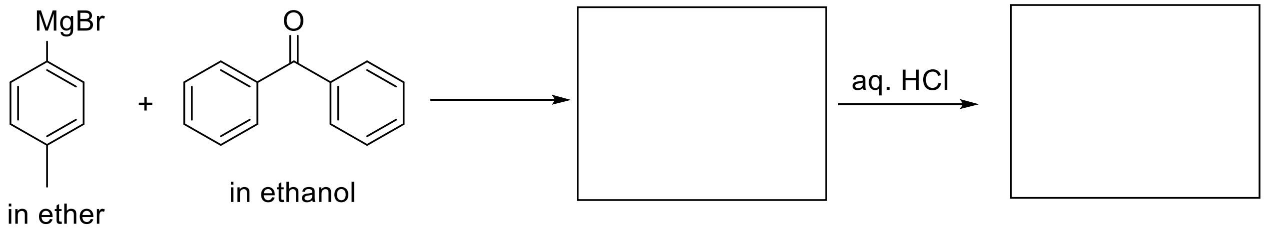
CHEM 344 Organometallic Chemistry Practice Problems (not for credit)

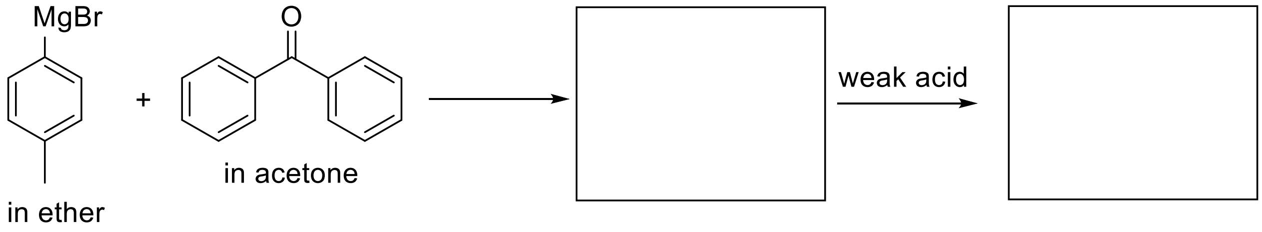
Name (print): TA name (print): ______________

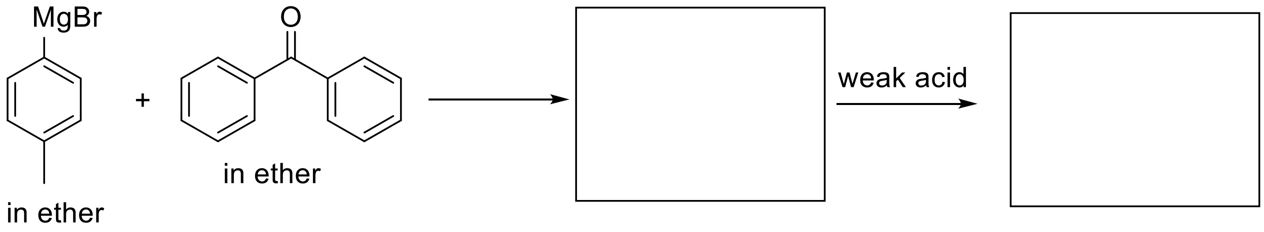
1) Careful choice of solvent is essential for the successful generation and reaction of a Grignard reagent.

a) Explain why anhydrous diethyl ether and tetrahydrofuran (THF) are common solvents for the generation of Grignard reagents.

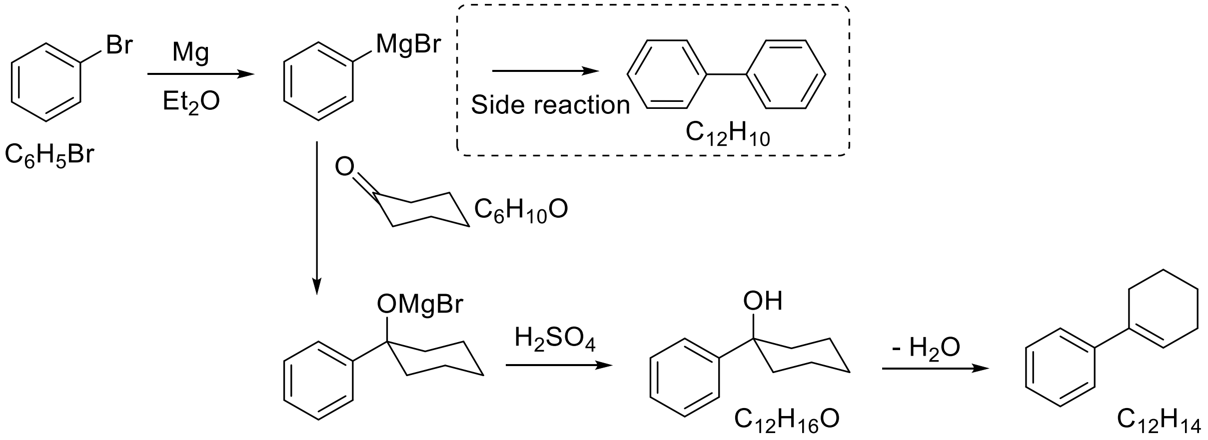
b) Show the major product(s) of the reaction of *p*-tolylmagnesium bromide (prepared in anhydrous diethyl ether) with benzophenone (dissolved in either ethanol, acetone, or diethyl ether).







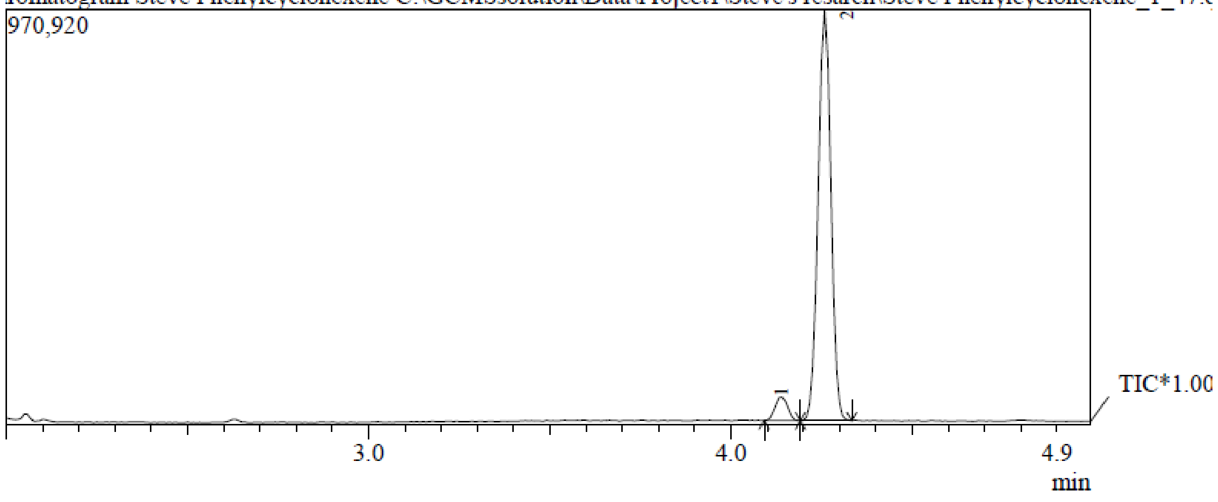
2) The reaction of PhMgBr with cyclohexanone followed by addition of acid produces 1-phenylcyclohexene as shown below.



The crude reaction mixture was analyzed by GC-mass spectrometry. Use the GC-MS data on the next page to identify the components of the crude product mixture and assess its purity.

Draw a plausible mechanism for the formation of the minor product. What does the formation of this product imply about the mechanism of formation of the Grignard reagent?

romatogram Steve Phenylcyclohexene C:\GCMSsolution\Data\Project1\Steve's resarch\Steve Phenylcyclohexene_1_47.c

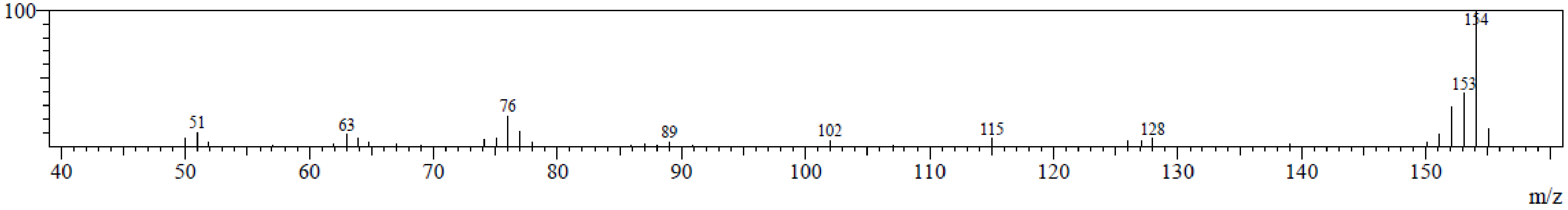


Peak Report TIC

Peak#	R.Time	Area	Area%
1	4.138	132097	5.32
2	4.258	2351497	94.68
		2483594	100.00

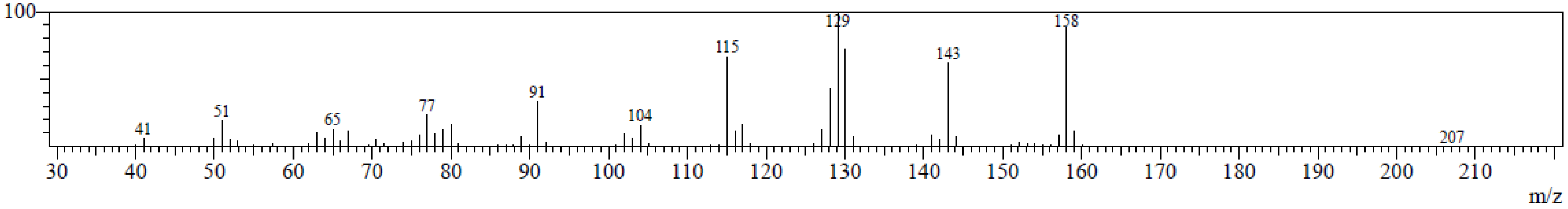
Spectrum

Peak#:1 R.Time:4.1(Scan#:258) MassPeaks:35

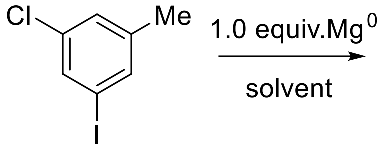


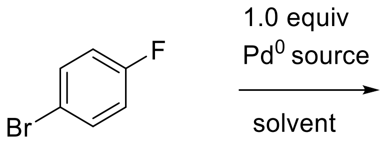
Spectrum

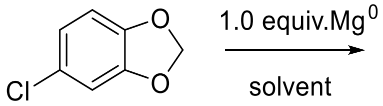
Peak#:2 R.Time:4.3(Scan#:272) MassPeaks:89



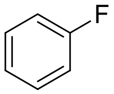
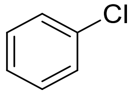
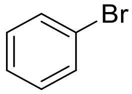
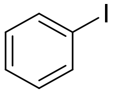
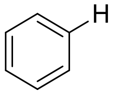
3) 3) Show the product and justify the chemoselectivity of each of the following oxidative addition reactions. Show the oxidation state of the metal in the product. The table of C-X bond dissociation enthalpies of halobenzenes may be useful.

a) 

b) 

c) 

C–X Bond Dissociation Enthalpies

Ph–X	ΔH°_{C-X} (kcal/mol)
	127
	97
	84
	67
	113

4) Transmetallation can be described by the following equilibrium:

$$\text{M-X} \;+\; \text{M'-R} \;\rightleftharpoons\; \text{M-R} \;+\; \text{M'-X}$$

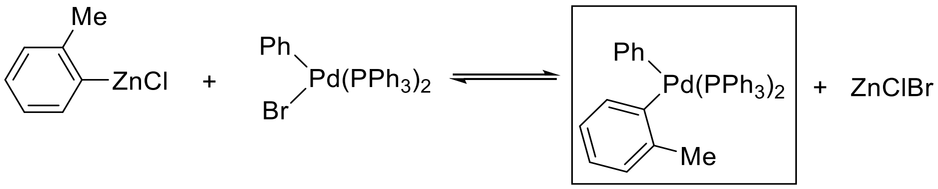
The process is thermodynamically favorable for the production of M-R if $X_M > X_{M'}$ (X = Pauling electronegativity, M/M' = metal, R = organic group, X= halide).

Show both products of the following transmetallation reactions. Label the starting materials as either M-X or M'-R, and the products as either M-R or M'-X. Draw a box around the transmetallation product that would be relevant to the catalytic cycle. For extra insight, you could calculate the % ionic character of the C-M bonds of M'-R and M-R.

$$\%\ ionic\ character = \left(\frac{X_C - X_M}{X_C}\right) * 100\ \%$$

Hints: Think about the relative polarities of the C–M bond in the starting material and the main product. Recall that the Pauling electronegativity of carbon, $X_{C,}$ is 2.55. The periodic table of electronegativity values for each element attached to this problem set may be useful. The rate of migration of groups from R_3SnX compounds is alkenyl > aryl > allyl > alkyl.

Example:



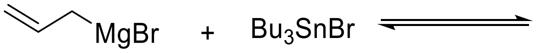
M'-R **M-X** **M-R** **M'-X**

X_{Zn} = *1.65* X_{Pd} = *2.20*

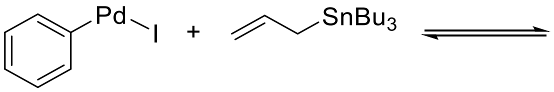
% ionic character C-Zn bond = [2.55- 1.65 / 2.55] x 100 = 35%

% ionic character C-Pd bond = 14 %

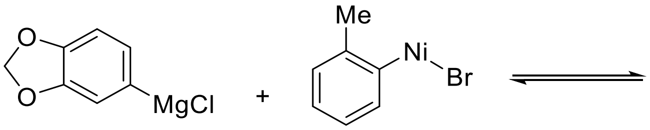
a)



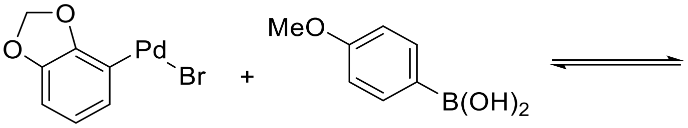
b)



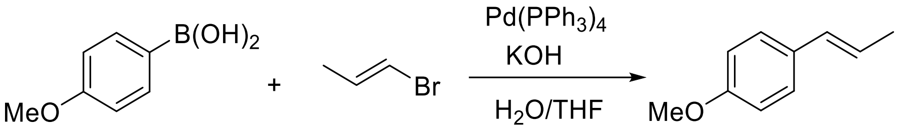
c)



d)



5) 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). The process involves the reaction of 4-methoxyphenylboronic acid and (*E*)-1-bromo-1-propene.

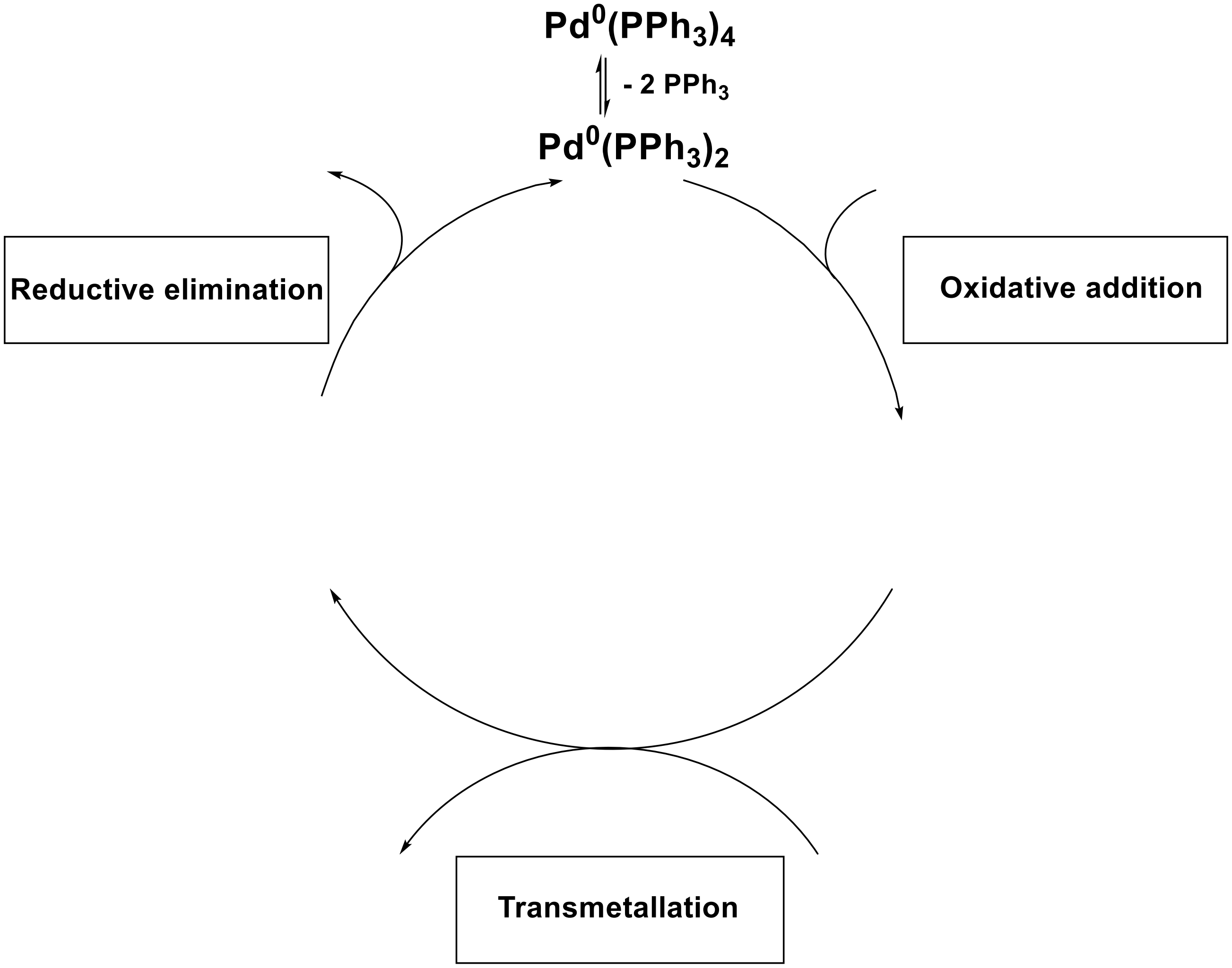


4-methoxyphenylboronic acid

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.

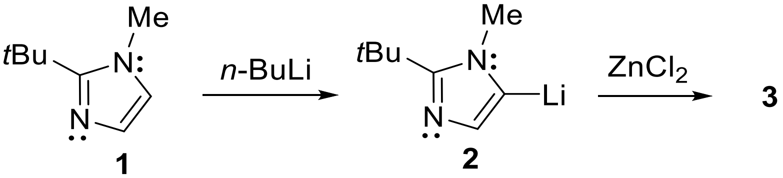
b) Complete the catalytic cycle for the Suzuki-Miyaura coupling reaction shown on page 7, drawing the appropriate reagents and products for each of the three labeled steps. The role of KOH in the reaction will be discussed in the Suzuki pre-lab session next week.



c) A researcher used (*E*)-1-chloro-1-propene in place of (*E*)-1-bromo-1-propene in the above reaction. Explain whether the oxidative addition of $Pd(PPh_3)_2$ into the C-Cl bond of (*E*)-1-chloro-1-propene will be faster or slower than the corresponding insertion into (E)-1-bromo-1-propene.

d) What is the driving force for the transmetallation process?

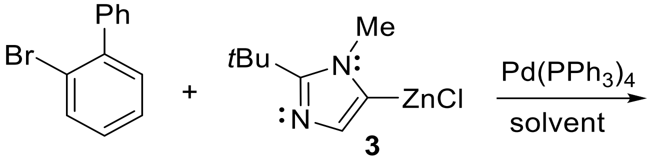
6) The Negishi reaction is a widely used Pd-catalyzed cross-coupling between an organozinc reagent and an organic halide. The catalytic cycle of the Negishi coupling is broadly similar to that of the Suzuki-Miyaura reaction. The preparation of organozinc reagent **3** via reaction of **2** (a lithiated *N*-methylimidazole) with $ZnCl_2$ is outlined below.



a) Draw an electron-pushing mechanism to show the formation of the organolithium species **2** by reaction of the *N*-methylimidazole precursor **1** with *n*-BuLi. Display the polarization of the C–Li bond in **2**. Is the carbon atom of the C–Li bond nucleophilic or electrophilic?

a) Show all products of the reaction of compound **2** with $ZnCl_2$ to produce compound **3**. What is the general name of this process? Rationalize the outcome of the reaction using Pauling electronegativity values and draw a box around the transmetallation product that would be relevant to the catalytic cycle.

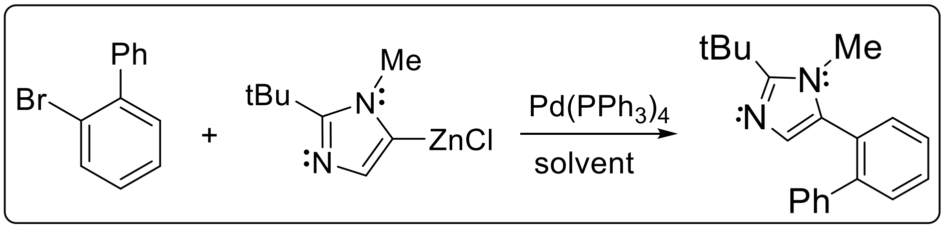
b) A Negishi coupling reaction between the organozinc reagent **3** and 2-bromobiphenyl was performed in the presence of the coordination complex [Pd(PPh_3)$_4$].

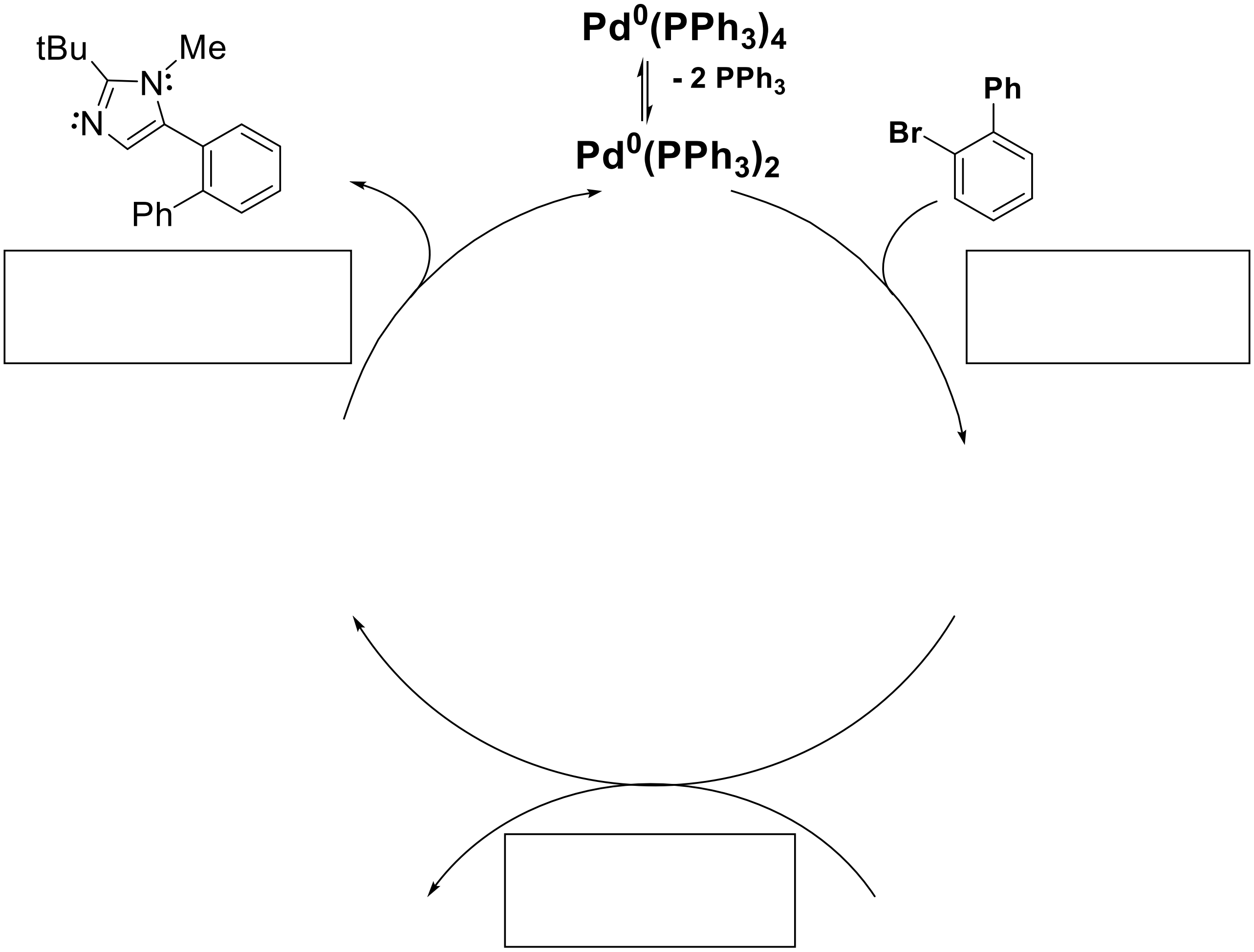


i) Show the organic product of the Negishi coupling reaction.

ii) List 3 reasons why metal-ligand coordination complexes such as [Pd(PPh_3)$_4$] are often more useful than elemental metals for organometallic catalysis.

c) Complete the catalytic cycle for the Pd-catalyzed Negishi cross-coupling reaction shown below. Clearly label each step, draw the appropriate reagents and products, and show the oxidation state of Pd in each step.





7) Draw and label the complete catalytic cycle for the Pd-catalyzed Stille cross-coupling of 2-iodotoluene and tributyl(vinyl)stannane shown below. The rate of migration of groups from R_3SnX compounds is alkenyl > aryl > allyl > alkyl.