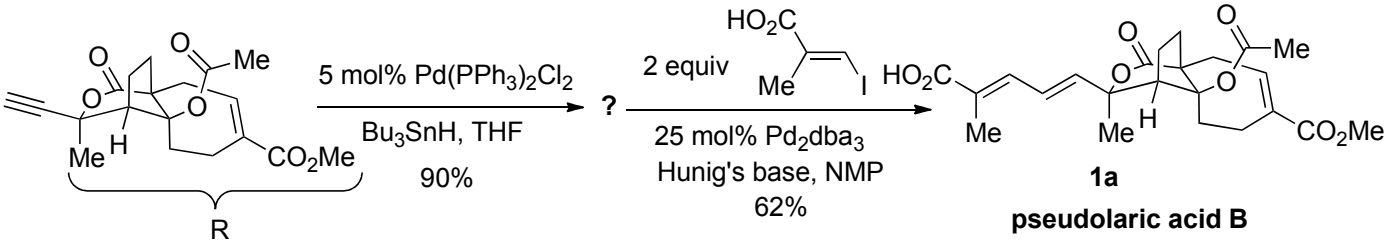
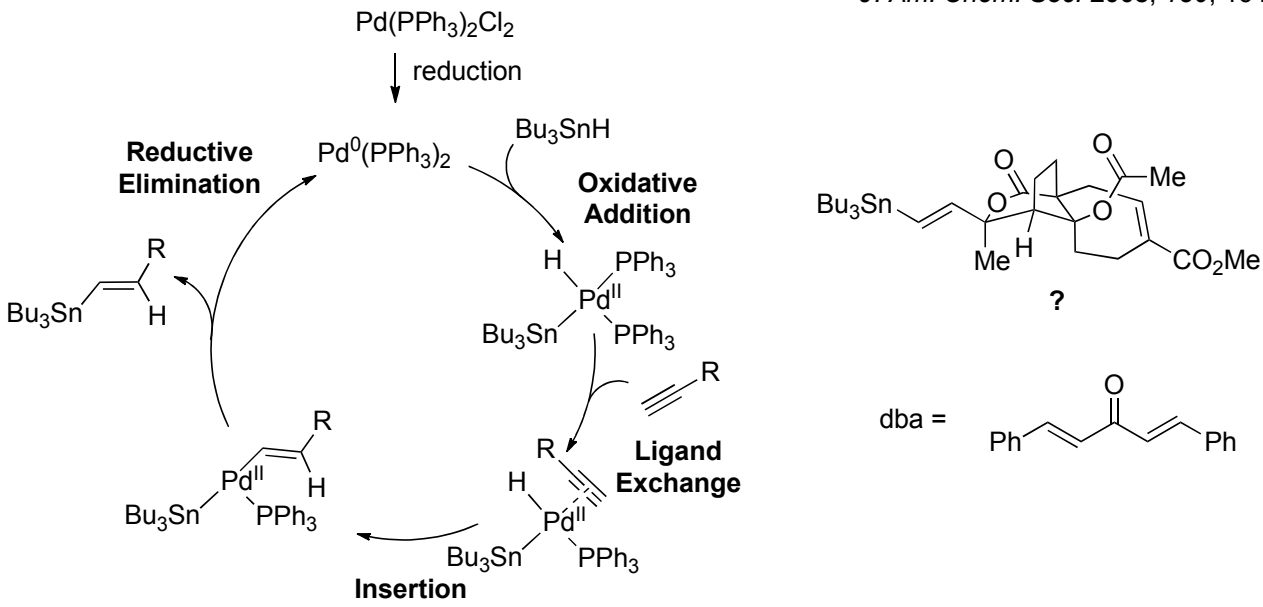
Series 4: Transition metals in organic synthesis - Solutions

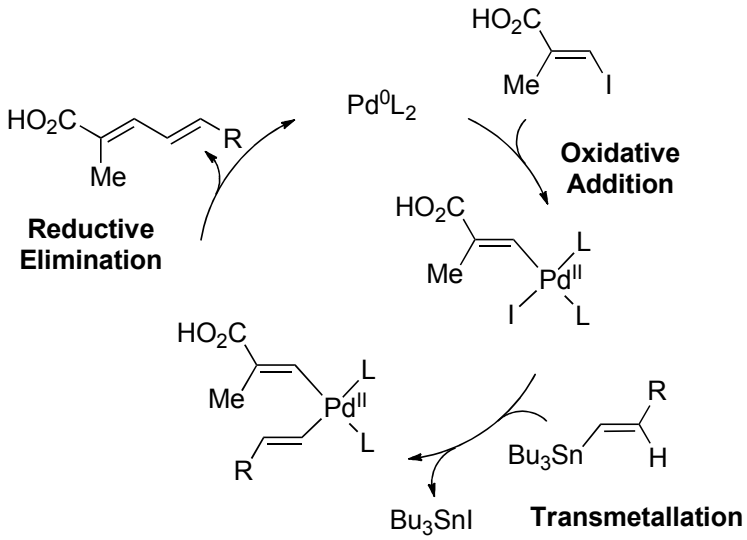
Exercise 1



J. Am. Chem. Soc. **2008**, *130*, 16424.

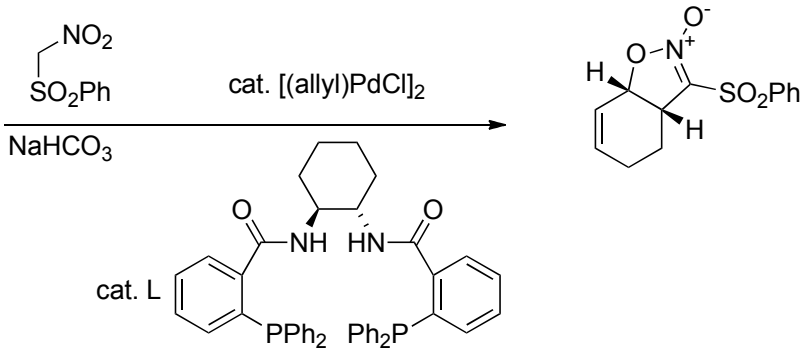


The first step in the reaction is a Pd-catalyzed hydrostannylation of a terminal alkyne, very similar to the general addition to olefins in the script (page 103). The Pd(II) precatalyst is first reduced to Pd(0), either by the phosphine or through the tributyltin hydride. After oxidative addition of the tributyltin hydride, coordination and insertion of the acetylene occurs. The insertion into the Pd-H bond is favored because of steric reasons. Finally, reductive elimination gives the vinyl stannane, which is the product obtained after the first step. As it is a *syn*-difunctionalization, the reaction generates the *trans* olefin with high selectivity.

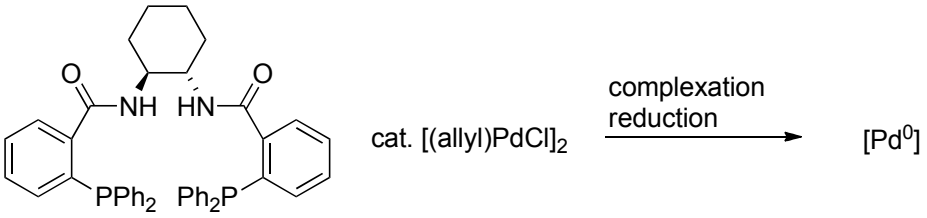


The second step is a classical Stille coupling, proceeding via oxidative addition, transmetallation and reductive elimination. The base is required to prevent protodematallation promoted by the acid. dba (dibenzylidene acetone) is a useful ligand for Pd(0). The mild conditions allows to construct the side chain of this complex natural product with good selectivity.

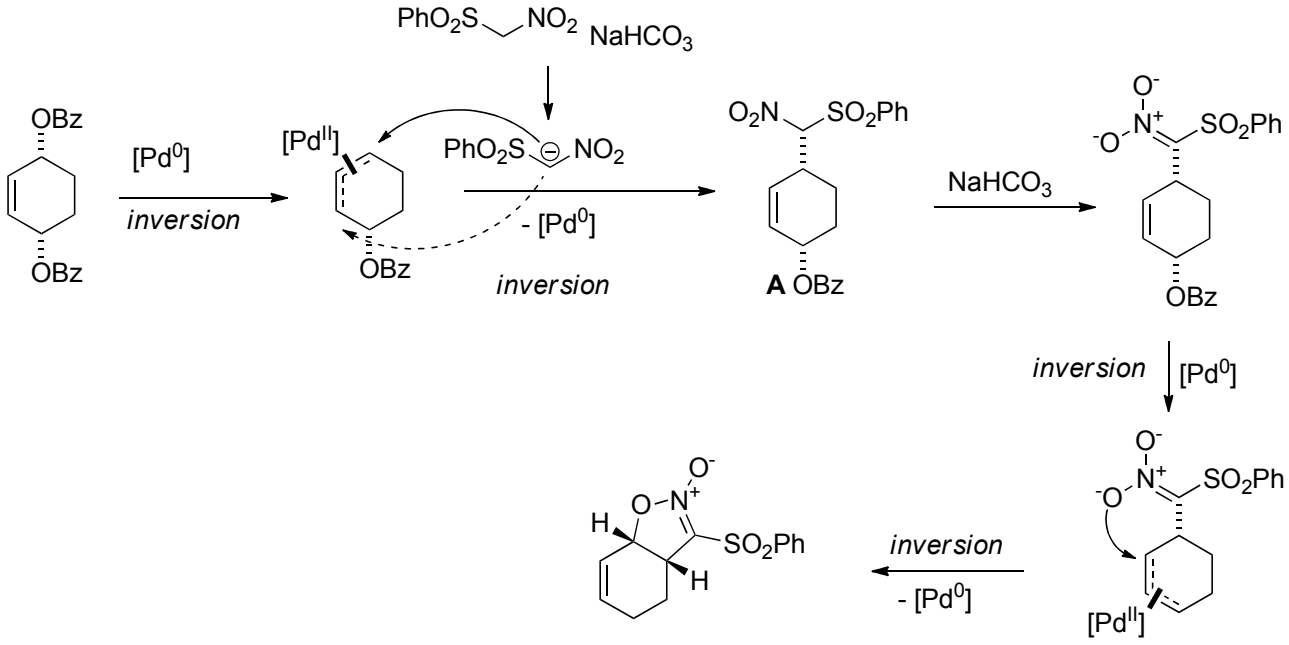
Exercise 2 Propose a mechanism for this reaction comprising two consequtive individual steps.



J. Am. Chem. Soc. 1998, 120, 1732-1740



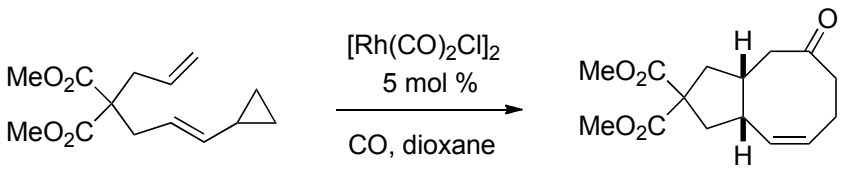
At first, the ligand complexes the palladium(II) metal. Under the reaction conditions a reductive elimination to a Pd(0)-complex [Pd^0] occurs. (The reaction is enantioselective, but we do not look a the transition state responsible for this selectivity.)



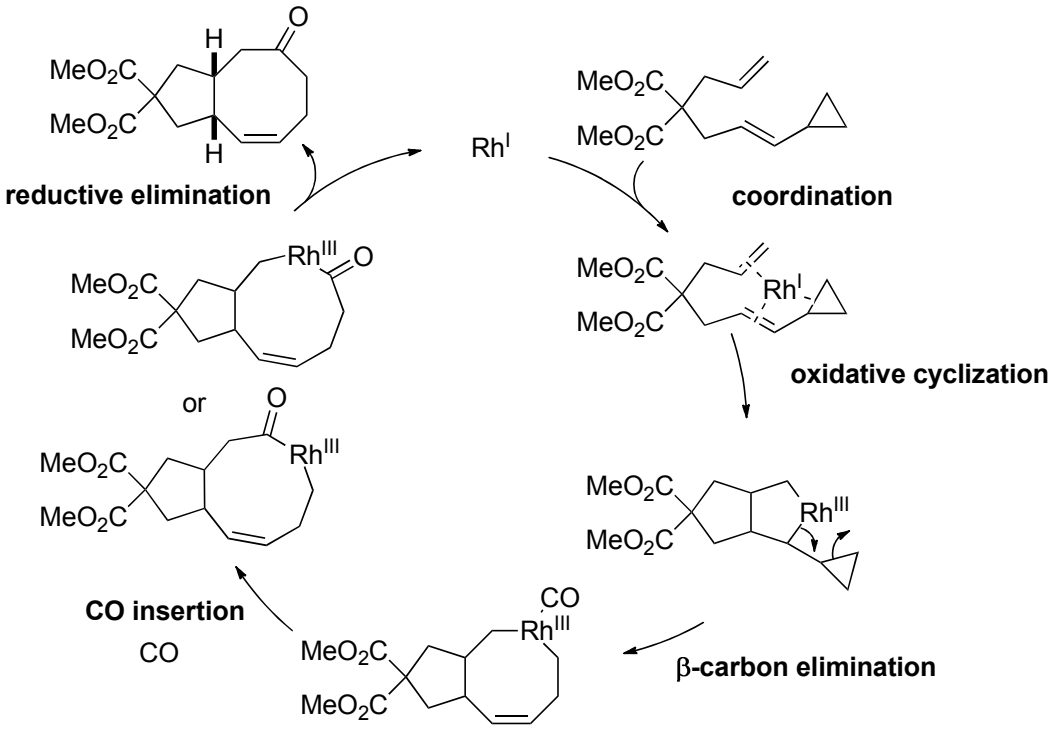
The reaction is overall a double palladium-catalyzed allylic alkylation. First, the symmetrical double allylic benzoate is selectively transformed the a pi-allyl-Pd(II)-complex. The chiral ligand decides which benzoate. This occurs under inversion of the configuration. The nitrosulfone is highly acidic (pka = 7.1). Thus it is deprotonated by a sodium bicarbonate and converted into a very good and soft C-nucleophile. This reacts again under inversion to give intermediate **A**. The alternative allylic position is sterically more congested and therefore not preferred.

The product **A** is still highly acidic and deprotonated to the nitronate. Next, a second pi-allyl-Pd(II)-formation occurs. As there is no more external nucleophile available, the anionic oxygen-atom of the nitro group is the attacking nucleophile. This closes the five-membered ring gives the product and releases the initial Pd(0)-catalyst.

Exercise 3



J. Am. Chem. Soc. **2007**, *129*, 10060.



This example of a [5+2+1] cycloaddition by Wender demonstrates the capacity of Rh catalysts for cyclization reactions. After coordination of the diene system, an oxidative cyclization occurs: the reaction of the two olefins form a metalacyclopentane. A beta-carbon elimination forms the metalacyclooctene. Until this step, everything is similar that for a normal [5+2] cycloaddition. However, under CO pressure, CO insertion is faster than reductive elimination and two different rhodium acyl complexes can be formed. Finally, reductive elimination gives the observed cyclooctanone. The observed diastereoselectivity for the ring junction is difficult to rationalize for this case.