

CHEM 344 Organometallic Chemistry Practice Problems (not for credit)

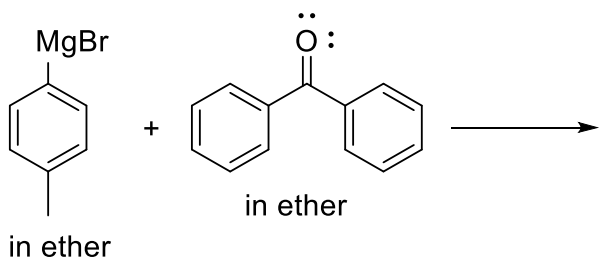
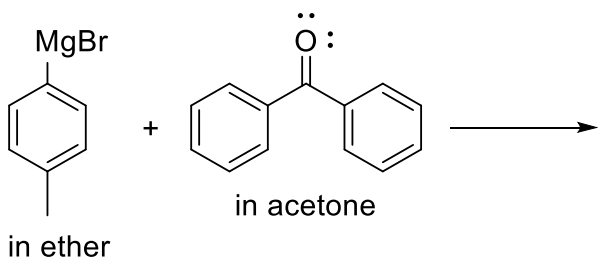
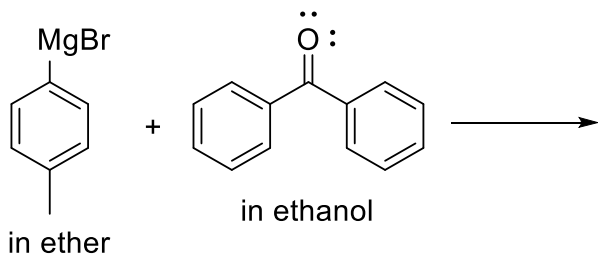
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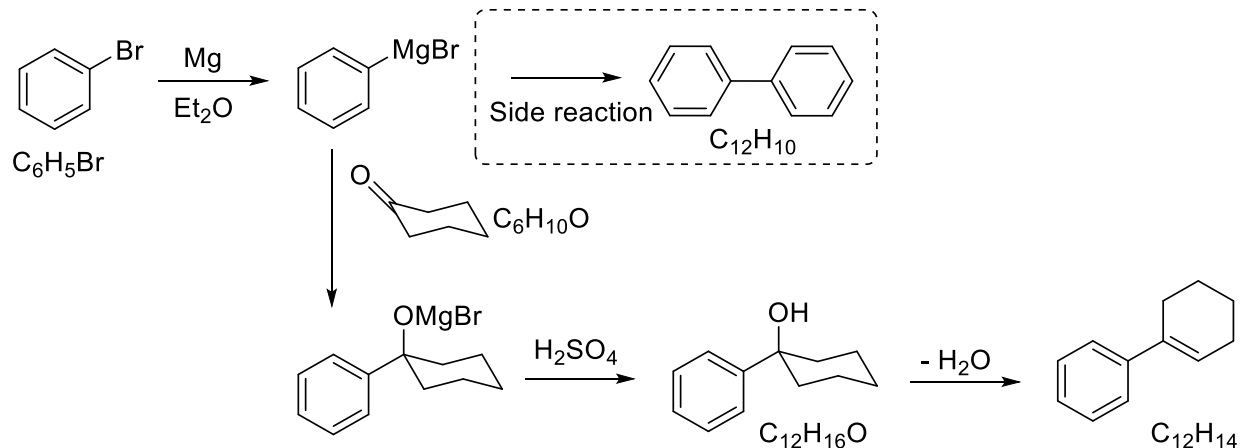
1) Careful choice of solvent is essential for the successful generation and reaction of a Grignard reagent.

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 4-methylphenylmagnesium bromide (prepared in anhydrous diethyl ether) with benzophenone (dissolved in either ethanol, acetone, or diethyl ether). Assume acidic workup in each case.



2) The reaction of PhMgBr with cyclohexanone ($C_6H_{10}O$) followed by addition of sulfuric acid produces 1-phenylcyclohexene ($C_{12}H_{14}$) as shown below.

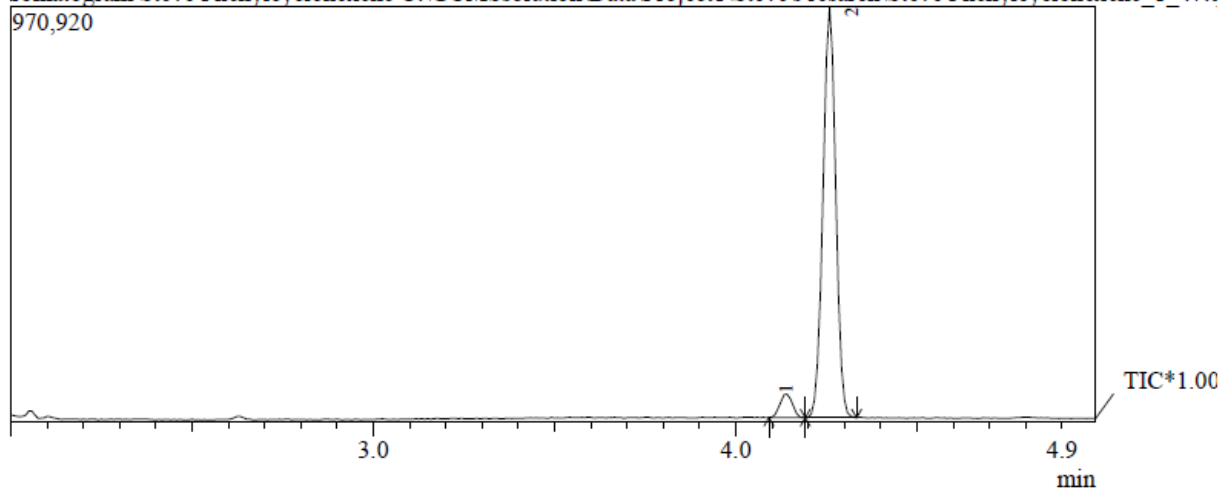


The crude reaction mixture was analyzed by GC-mass spectrometry. Use the GC-MS data on the next page to identify the components of the crude product mixture and assess its purity.

Draw a plausible electron-pushing mechanism for the formation of the major and minor products starting from bromobenzene.

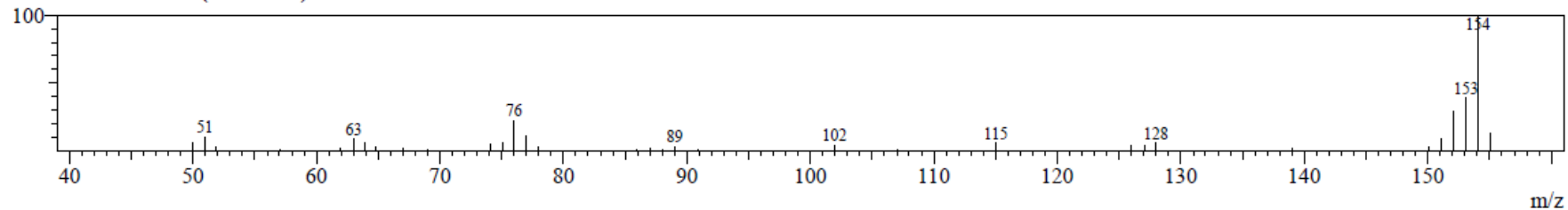
romatogram Steve Phenylcyclohexene C:\GCMSsolution\Data\Project1\Steve's resarch\Steve Phenylcyclohexene_1_47.c

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



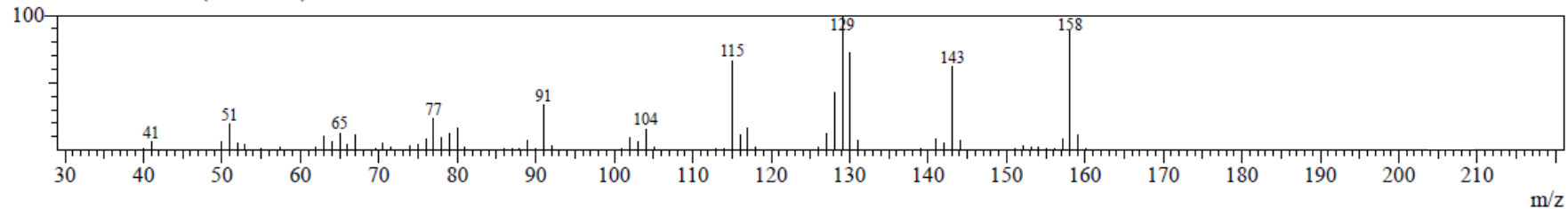
Spectrum

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

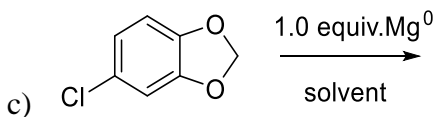
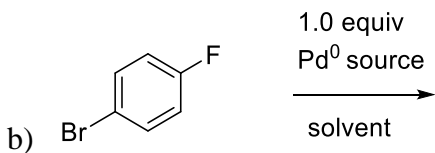
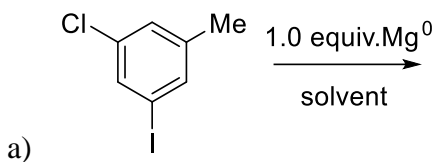


Spectrum






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



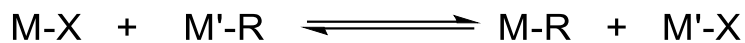
- 3) 3) Show the product and justify the chemoselectivity of each of the following oxidative addition reactions. Show the oxidation state of the metal in the product. The table of C-X bond dissociation enthalpies of halobenzenes may be useful.



C-X Bond Dissociation Enthalpies

Ph-X	$\Delta H^\circ_{\text{C-X}}$ (kcal/mol)
	127
	97
	84
	67
	113

4) Transmetallation follows oxidative addition in a typical Pd-catalyzed coupling cycle. The process of transmetallation can be described by the following equilibrium:



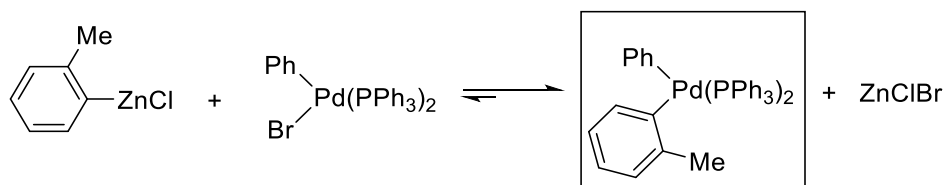
The process is thermodynamically favorable for the production of M-R if $X_M > X_{M'}$ (X = Pauling electronegativity, M/M' = metal, R = organic group, X = halide).

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.

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

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 (Appendix Q in CHEM 344 lab manual) 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

$$X_{Zn} = 1.65$$

$$X_{Pd} = 2.20$$

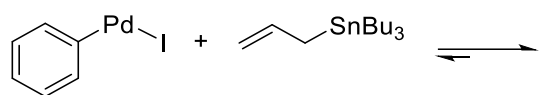
$$\% \text{ ionic character C-Zn bond} = [2.55 - 1.65 / 2.55] \times 100 = 35\%$$

$$\% \text{ ionic character C-Pd bond} = 14 \%$$

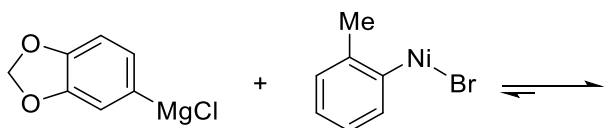
a)



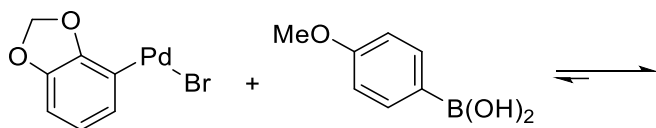
b)



c)



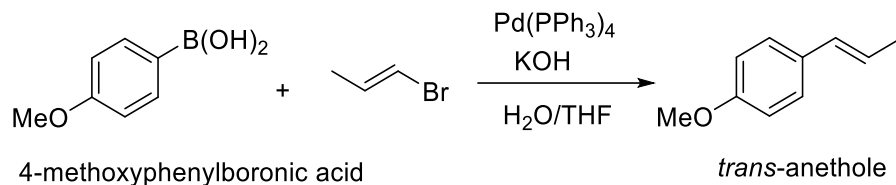
d)



e)

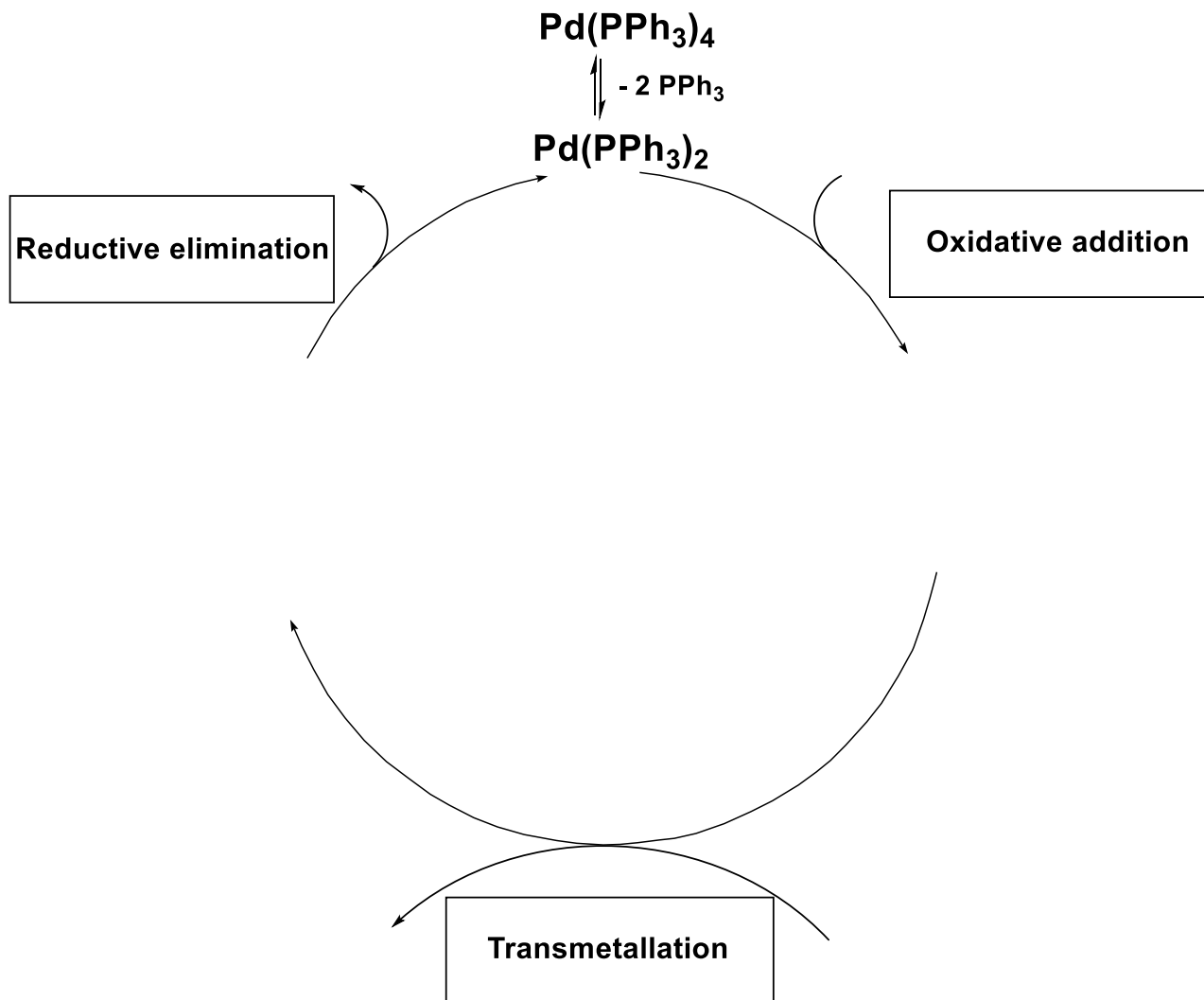


- 5) Suzuki-Miyaura coupling reactions typically occur between aryl or alkenyl halides and an arylboronic acid. An example of such a reaction is shown below for the synthesis of the food flavoring compound *trans*-anethole (*trans*-1-methoxy-4-(1-propenyl)benzene). The process involves the reaction of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



- 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.

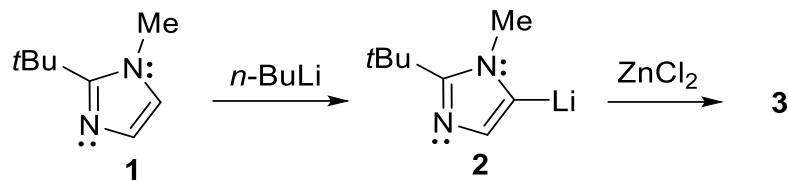
- b) Complete the catalytic cycle for the Suzuki-Miyaura coupling reaction to form *trans*-anethole (shown on the previous page), drawing the appropriate reagents and products for each of the three labeled steps.



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 $\text{Pd}(\text{PPh}_3)_2$ 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 one of the main driving forces for the transmetallation process?

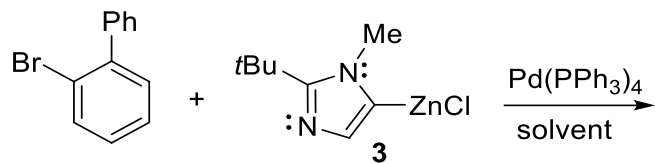
6) The Negishi reaction is a Pd-catalyzed cross-coupling between an organozinc reagent and an organic halide. The catalytic cycle of the Negishi coupling is similar to that of the Suzuki-Miyaura reaction. The preparation of organozinc reagent **3** via reaction of the organolithium species **2** (a lithiated *N*-methylimidazole) with ZnCl₂ is outlined below.



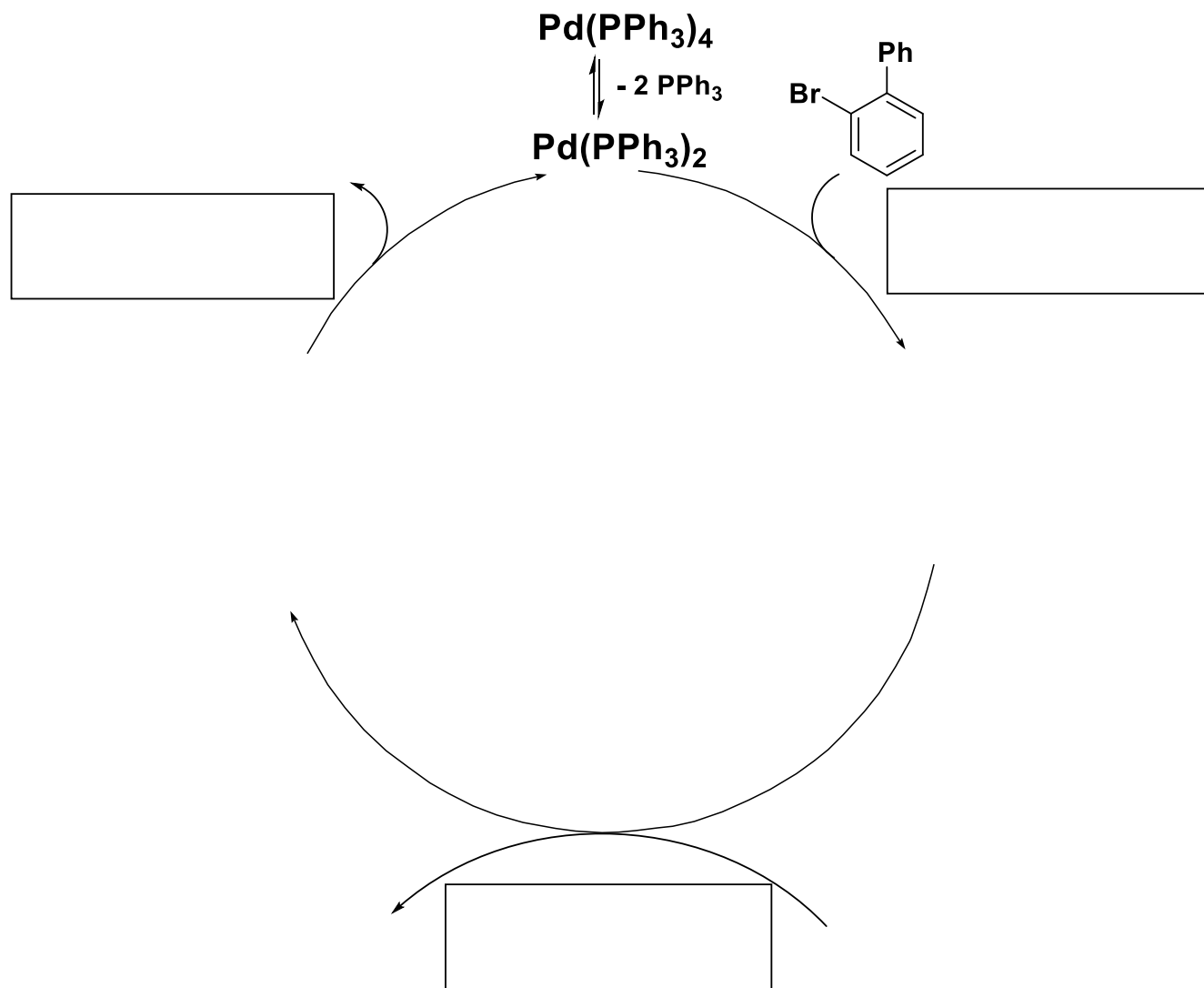
a) Draw an electron-pushing mechanism to show the formation of **2** by reaction of the *N*-methylimidazole precursor **1** with *n*-BuLi. Display the polarization of the C–Li bond in **2**. Is the carbon atom of the C–Li bond nucleophilic or electrophilic?

a) Show all products of the reaction of compound **2** with ZnCl₂ 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 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 $[\text{Pd}(\text{PPh}_3)_4]$. Show the products of the Negishi coupling reaction.



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



7) The Pd-catalyzed Stille cross-coupling allows for the preparation of thiophene-based liquid crystalline materials (*J. Org. Chem.* **2008**, *73*, 830-839). Draw and label the complete catalytic cycle for the reaction shown below. The reactivity of organic groups in R_3SnX compounds is vinyl > aryl > allyl > alkyl.

