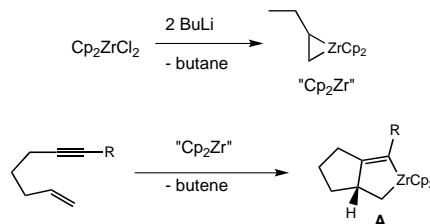
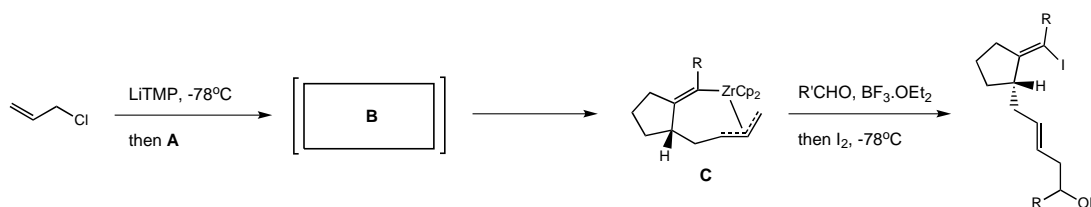


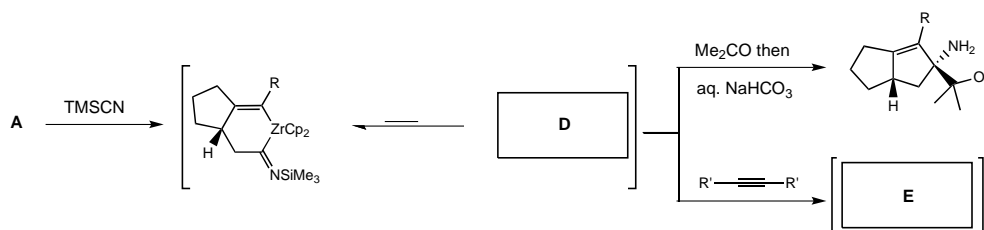
1) Elaboration of Zirconacycles. The intramolecular reductive coupling of 1,*n*-dienes, -enynes, and -diynes induced by the electrophilic zirconocene equivalent "Cp₂Zr" gives zirconacyclopentenes such as **A**. A number of methods for the elaboration of the resulting zirconacycles have been developed.



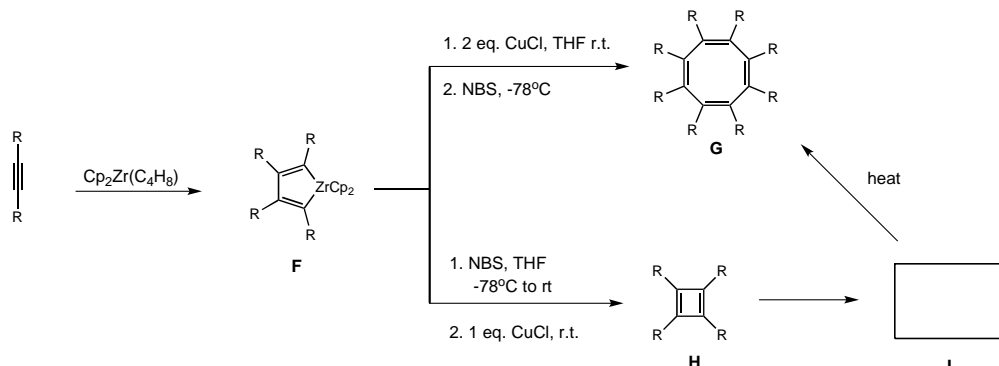
(A) Provide a mechanism for the formation of "Cp₂Zr" and its conversion to allyl complex **C**, which can be functionalized by insertion of electrophiles into the pi-allyl complex followed by proto- or halogenolysis.



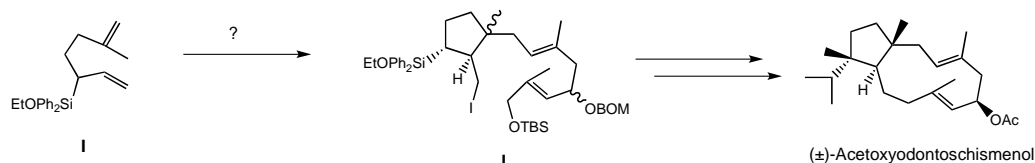
(B) Alternatively, insertion of TMSCN, presumably via the isocyanide isomer, into **A** leads to a ring-expanded iminoacyl complex. Trapping of this species with an electrophile leads to a substituted cyclopentenylamine, implying the intermediacy of species **D**. Insertion of an alkyne into **D** gives complex **E**, predict their structures and provide a mechanism for the process from **A**.



(C) Zirconacyclopentadiene **F** is formed by the intermolecular cyclization of alkynes. Transmetalation to copper and low temp. halogenolysis gives cyclooctatetraene **G** while reversing the order of these steps and using less copper cleanly gives **I**. Explain this with a detailed mechanism and also account for the conversion of cyclobutadiene **H** to **I** and then **G** at elevated temperatures.

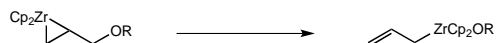


(D) Whitby used a one-pot, three component coupling mediated by zirconium to assemble all the carbons of the *trans*-bicyclo[9.3.0]tetradecane ring system in his synthesis of Acetoxodontoschismenol. Provide reagents and a mechanism for the conversion of **I** to **J**.

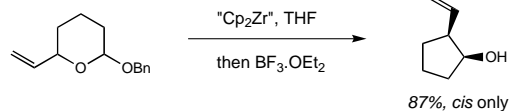


2) Zirconocene and Carbohydrates

(A) Complexes of "Cp₂Zr" and allyl ethers are known to generate allylic zirconiums:

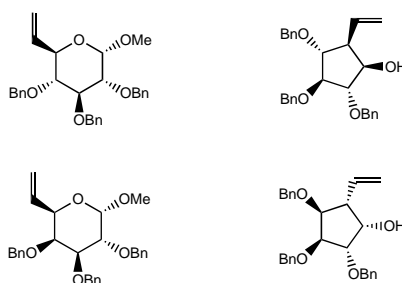


This chemistry has been used by Taguchi to develop a stereoselective ring contraction of vinyl carbohydrate derivatives. In the case of pyranoside substrates, the stereochemical relationships between the new chiral centers and inherent carbohydrate substituents were heavily dependent on the stereochemistry of the 4-substituent. Provide a mechanism for the reaction which accounts for the following stereochemical observations. (An NMR study of the complex formed prior to addition of BF₃·OEt₂ reveals the presence of a *cis* disubstituted olefin)

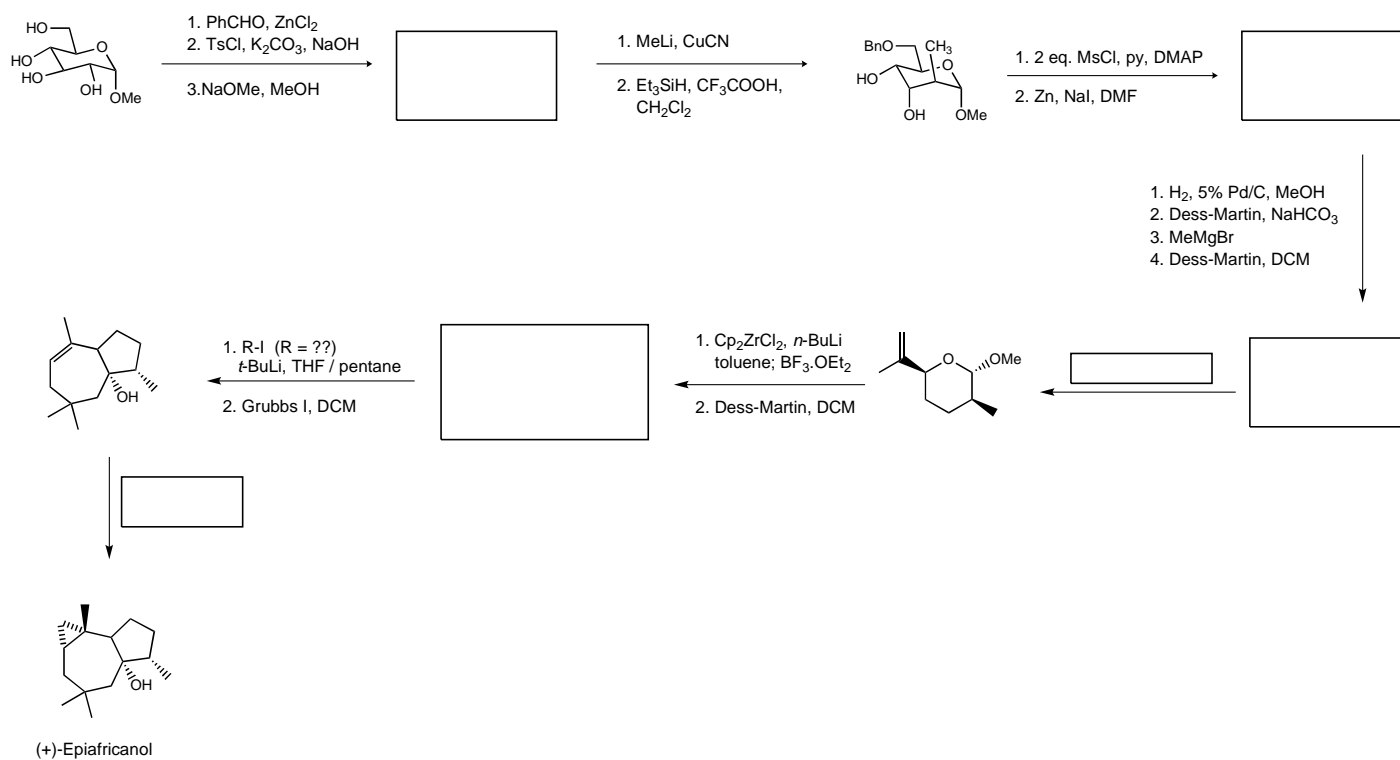


Reactant

Product



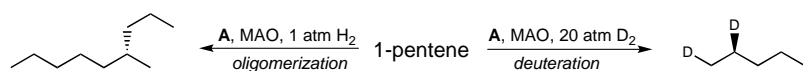
(B) Sugar in, terpene out: Paquette made use of the above transformation in his synthesis of (+)-Epiatricanol. Fill in the missing reagents and intermediates.



3) Chiral Zirconocenes

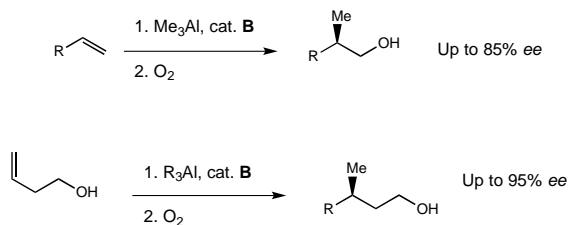


(A) C₂-symmetric *ansa*-metallocene (EBTHI)ZrCl₂ **A** has been shown to catalyze the asymmetric transformation of olefins in two related processes: polymerization (Ziegler-Natta process) and hydrogenation. An interesting observation was made by Weymouth: the induced stereochemistry of hydrogenation is opposite to that of similar oligomerization reactions using the same catalyst, for example:

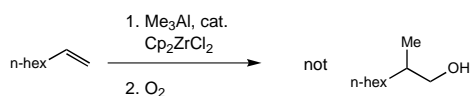


Assuming that olefin coordination is the enantioselective step, rationalize this observation with an analysis of the transition states for these two transformations.

(B) While much of the chemistry of chiral zirconocenes is dominated by polymerization reactions, an interesting enantioselective carboalumination of alpha-olefins has been developed by Negishi which is catalyzed by the neomenthyl-derived (NMI)₂ZrCl₂ **B**. After aerobic oxidation of the resulting alkylmetal species, 2-methyl-1-alkanols are obtained in high yields and with good *ee*. The reaction has been iteratively applied to the synthesis of reduced polypropionate natural products.

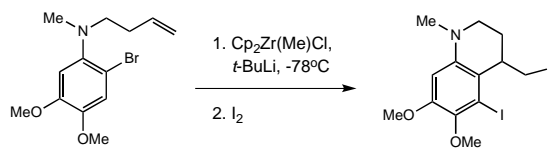


The development of this reaction had an interesting twist. After his initial discovery of methylalumination of alkynes catalyzed by Cp₂ZrCl₂, Negishi examined the analogous reaction of monosubstituted alkenes. Using Me₃Al / Cp₂ZrCl₂ and 1-octene he obtained a mixture of two alkenes with a trace amount of the expected alcohol, and yet the asymmetric version using (NMI)₂ZrCl₂ was found to work as advertised above. It was later found the expected alkylzirconium does form transiently. Explain what's going on with a catalytic cycle for the following reaction, predict the actual product(s) and rationalize why this doesn't happen with the neomenthyl-derived catalyst **B**:

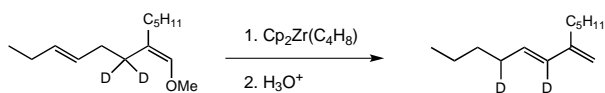


4) Assorted zirconocene madness. Provide mechanisms for the following transformations:

(A) Buchwald applied zirconocene to aromatic chemistry:



(B) Follow "Cp₂Zr" as it has its way with this diene:



(C) 10 C-C bonds formed in one pot, 2 broken. Enjoy.

