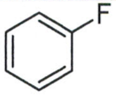
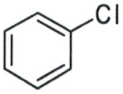
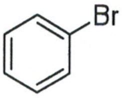
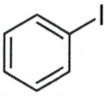
CHEM 344 Organometallic Chemistry Practice Problem Set (not for credit)

Summer 2013

Name (print): **ANSWER KEY**

1) The strength of the C-X bond of halobenzenes Ph-X was explored via computational chemistry in Chapter 5.

a) Explain the experimental bond dissociation enthalpy values shown below.

Ph-X	$\Delta H_{C\text{-}X}°$ (kcal/mol)
	127
	97
	84
	67

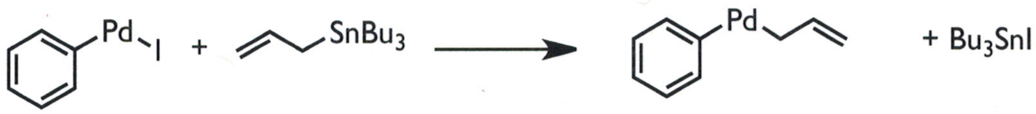
Larger ΔH° value = stronger C-X bond. With the increasing bond strength, the C-X bond distance will decrease. Stronger bond = shorter bond.

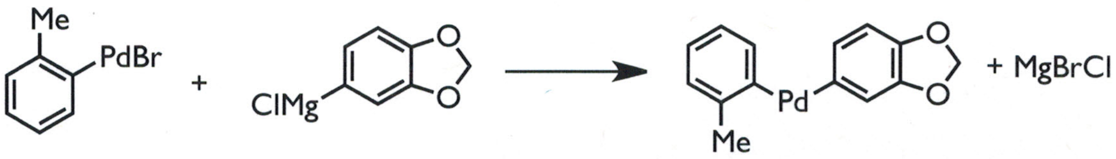
b) Briefly explain which of the above halobenzenes is the least reactive toward the oxidative addition of a metal such as Mg or Pd.

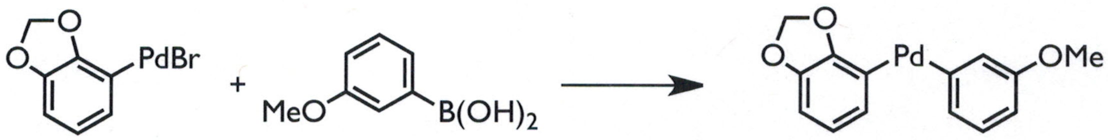
Fluorobenzene is the least reactive because the C-F bond is the strongest of the series and thus the oxidative addition step is most difficult.

2) Show all products of the following transmetallation reactions. The electronegativity values for each element shown in the handout may be useful (think about the nature of the C-M bond in the product(s)).

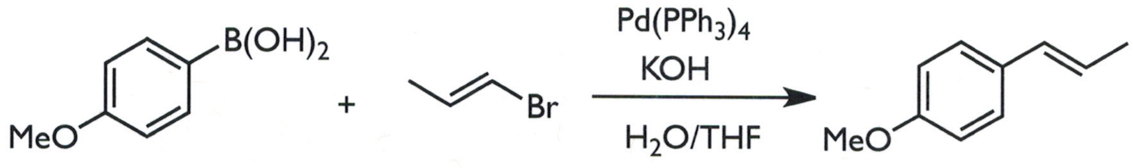
$2\ BuLi + CuI \longrightarrow Bu_2CuLi + LiI$





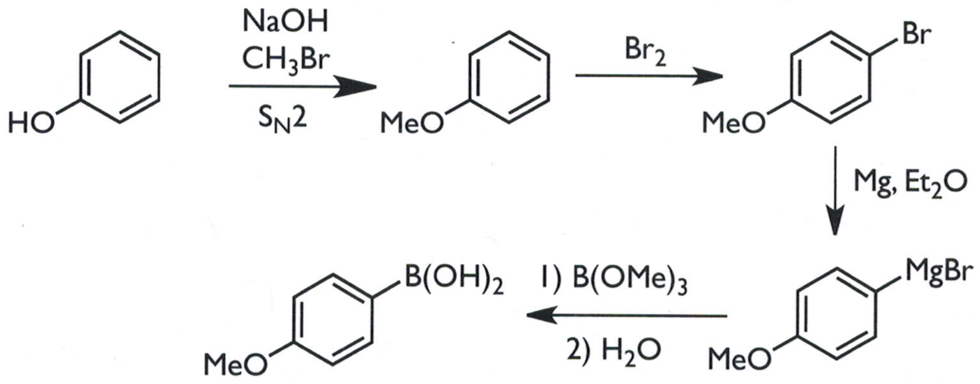


3) Suzuki-Miyaura coupling reactions typically occur between aryl or alkenyl halides and an arylboronic acid. An example of such a reaction is shown below for the synthesis of the food flavoring compound *trans*-anethole (*trans*-1-methoxy-4-(1-propenyl)benzene).

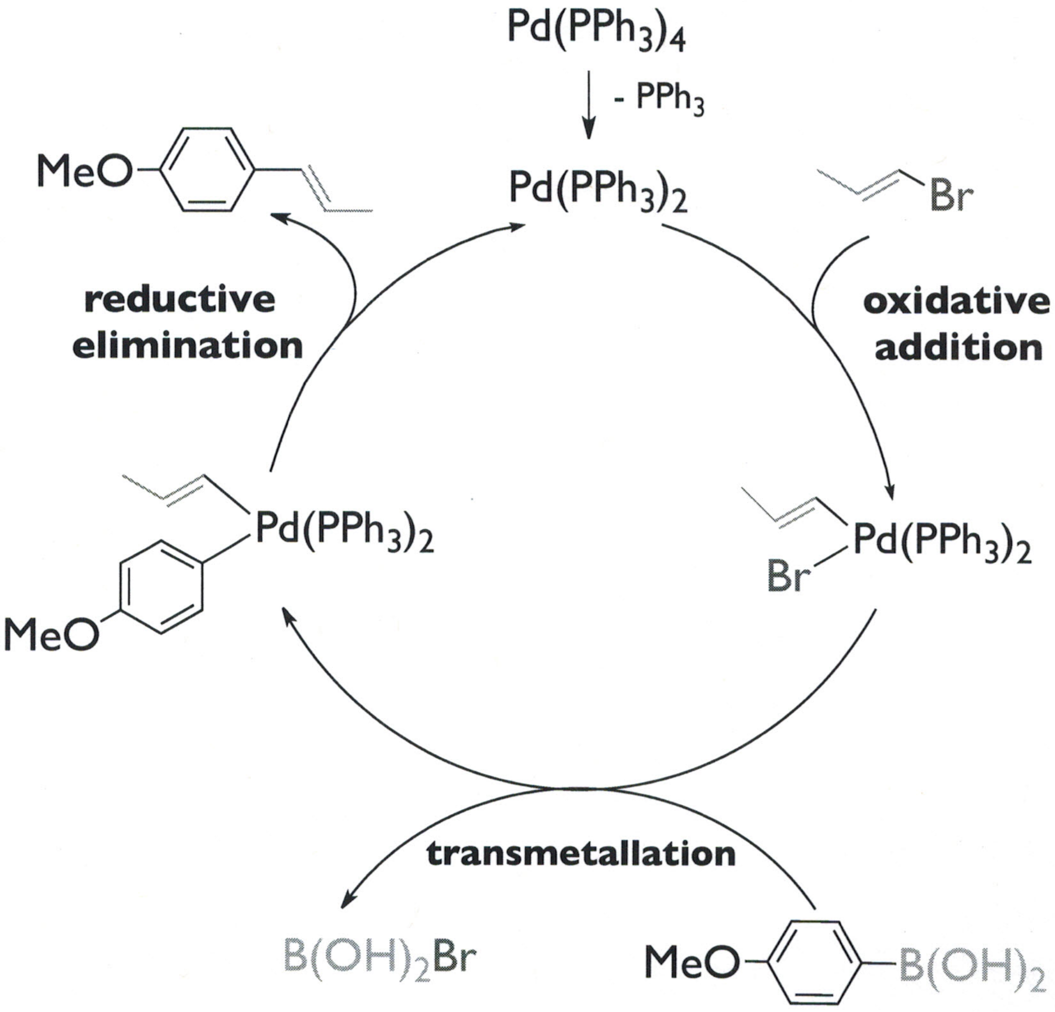


4-methoxyphenylboronic acid *trans*-anethole

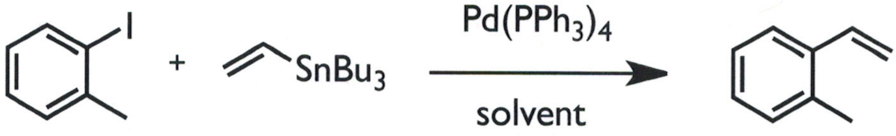
a) Propose a synthesis of 4-methoxyphenylboronic acid starting from phenol. Recall that trimethylborate, B(OMe)$_3$, reacts as an electrophile toward Grignard reagents. Show all isolated intermediates/products formed. You do not need to give a mechanism for the individual steps.

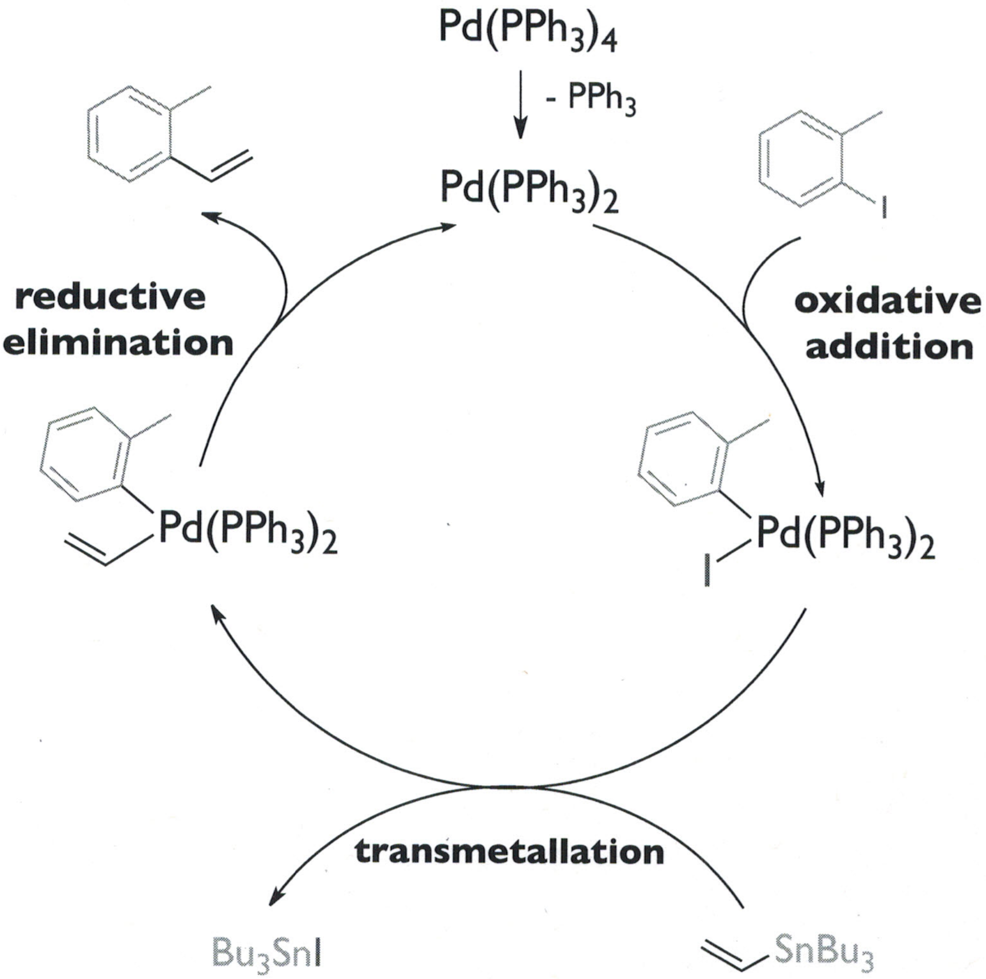


b) Complete the catalytic cycle for the Suzuki-Miyaura coupling reaction shown above, drawing the appropriate reagents and products of each of the three labeled steps. The role of KOH in the reaction will be discussed in the Suzuki pre-lab session next week.

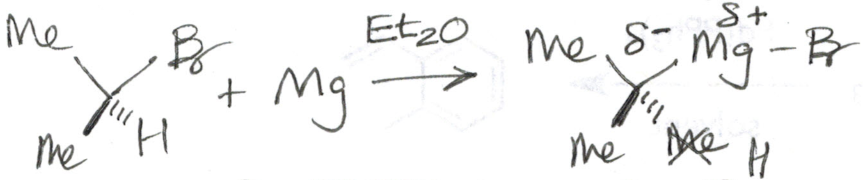


c) Draw and label the full catalytic cycle for the Stille coupling of 2-iodotoluene and tributyl(vinyl)stannane shown below.





4) Draw the balanced reaction for the formation of isopropylmagnesium bromide in diethyl ether and show the charge distribution along the carbon-metal bond. Explain why diethyl ether is a common solvent for the generation of Grignard reagents.



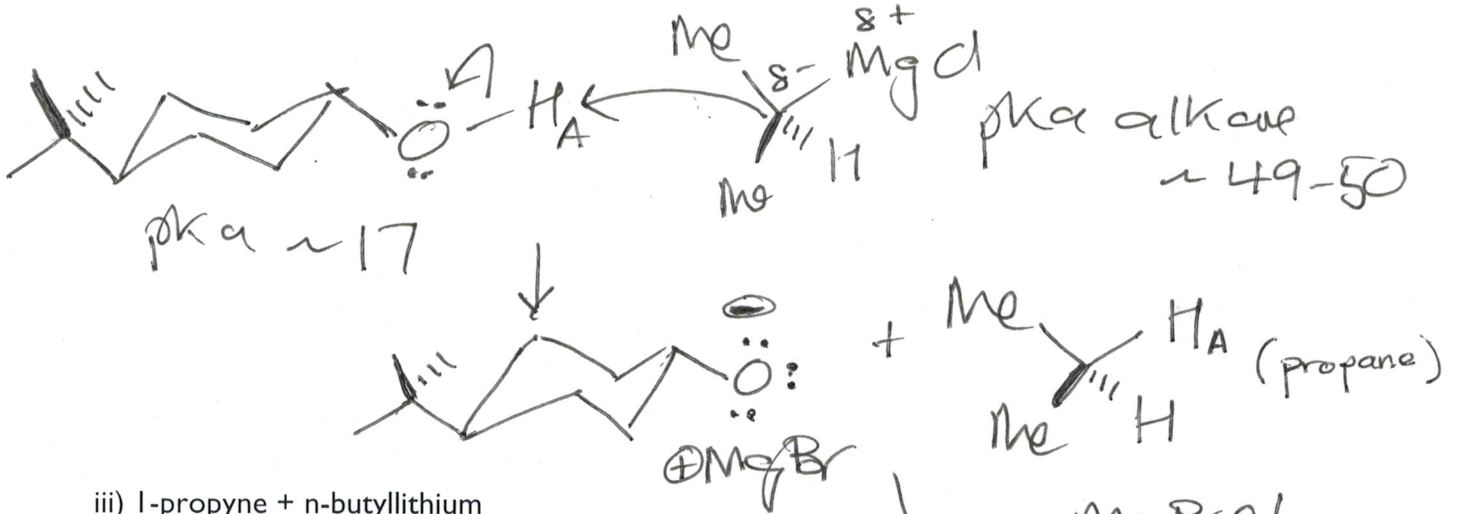
C-atom is ⊖ve charged

Et₂O is a coordinating solvent, helps to stabilize + increase solubility of RMgX.

Point of this question is to be aware of what you react the organometallic reagent with!

5) Draw the electron-pushing mechanism and show the product(s) of the following reactions (assume 1:1 stoichiometry, appropriate solvents, and aq. HCl workup of the reaction mixture).

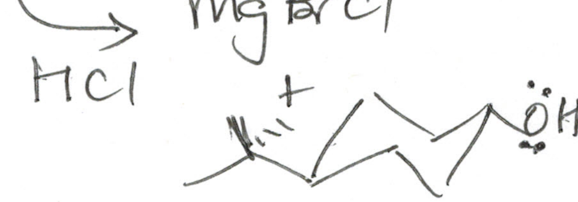
i) *trans*-4-tert-butyl-cyclohexanol + isopropylmagnesium bromide



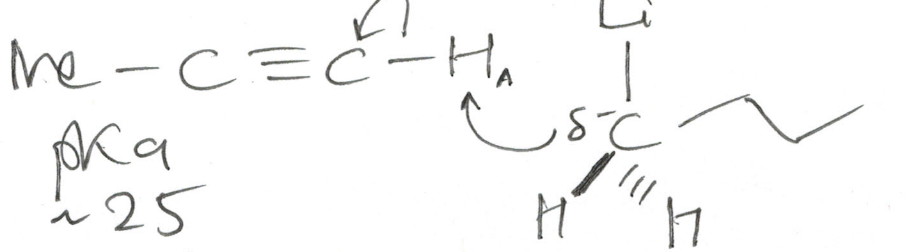
pKa ~17

pKa alkane ~49-50

(propane)

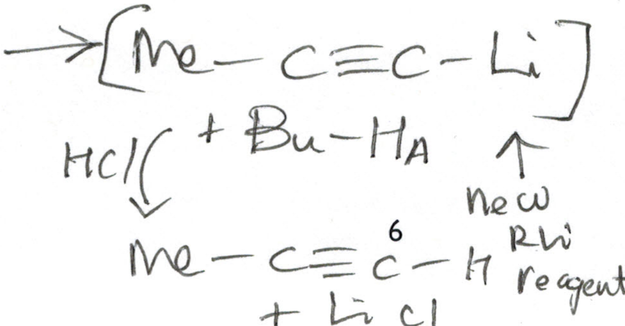


iii) 1-propyne + n-butyllithium



pKa ~25

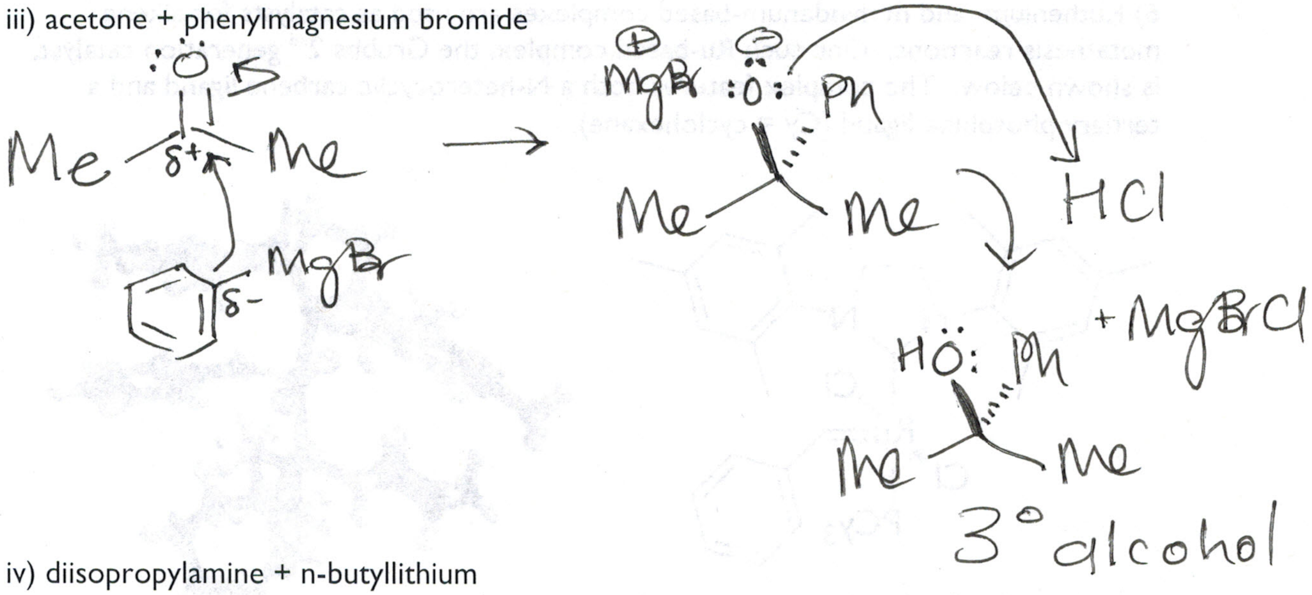
pKa alkane ~ 49-50



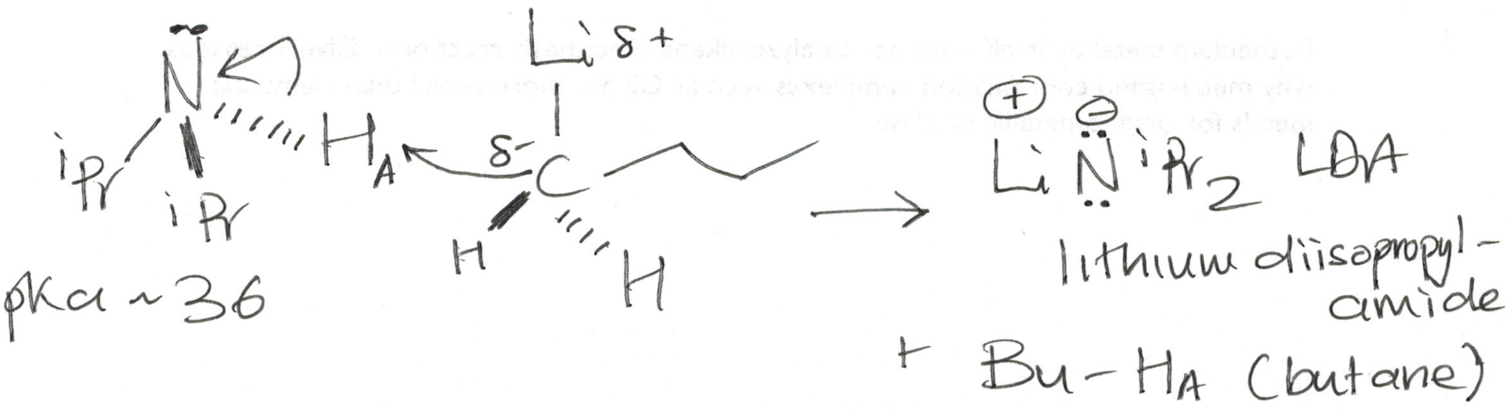
new RLi reagent

In real life would not work up with HCl b/c point of rxn would be to make new RLi reagent

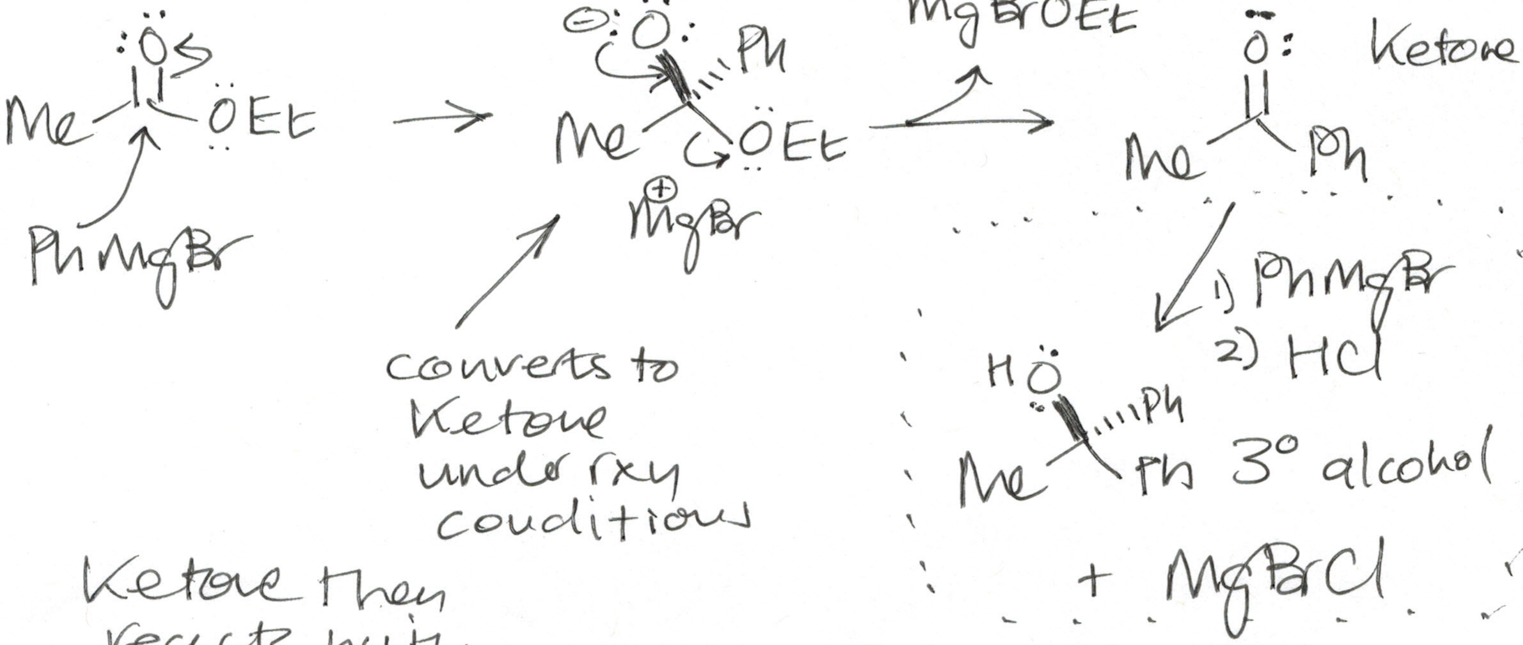
iii) acetone + phenylmagnesium bromide



iv) diisopropylamine + n-butyllithium



v) ethyl acetate + phenylmagnesium bromide

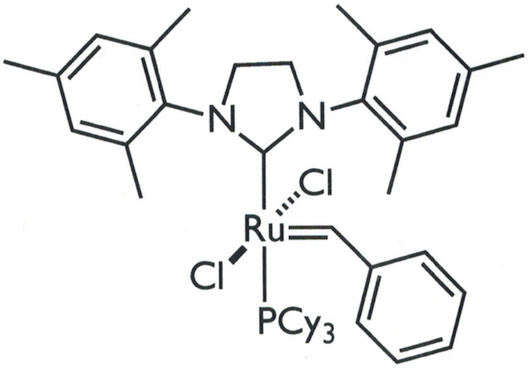


converts to Ketone under rxn conditions

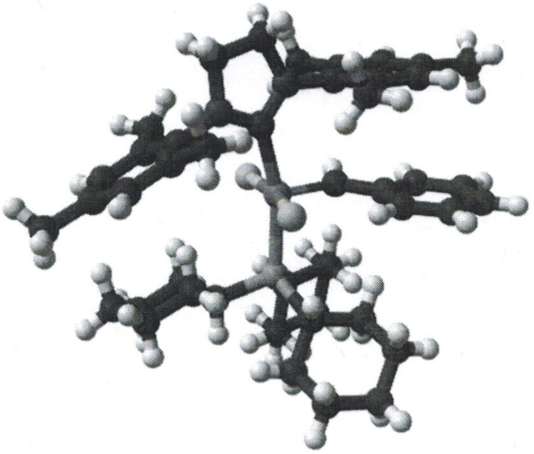
Ketone then reacts with 2nd equiv of ~~Mg~~ PhMgBr to produce 3° alcohol

1:1 would yield a mix of products + starting materials.

6) Ruthenium- and molybdenum-based complexes are used as catalysts for alkene metathesis reactions. One such Ru-based complex, the Grubbs 2nd generation catalyst, is shown below. The complex features both a N-heterocyclic carbene ligand and a tertiary phosphine ligand (Cy = cyclohexane).



Grubbs 2nd generation catalyst



Ruthenium metal by itself does not catalyze alkene metathesis reactions. Give 3 reasons why metal-ligand coordination complexes such as G2 are more useful than elemental metals for organometallic catalysis.

i) Metal-ligand complexes are soluble in a wide range of organic solvents, thus allowing homogeneous catalysis (catalysis in solution).

Homogeneous catalysis is more attractive than heterogeneous b/c it allows easier access to and control of the active site, easier alteration of the system in general, milder conditions and also easier study of the system leading to fuller understanding of the mechanism. One advantage of heterogeneous catalysis is that the metal catalyst quite easy to separate from the product – this can sometimes be a problem for the purification of pharmaceuticals etc. made via homogeneous catalysis.

ii) Ligands can dissociate from the metal atom to open an active site(s) for catalytic cycle to begin/continue.

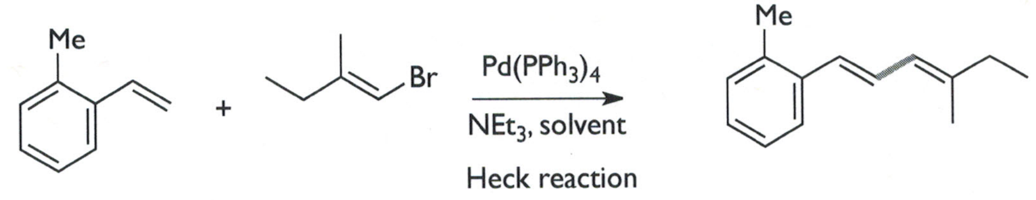
This is the "just right" bonding referenced in the slides. For example, $Pd(PPh_3)_4$ is a yellow solid that can be stored indefinitely under N_2 (i.e. is "stable") but, in solution in the presence of an aryl bromide, a Pd-P bond will break and create an active site for oxidative addition, thus beginning the catalytic cycle.

iii) Ligands control the size and shape of the active site of the metal catalyst.

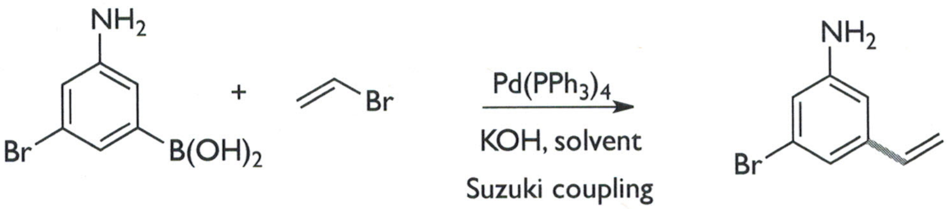
This allows improved selectivity for a particular product. In many cases, a specific ligand or set of ligands can control the size and shape of the reactive pocket on the metal to such an extent that only one enantiomer of a chiral product is produced – this is more difficult to achieve with heterogeneous catalysts.

7) Draw the products of the following organometallic reactions.

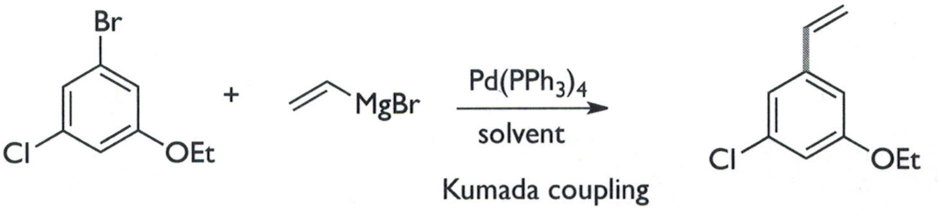
a)



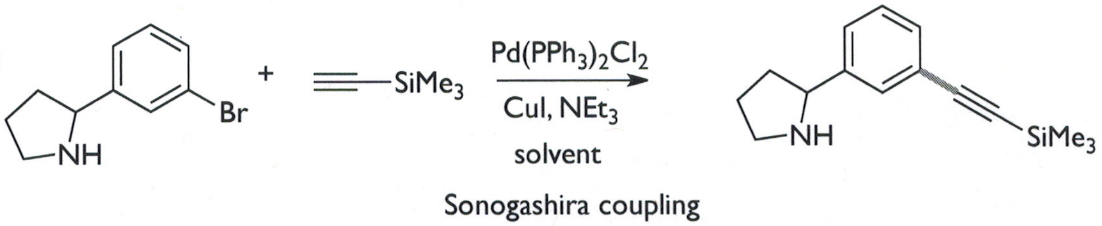
b)



c)

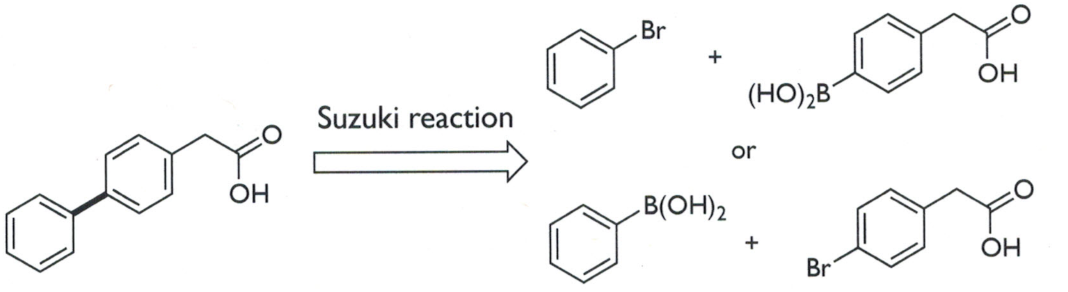


d)



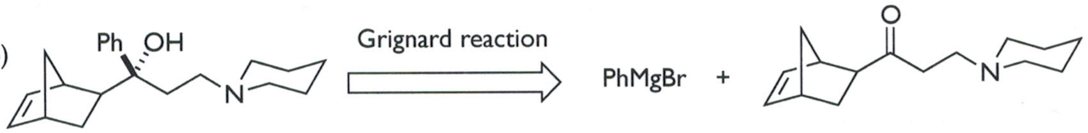
8) Each of the following compounds can be synthesized by either a Grignard reaction or by a Pd-catalyzed coupling reaction. The bond generated by the organometallic reaction is in **bold**. Draw starting materials that could be used for each target compound and name each reaction used to form each **bold** bond.

a)

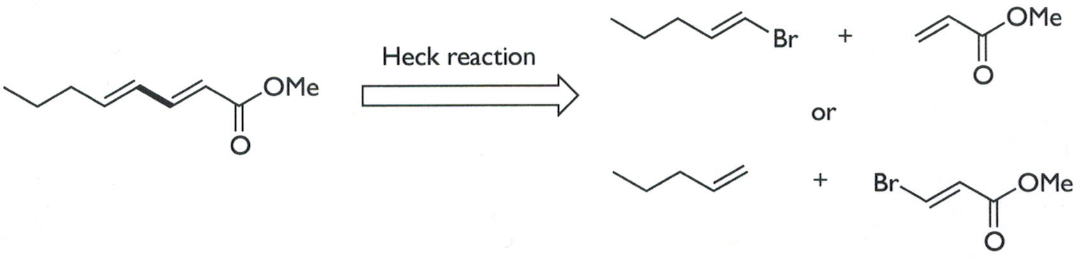


could iodide instead of bromide for either ArX

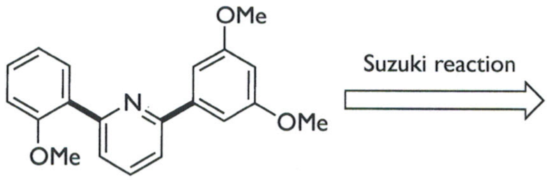
b)



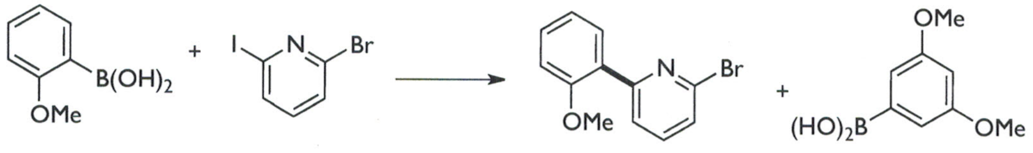
c)

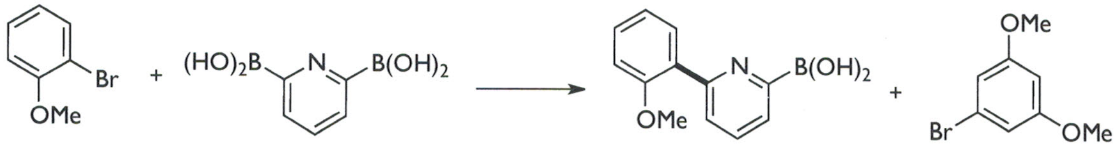


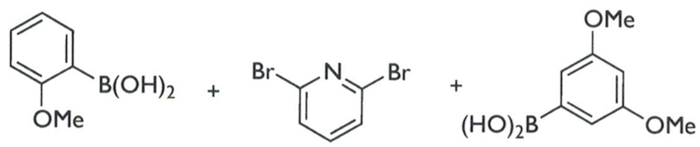
d)



A number of plausible routes
some will be better than others







would lead to mixture of products