Chemistry of Palladium

Heck Reaction

Sonogashira Reaction

Suzuki-Miayura Coupling

Carbonylation of Aryl Halides

Palladium based reagents in organic synthesis (Pd)

The **Heck reaction** (also called the **Mizoroki-Heck reaction**)

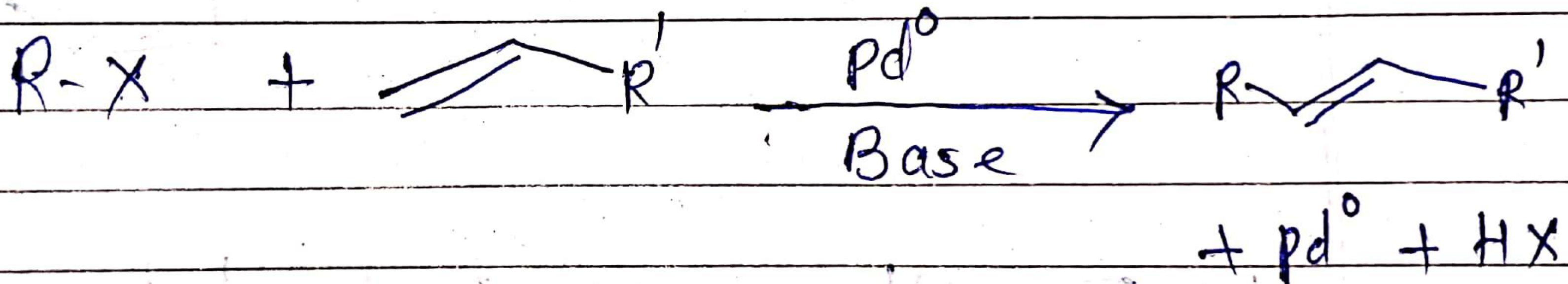
- It is the chemical reaction of an unsaturated halide (or triflate) with an alkene in the presence of a base and a palladium catalyst (or palladium nanomaterial-based catalyst) to form a substituted alkene.

- It is named after Tsutomu Mizoroki and Richard F. Heck. Heck was awarded the 2010 Nobel Prize in Chemistry, (which he shared with Ei-ichi Negishi and Akira Suzuki,) for the discovery and development of this reaction.

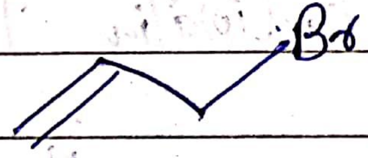
- This reaction was the first example of a carbon-carbon bond-forming reaction that followed a Pd(0)/Pd(II) catalytic cycle, the same catalytic cycle that is seen in other Pd(0)-catalyzed cross-coupling reactions. The Heck reaction is a way to substitute alkenes.

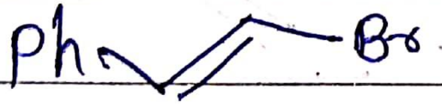
Heck Reaction

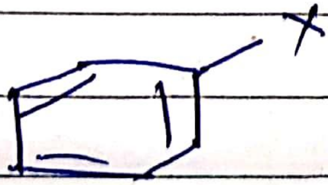
palladium is used as catalyst.
C-C bond formation (Cross-coupling Reaction)



R =





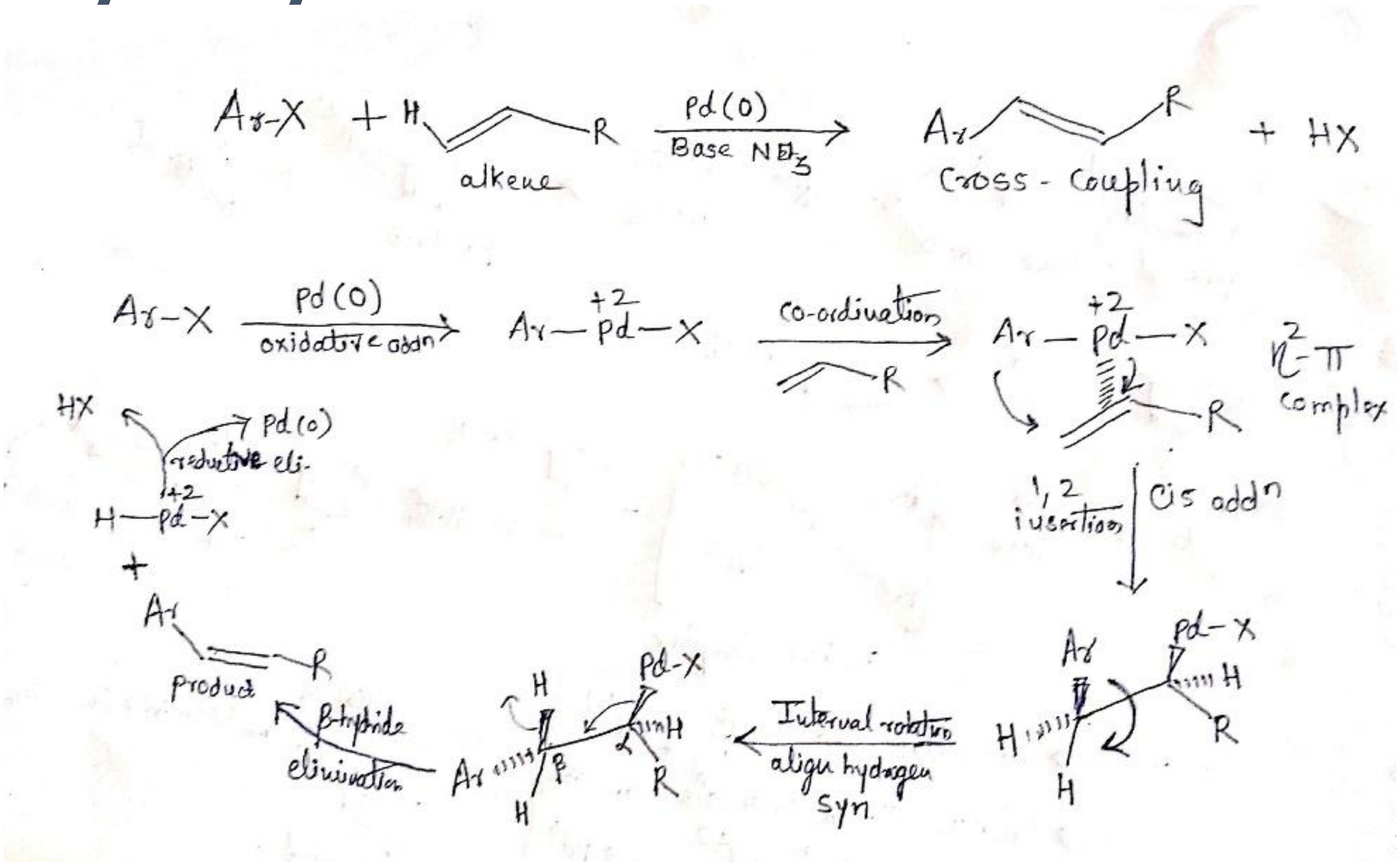


(Cl, Br, I, OTs)

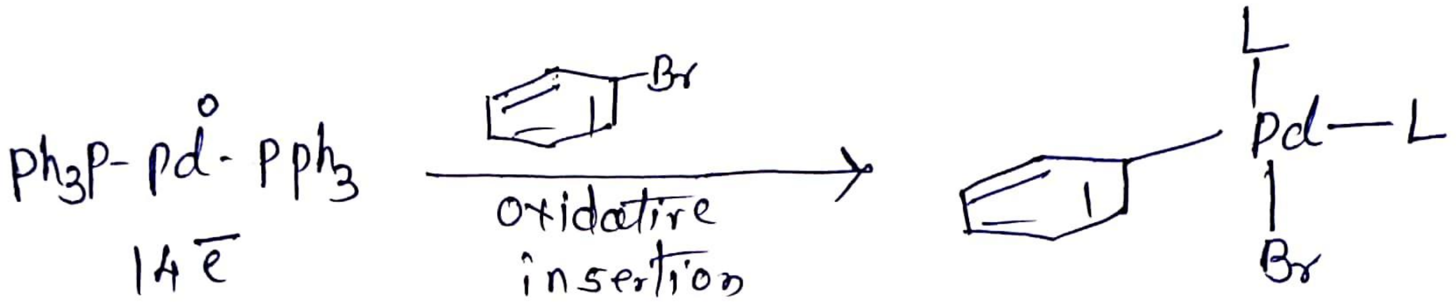
R' = alkyl, Aryl, -OR, -CO_2R

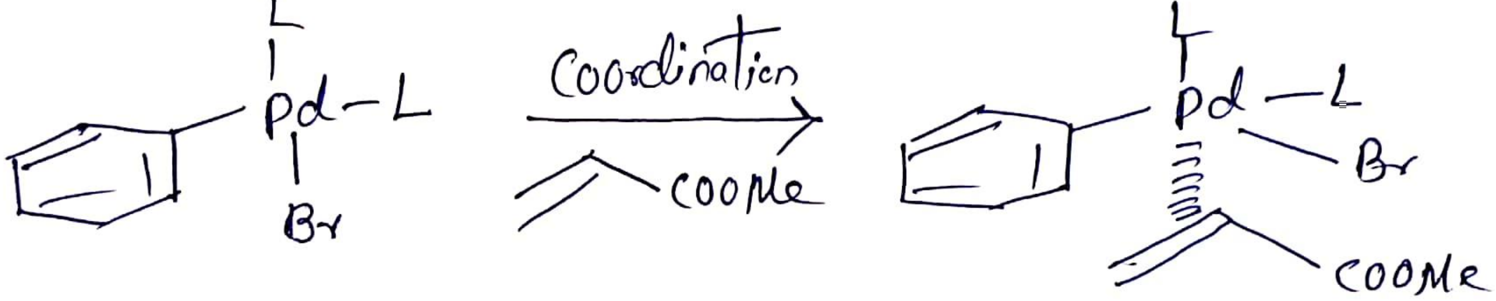
Base - $Et_3\ddot{N}$, NaOMe or
aq. Na_2CO_3

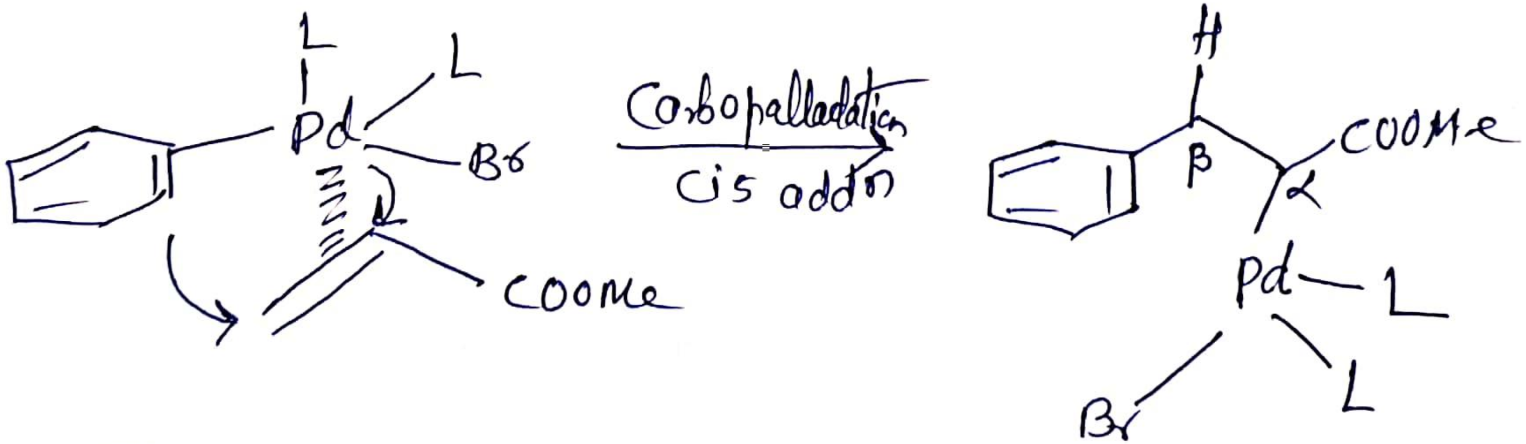
Catalytic Cycle of Heck Reaction



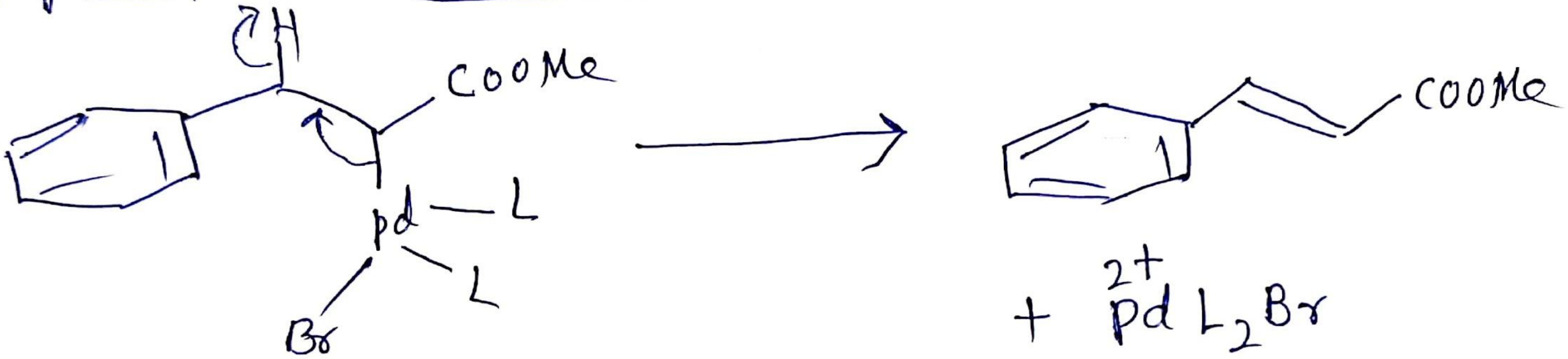
Mechanism of Heck Reaction

①


②


③


④ β-Hydride elimination



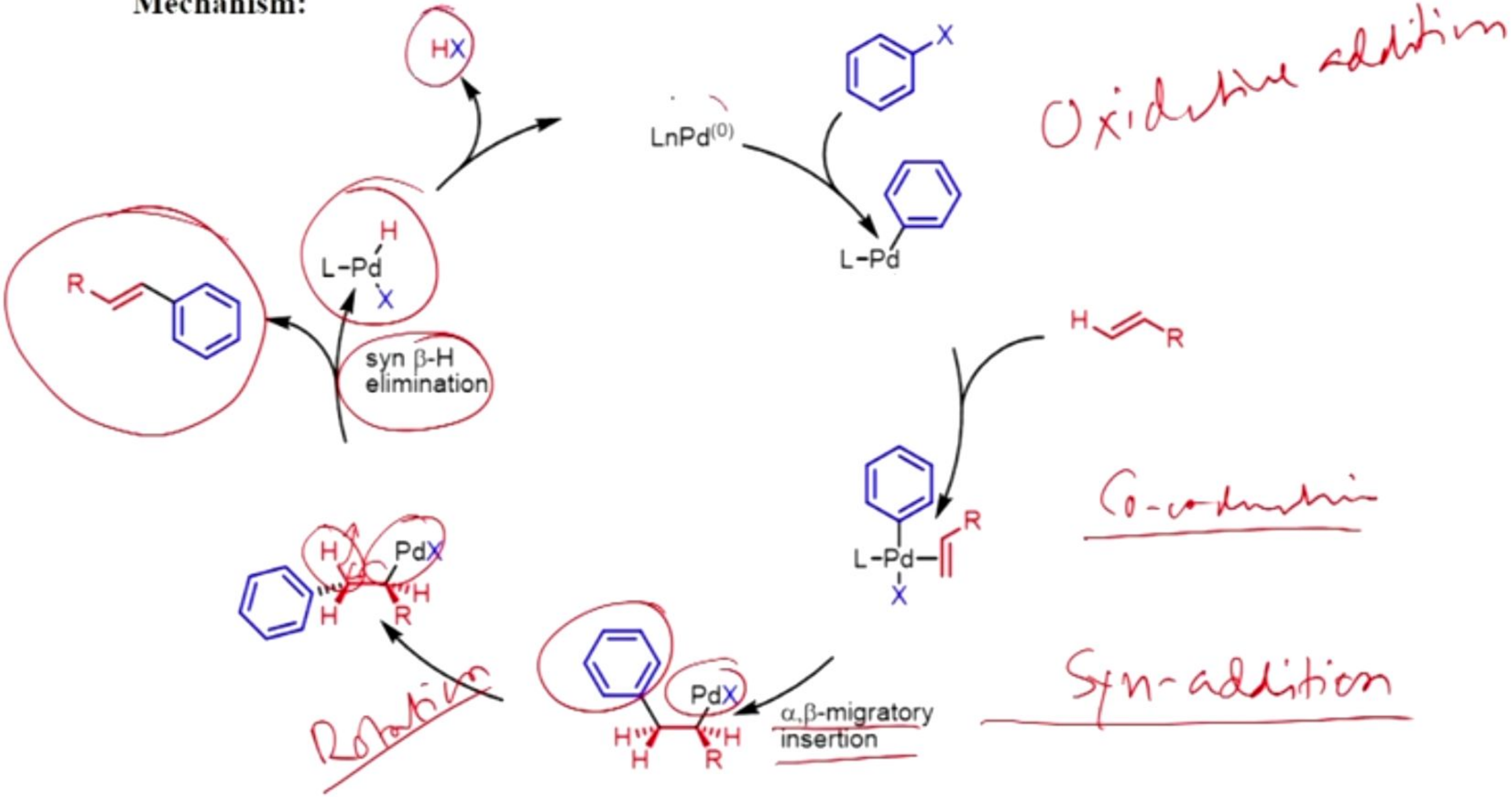
⑤ Regeneration of Catalyst

$$\overset{+2}{Pd}L_2Br + \underset{\text{Base}}{Et_3N} \longrightarrow \overset{0}{Pd}L_2 + Et_3\overset{+}{N}H + \overset{\ominus}{Br}$$

Palladium based reagents in organic synthesis

(Pd)

Mechanism:



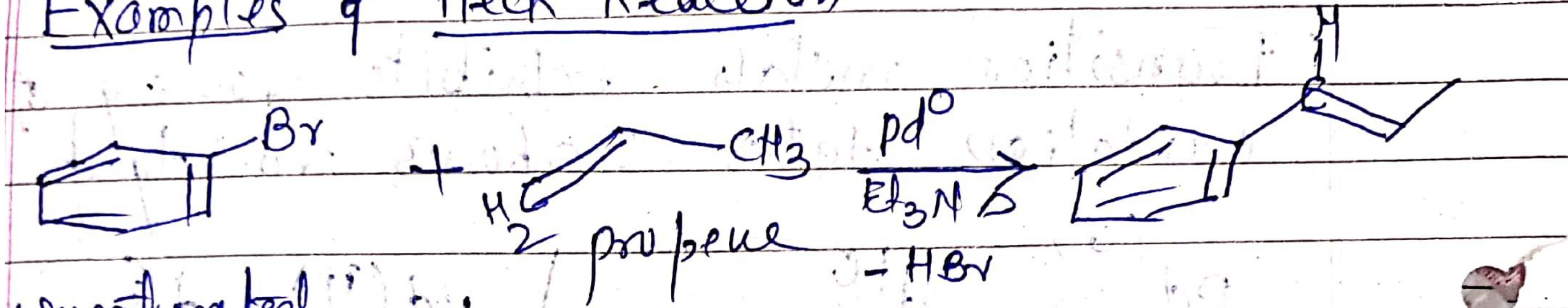
Oxidative addition

Co-ordination

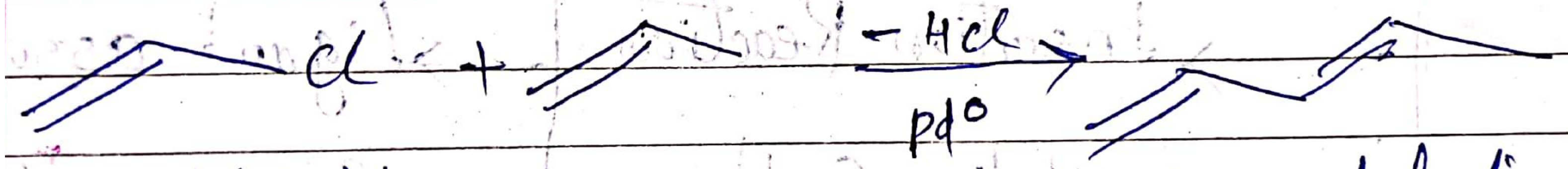
Syn-addition

Rotation

Examples of Heck Reaction

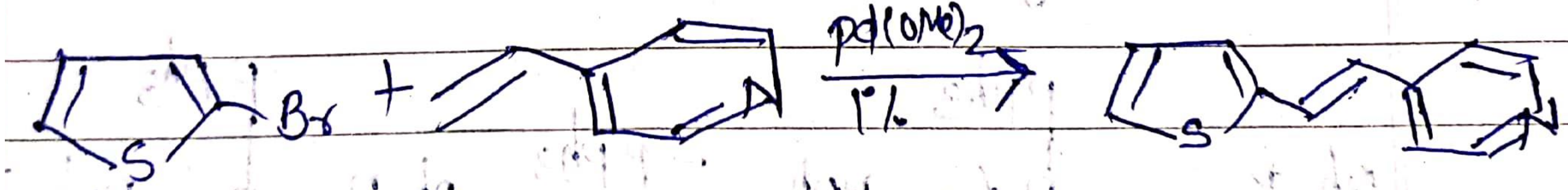


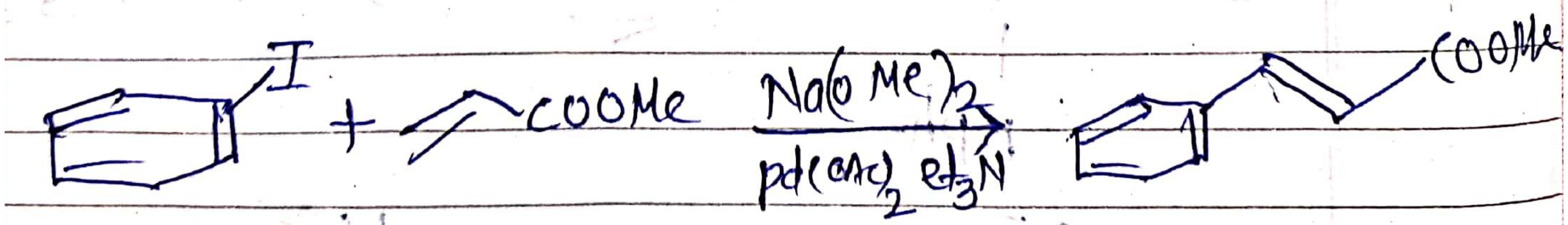
Unsaturated halide



Vinyl chloride

conjugated diene

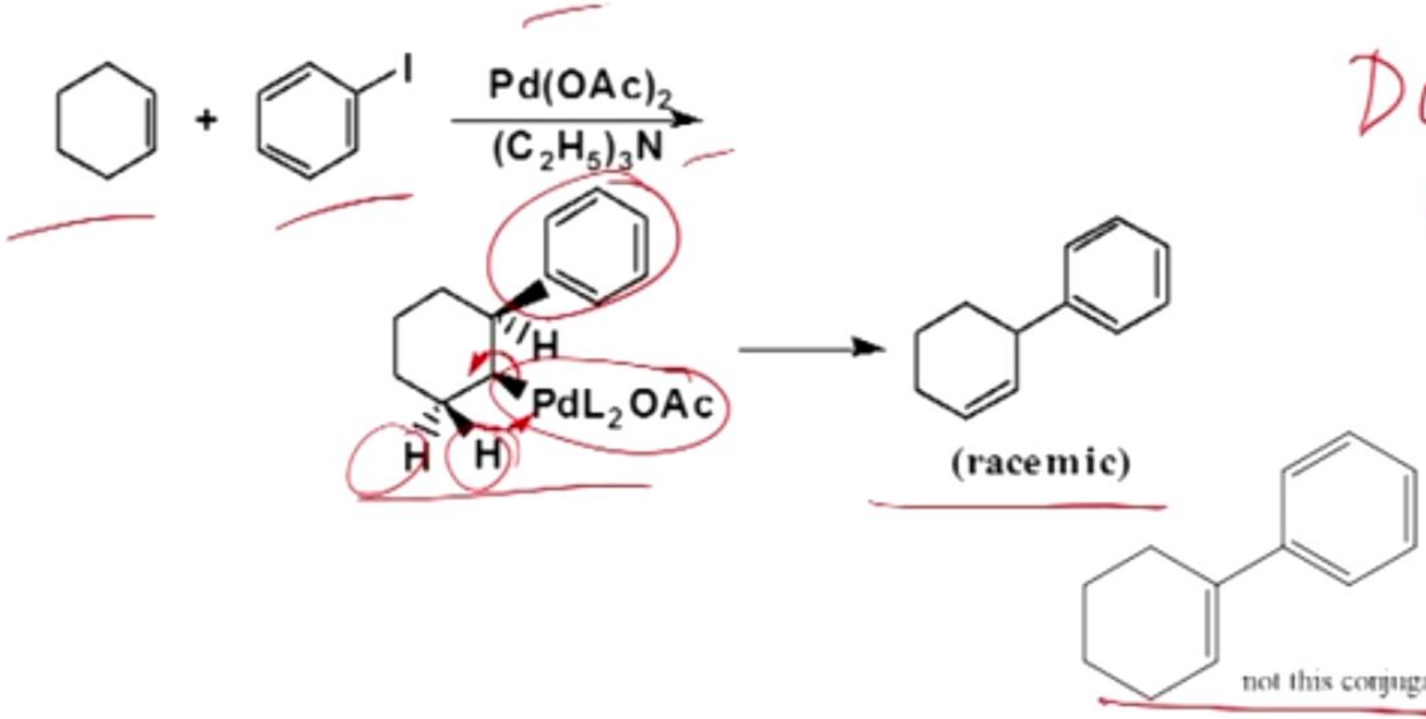




Palladium based reagents in organic synthesis
(Pd)

If the R group has no H for *syn* elimination, then a β H may be abstracted elsewhere.

The β H should be brought into position for *syn* elimination with the Pd.



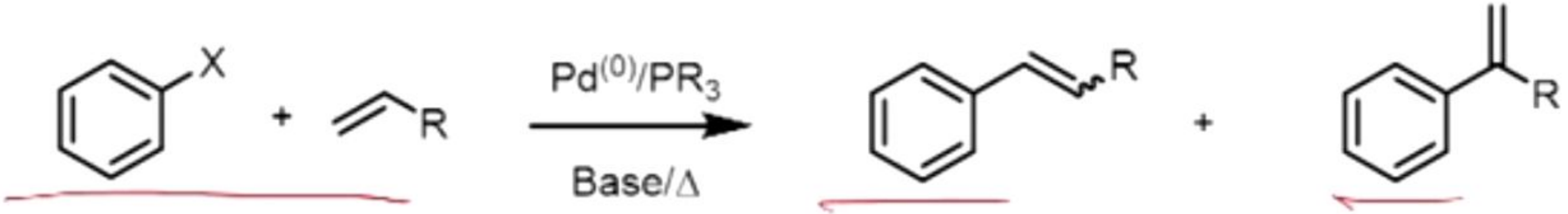
(racemic)

not this conjugated product

Double bond changes its place.

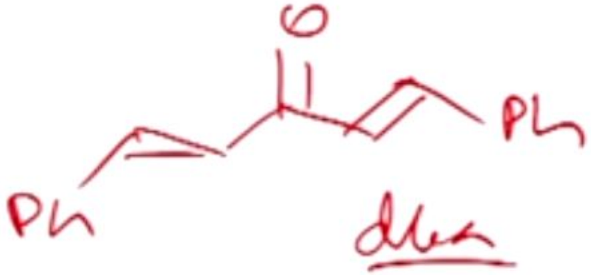
Palladium based reagents in organic synthesis
(Pd)

Good additives



$\overset{2}{Pd}_2(dba)_3$

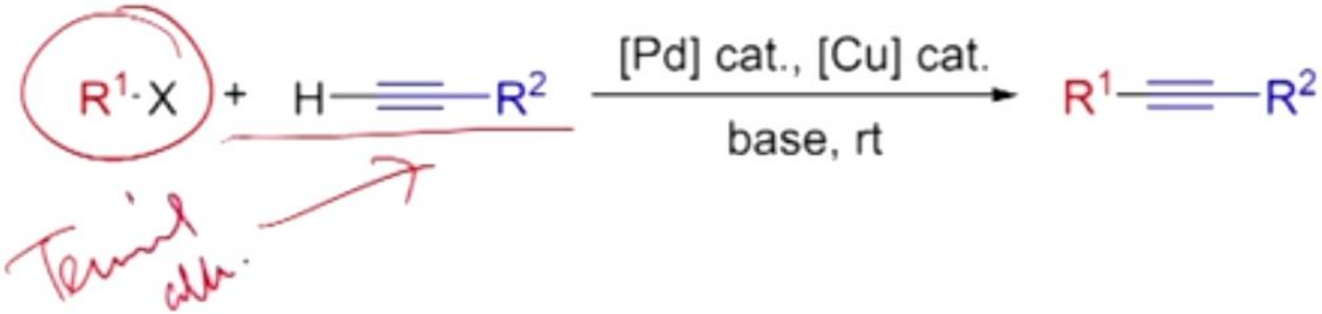
Pd	$Pd_2(dba)_3$	$\overset{II}{Pd}(OAc)_2$	$\overset{0}{Pd}(PPh_3)_4$
Ligands	PPh_3	$PtBu_3$	1:1 P:Pd
Solvents	Dioxane	DMF	MeCN
Base	Et_3N	Cs_2CO_3	Cy_2NMe



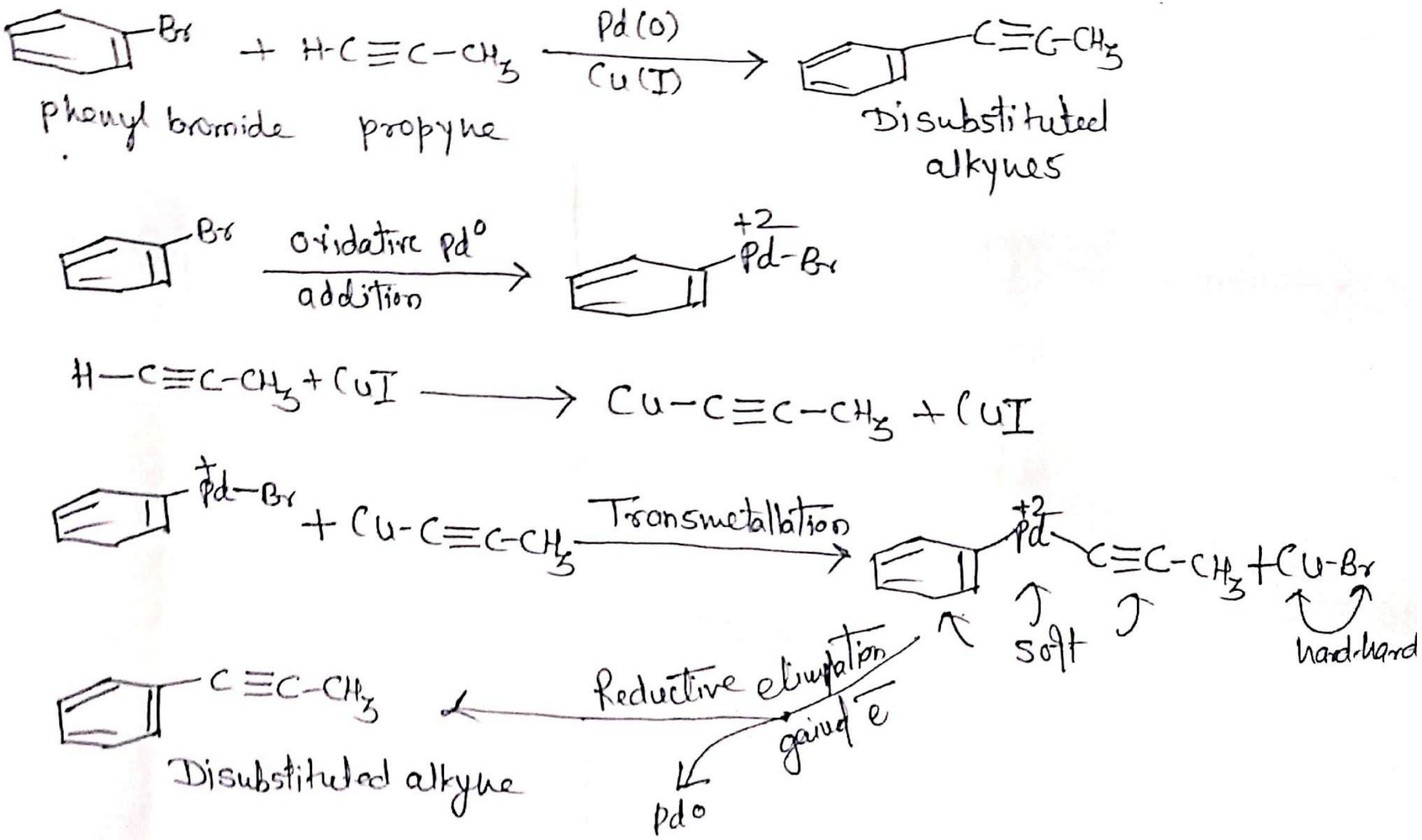
Palladium based reagents in organic synthesis
(Pd)

Sonogashira coupling

- The **Sonogashira reaction** is a cross-coupling reaction used in organic synthesis to form carbon–carbon bonds.
- It employs a palladium catalyst as well as copper co-catalyst to form a carbon carbon bond between a terminal alkyne and an aryl or vinyl halide.
- The Sonogashira cross-coupling reaction has been employed in a wide variety of areas, due to its usefulness in the formation of carbon–carbon bonds. The reaction can be carried out under mild conditions, such as at room temperature, in aqueous media, and with a mild base, which has allowed for the use of the Sonogashira cross-coupling reaction in the synthesis of complex molecules.
- Its applications include pharmaceuticals, natural products, organic materials, and nanomaterials

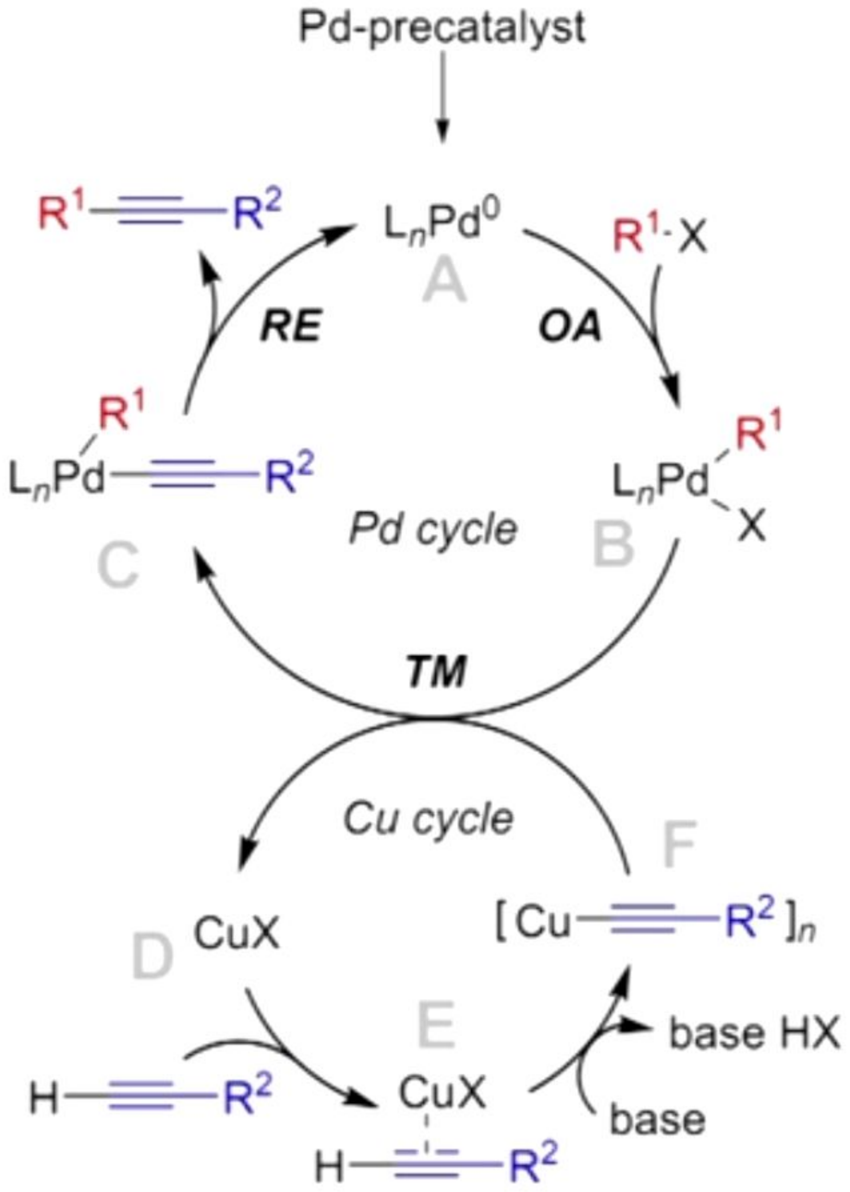


$$R^1\text{-}X + H\text{—}\equiv\text{—}R^2 \xrightarrow[\text{base, rt}]{\text{[Pd] cat., [Cu] cat.}} R^1\text{—}\equiv\text{—}R^2$$


Br
+ H-C≡C-CH3
Pd (0)
Cu (I)
C≡C-CH3
phenyl bromide
propyne
Disubstituted alkynes
Br
Oxidative pd°
addition
+2
Pd-Br
H—C≡C-CH3 + CuI
Cu-C≡C-CH3 + CuI
+
Pd—Br
+ Cu-C≡C-CH3
Transmetallation
+2
Pd
C≡C-CH3 + Cu-Br
soft
hard-hard
Reductive elimination
gained e
pd°
C≡C-CH3
Disubstituted alkyne

Palladium based reagents in organic synthesis

(Pd)



Suzuki-Miayura Cross Coupling Reaction

- Carbon Carbon bond formation
- Most useful industrial reaction
- Use of Boronic ester
- Reaction can run in water or organic solvent
- Reaction requires base

General Mechanism of Suzuki-Miayura Reaction

- Oxidative Addition-Insertion of palladium to Aryl halide

Ar-X + pd(0) →Ar-pd(II)-X

- Formation of active complex using base and boronic ester

$(RO)_2BR_2$ + base → $(RO)_2BR_2OH$

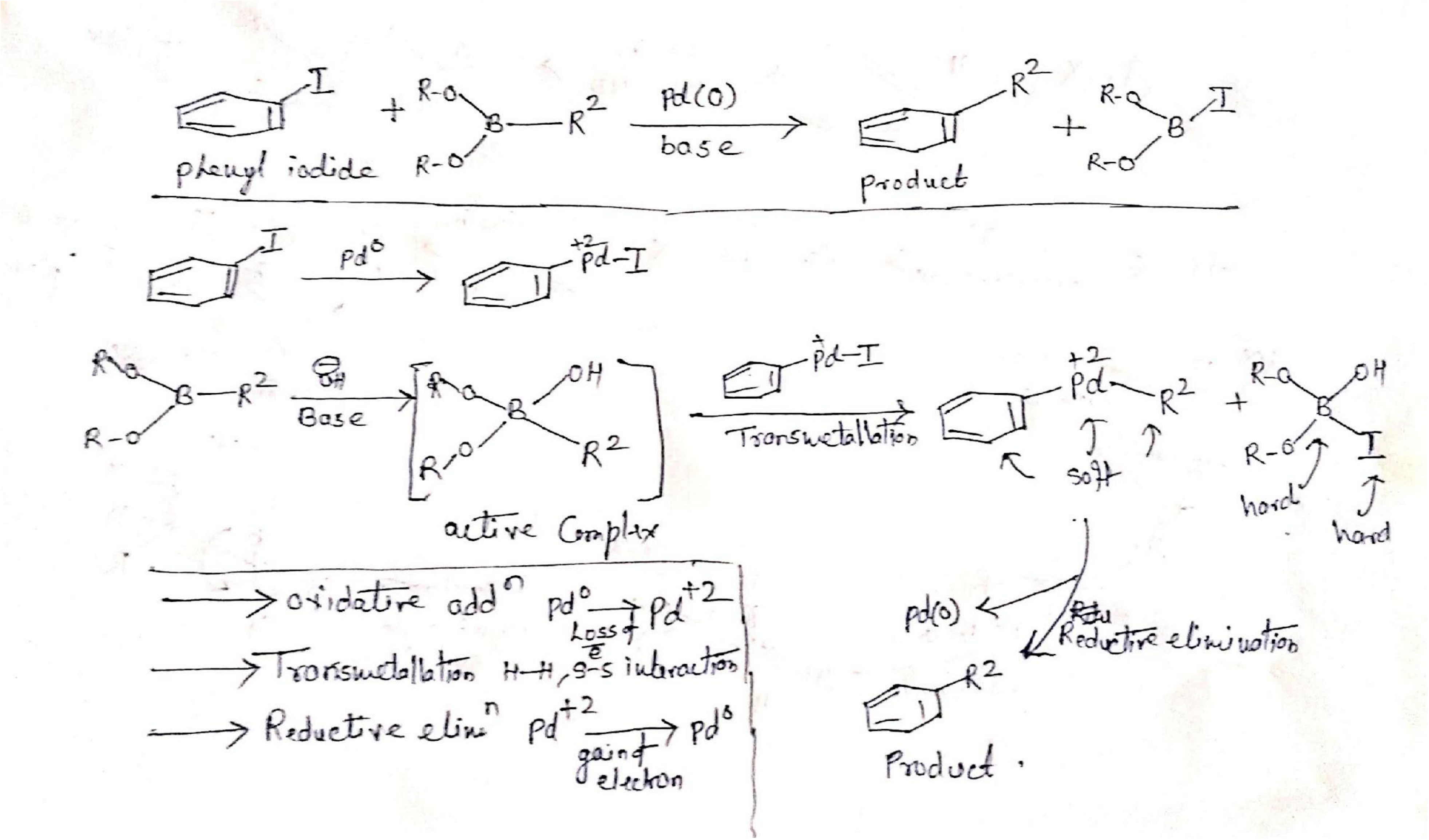
- Transmetallation-Hard-Hard and Soft-Soft interaction

Ar-pd-X + $(RO)_2BR_2OH$ → Ar-pd(II)-R_2 + $(RO)_2BXOH$

Reductive Elimination

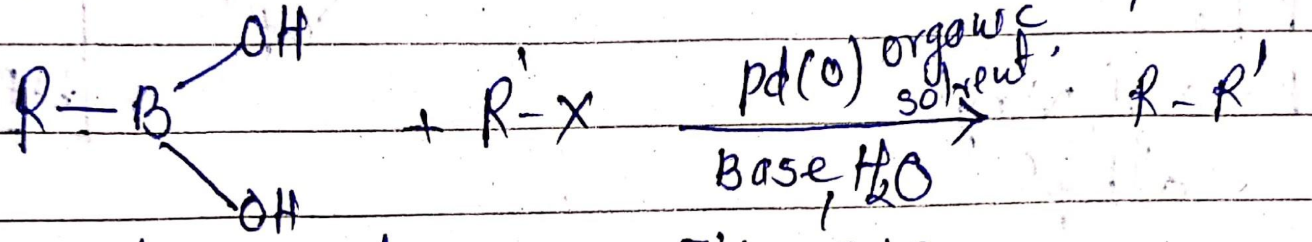
Ar-pd(II)-R_2 → pd(0)(catalyst) +Ar-R2(product)

Mechanism of Suzuki-Miayura Reaction



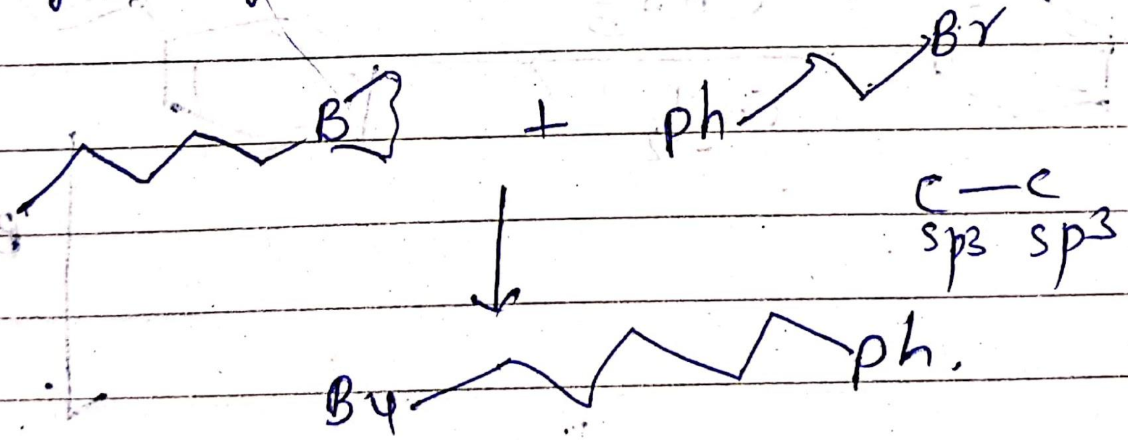
Suzuki Reaction

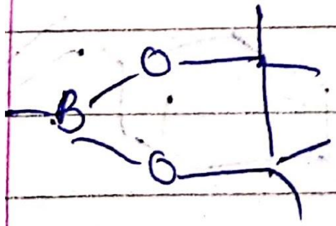
powerful method for formation of C-C-bond

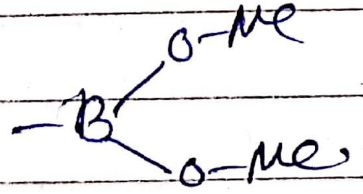


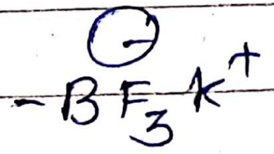
Borolic acid.

R- Aryl, alkyl

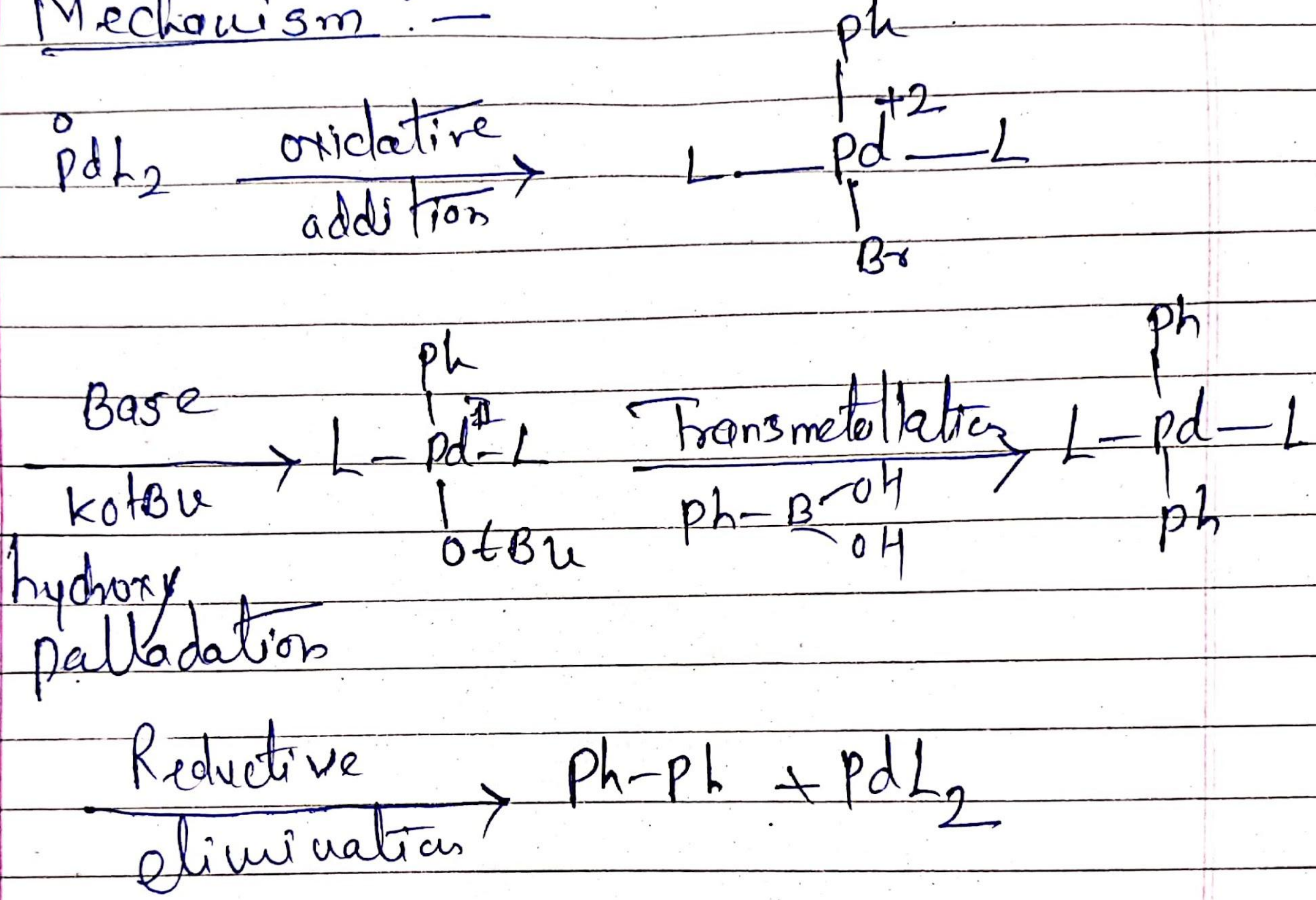


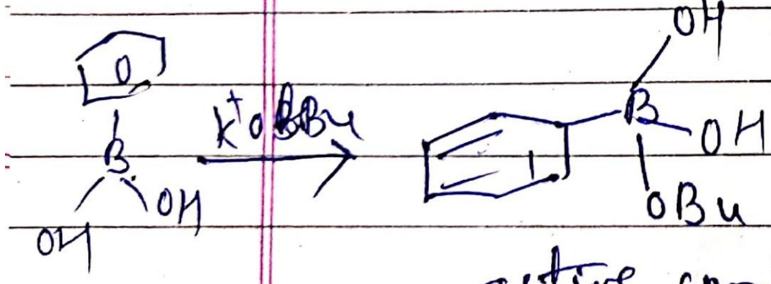




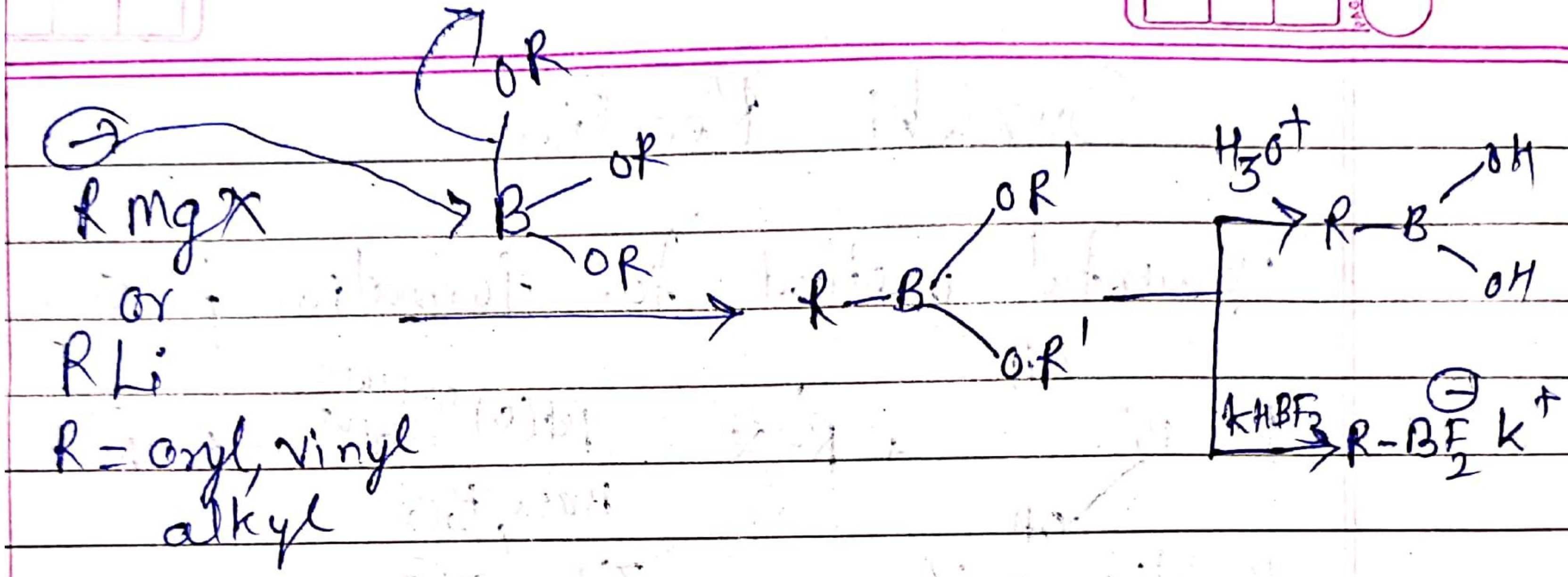


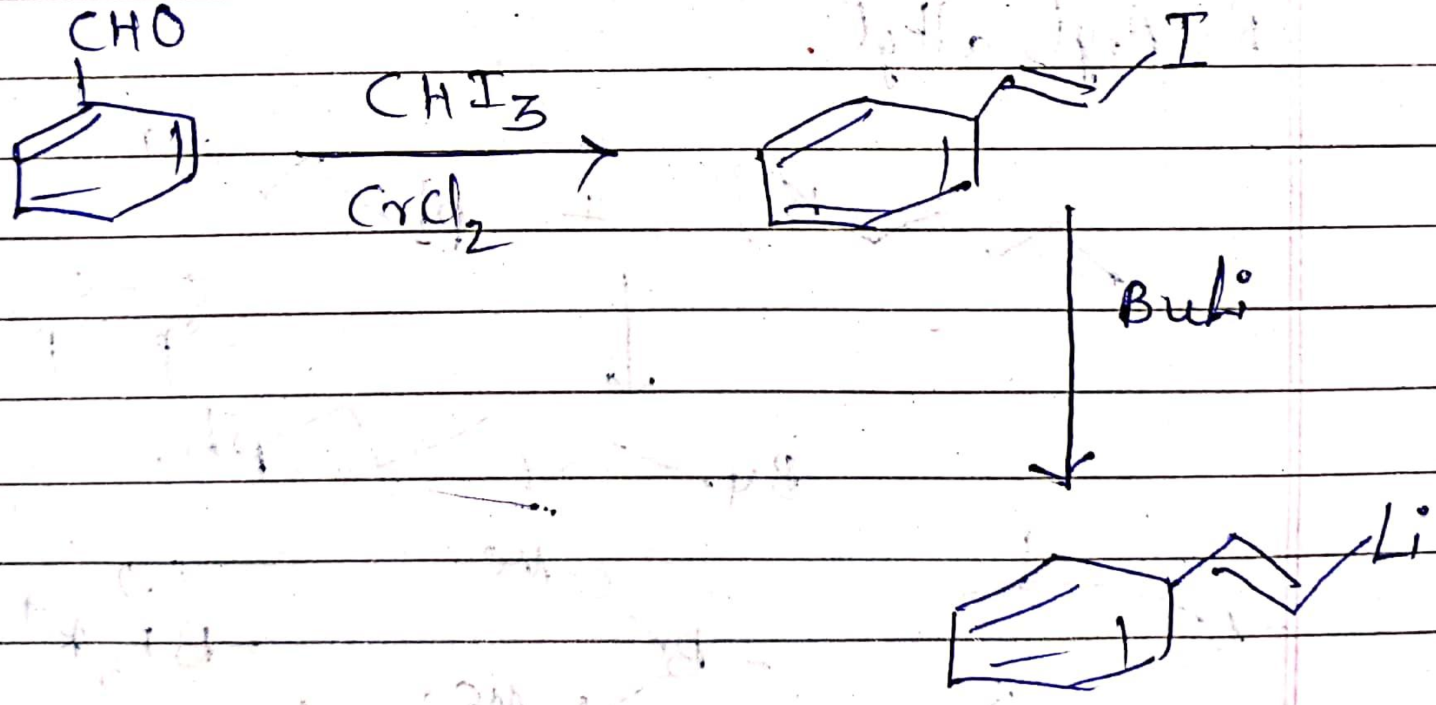
Mechanism :—





active complex


RMgX
or
RLi
R = aryl, vinyl
alkyl
OR
OR
OR
OR'
R–B
OR'
H3O+
R–B
OH
OH
KHBF3
R-BF2 k+


CHO
CHI3
CrCl2
I
BuLi
Li

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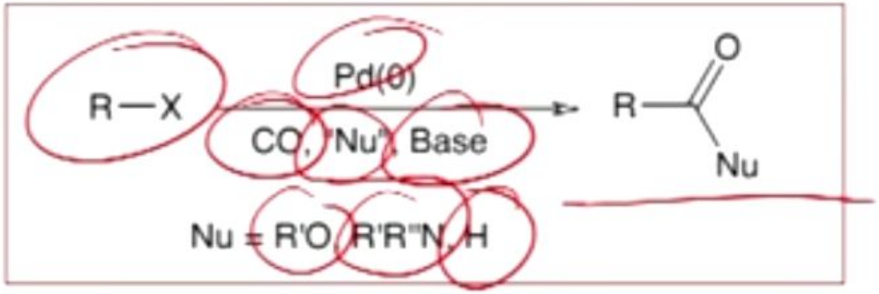
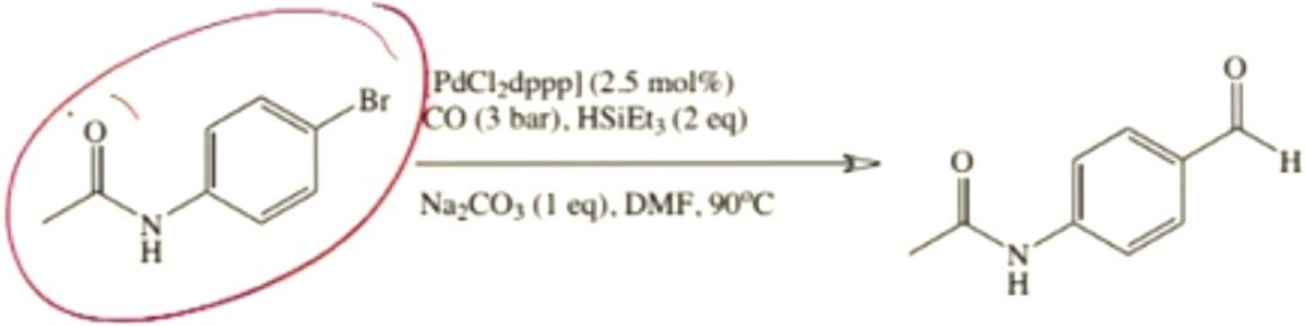
(Pd)

Palladium catalysed carbonylation

As with most palladium mediated C-C bond forming reactions palladium catalysed carbonylation is compatible with a range of functional groups. This gives it significant advantages over standard organolithium and Grignard chemistry for the synthesis of aryl aldehydes, acids, esters and amides.



Aldehyde ($H^{(-)}$)



Palladium based reagents in organic synthesis

(Pd)

Example:

Mechanism