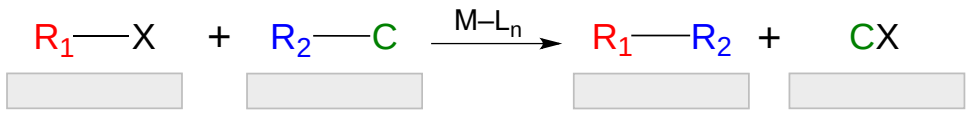
## **CONCEPT:** OVERVIEW OF CROSS-COUPLING GENERAL REACTIONS

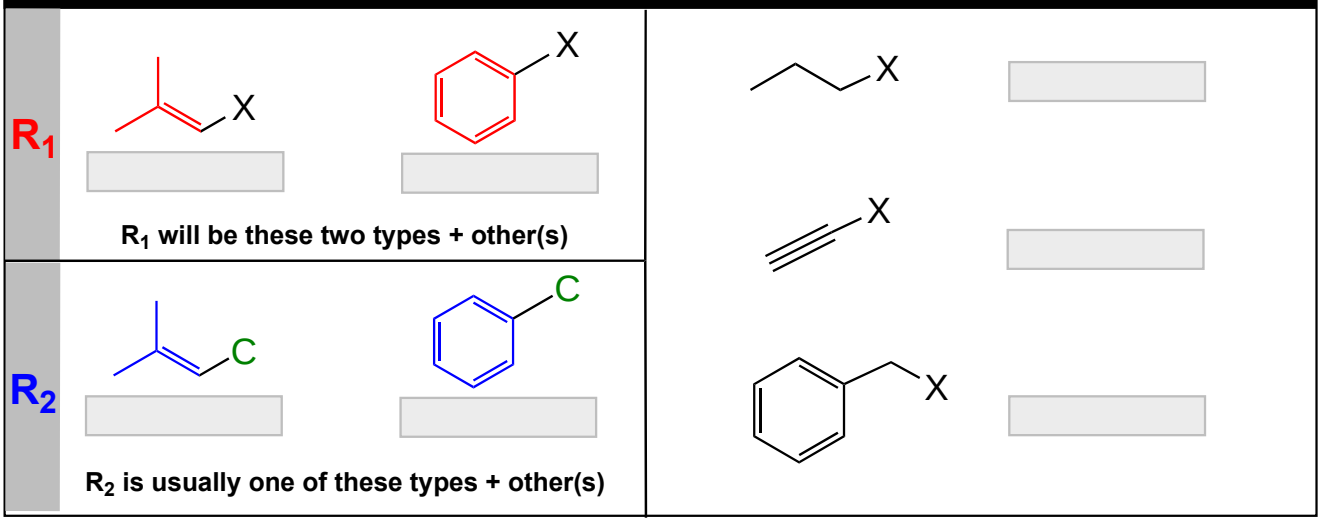
- These reactions involve synthetic transformations that combine a(n) _____ agent with a(n) _____.
  - □ 2 driving forces: Formation of highly _____ products + the catalyst following the ____ or ____ electron rule.

**Cross-Coupling Reaction**



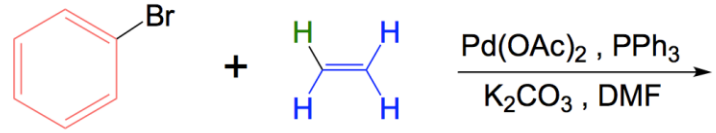

- The $R_1$ group in the reaction can be an _____, _____, _____, _____, or _____.
  - □ The carbon halide being used is dependent on the type of coupling reaction.

**Carbon Halides**

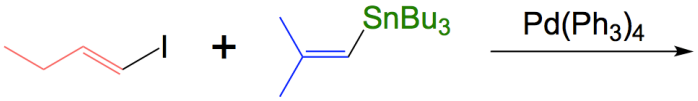



- The Coupling Agent (**C** group) in the reaction is also dependent on the type of coupling reaction.

**EXAMPLE:** The Heck reaction is a well-known coupling reaction that involves the combining of a carbon halide with an alkene. Base on the example provided determine a possible coupling product.




**PRACTICE:** In the Stille reaction, an organostannane compound reacts with a carbon halide in order to form a new carbon-carbon bond. What would be the final product from the following Stille coupling reaction?



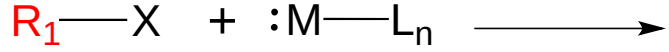
## **CONCEPT:** CROSS-COUPLING REACTION MECHANISMS

- The detailed mechanisms for many of these reactions are still debated, but it is accepted that all of them follow 3 stages:
  - □ These stages include (1) oxidative addition, (2) transmetallation and (3) reductive elimination.

### 1. Oxidative Addition

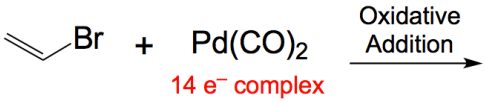
- A transition metal complex, M—$L_n$, reacts with a carbon halide by inserting itself into the $R_1$—X bond.
  - □ This step can happen by a variety of mechanisms, but a _____ (one-step) process is most common.

**Oxidative Addition**

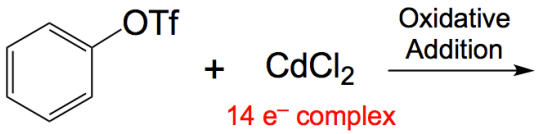


- □ Both of the new bonds formed behave like _____-type ligands, which causes the electron count to _____ by 2.
- □ Recall, this part of the cycle is driven by the _____ or _____ electron rule.

**EXAMPLE:** Determine the new palladium complex that forms during this oxidative addition step.




**PRACTICE:** Determine the new cadmium complex that forms during this oxidative addition step.

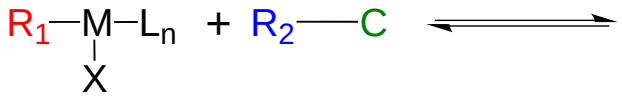


## **CONCEPT:** CROSS-COUPLING REACTION MECHANISMS

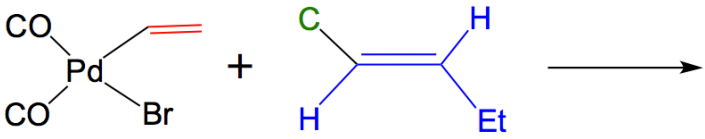
### 2. Transmetallation

● The $R_2$ group of the coupling agent is transferred to the metal complex, while at the same time the _____ group leaves.

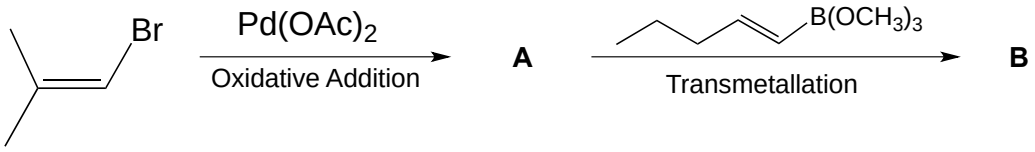
**Transmetallation**




□ The term "transmetallation" generally involves the interchanging of ligands between two metals or metalloids.



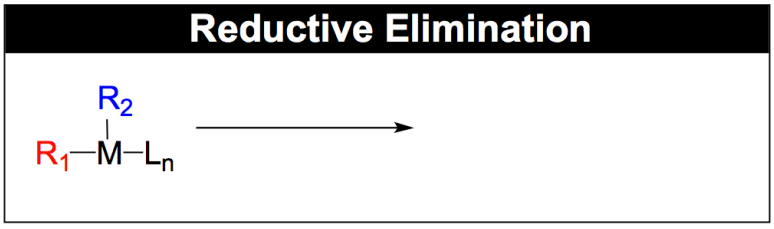

**EXAMPLE:** Determine the product(s) formed in the following reaction sequence.



## **CONCEPT:** CROSS-COUPLING REACTION MECHANISMS

### 3. Reductive Elimination

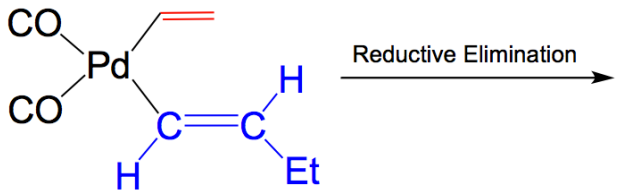
- Both the _____ and _____ leave the metal complex and form a sigma bond between one another to end the reaction.
  - □ This step is basically the opposite of the oxidative addition step.
  - □ It is not always a typical elimination that generates a pi bond.




### Stereochemistry

- Typically, reductive elimination generally results in the _____ of stereochemistry.

**EXAMPLE:** Determine the final product in the following reaction.




16 $e^-$ complex

- □ Reduction is seen as the gaining of electrons and a _____ in an element's oxidation number.
- □ When the two _____-type ligands are lost the oxidation state of the metal decreases by 2.
- □ At the same time, the formation of a conjugated product allows for the unstable catalyst to be regenerated.

### Mechanism Cycle

- These 3 stages together help to form a _____ cycle to show product formation and catalyst regeneration.