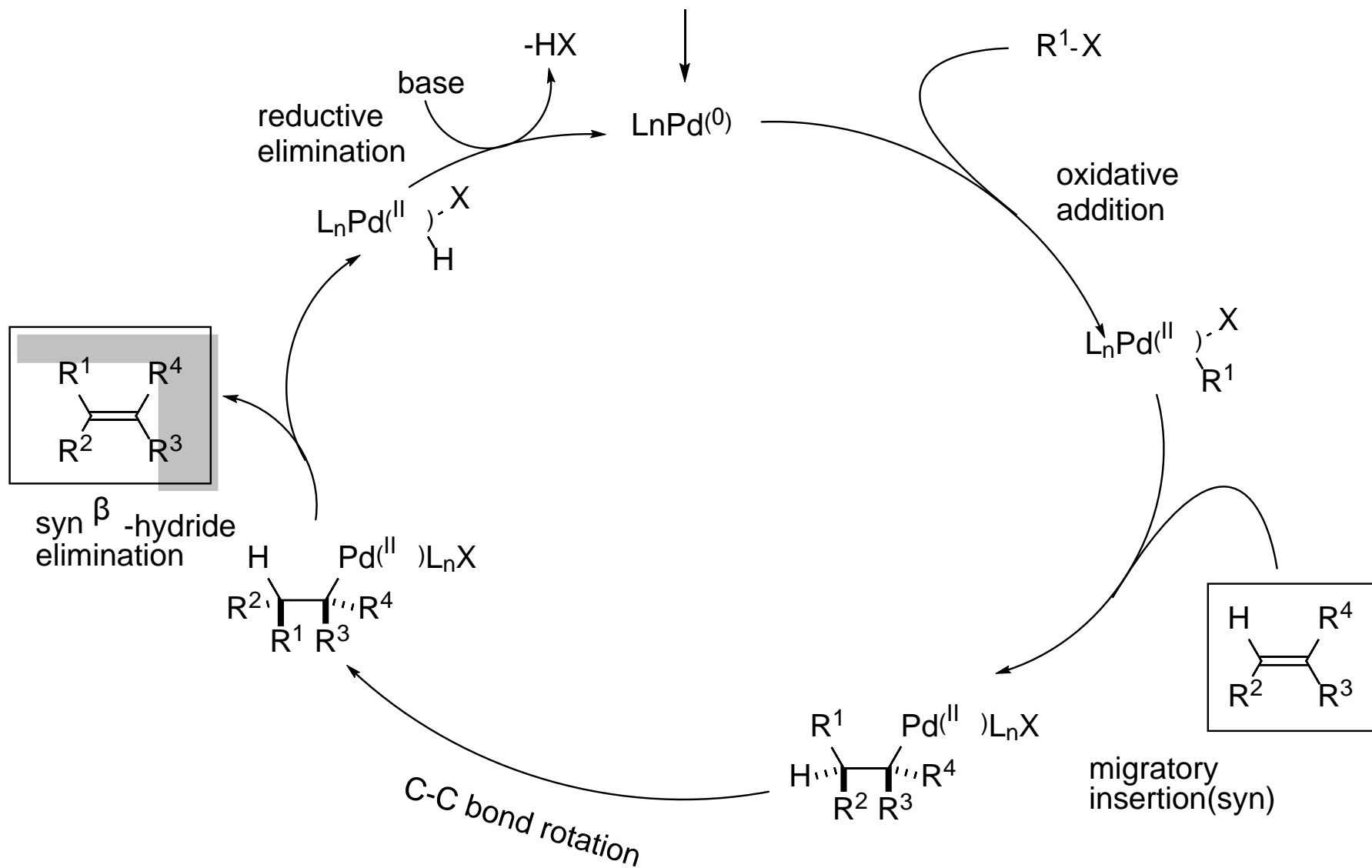
10) the Heck reaction is stereospecific as the migratory insertion of the palladium complex into the olefin and the β -hydride elimination both proceed with syn stereochemistry.

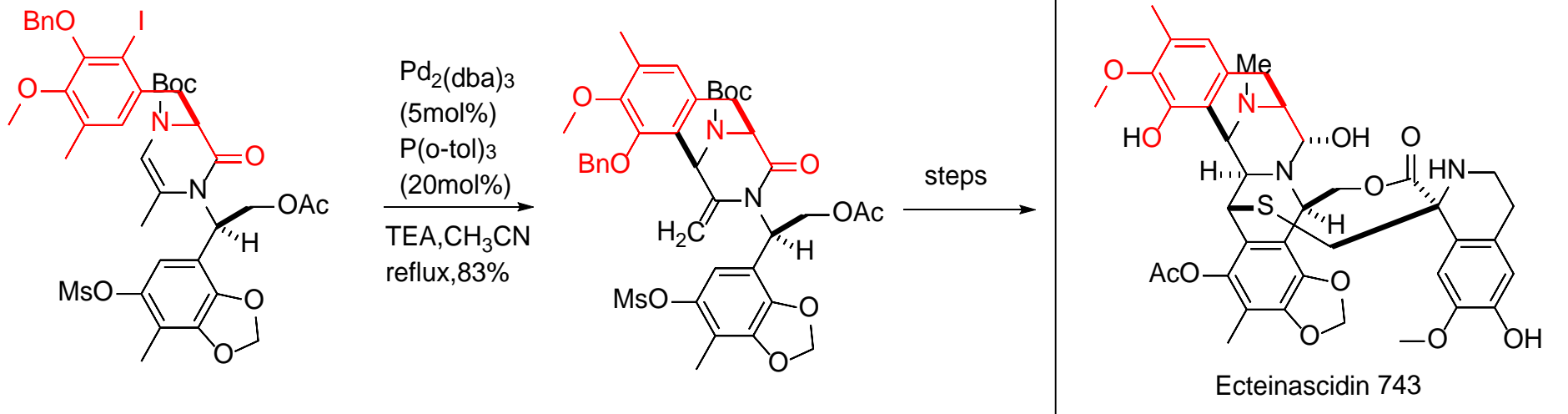
There are a couple of drawbacks of the Heck reaction: 1) the substrates cannot have hydrogen atoms on their β -carbons, because their corresponding organopalladium derivatives tend to undergo rapid β -hydride elimination to give olefins; and 2) aryl chlorides are not always good substrates because they react very slowly.

Several modifications were introduced during the past decade: 1) asymmetric versions; 2) generation of quaternary stereocenters in the intramolecular Heck reaction; 3) using water as the solvent with water-soluble catalysts; and 4) heterogeneous palladium on carbon catalysis.

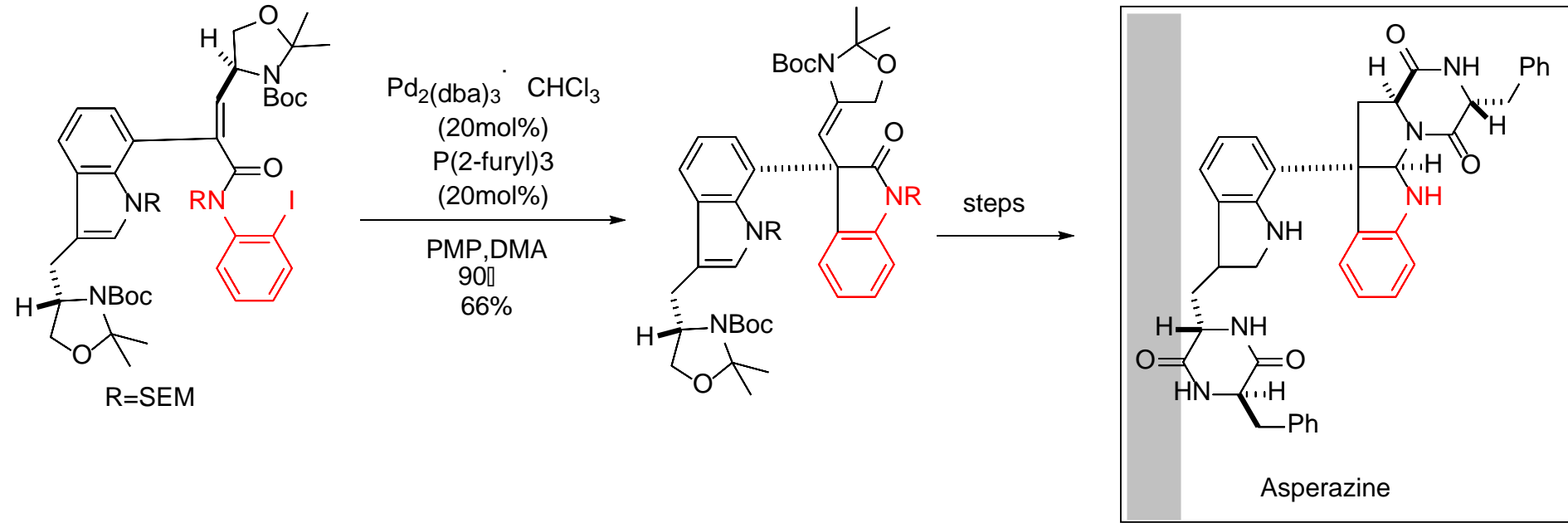
Mechanism

Pd(0) or Pd(II) complexes (precatalysts)

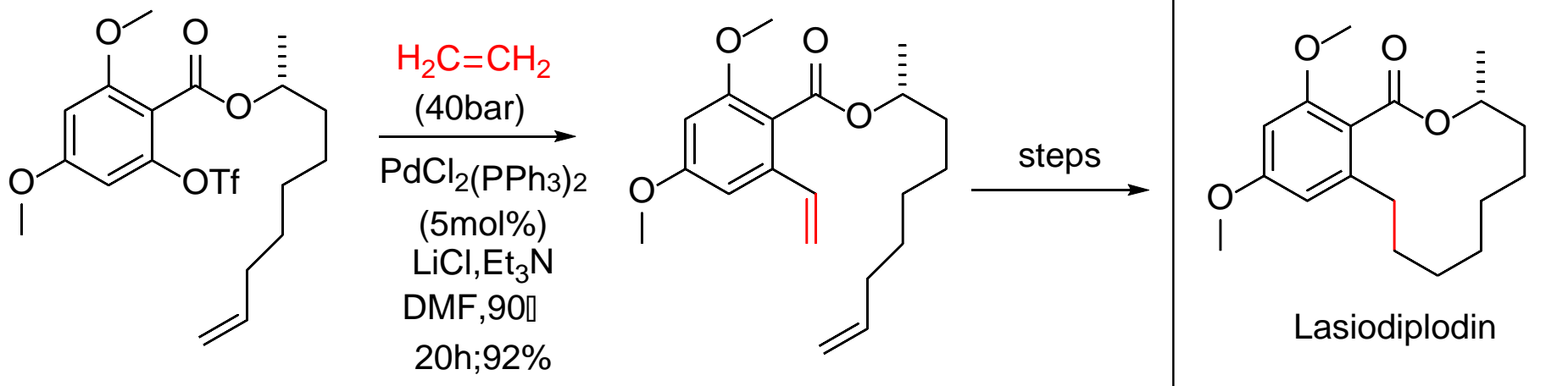




Applications



Applications



Applications