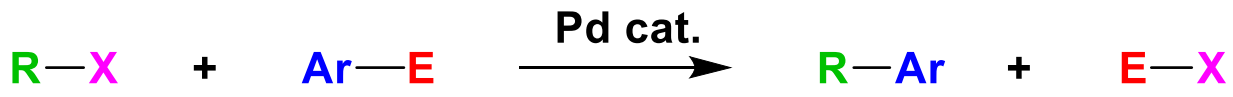
Palladium Catalyzed Coupling Reactions: 2010 Nobel Prize to Suzuki, Negishi & Heck

- See various books – *e.g.* Diederich and Stang, Metal-Catalyzed Cross Coupling Reactions, Wiley-VCH, 1998.

(1) Direct C–C Bond Forming Reactions :



R = usually an aryl or vinyl group

X = I, Br, OTf, Cl, (F), (OTs)

E =	**$B(OR)_2$ or $B(OH)_2$**	**Suzuki**
	SnR_3	**Stille**
	SiR_3	**Hiyama**
	MgX	**Kumada** ⇐ Often a Ni cat. instead of Pd
	ZnX	**Negishi** [e.g. $NiCl_2(PR_3)_2$ or $Ni(COD)_2$ + n PR_3]

- Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176.
- Fu, G. C. *JACS*, **2001**, 10099; *JACS*, **2003**, 5616; *JACS*, **2003**, 14726; *JACS*, **2004**, 1340; *JACS*, **2005**, 4594.

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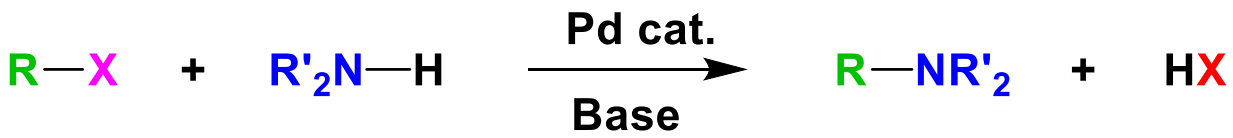
(2) Direct C–N Bond Forming Reactions :



- Hartwig *Angew. Chem. Int. Ed.* **1998**, *37*, 2046.

Hartwig-Buchwald coupling (can also use $R'_2N–SnR_3$)

- Also possible to couple ArX and Ar'EH (E = O or S) to give ArEAr' → Hartwig *JACS* **2006**, 2180 and references therein.

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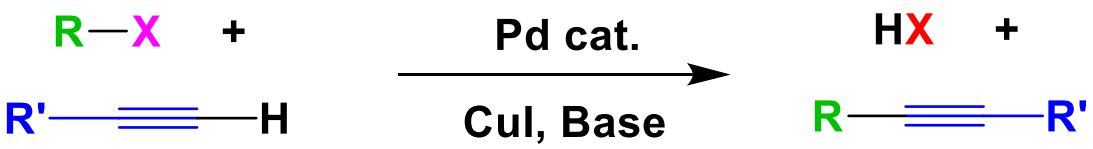
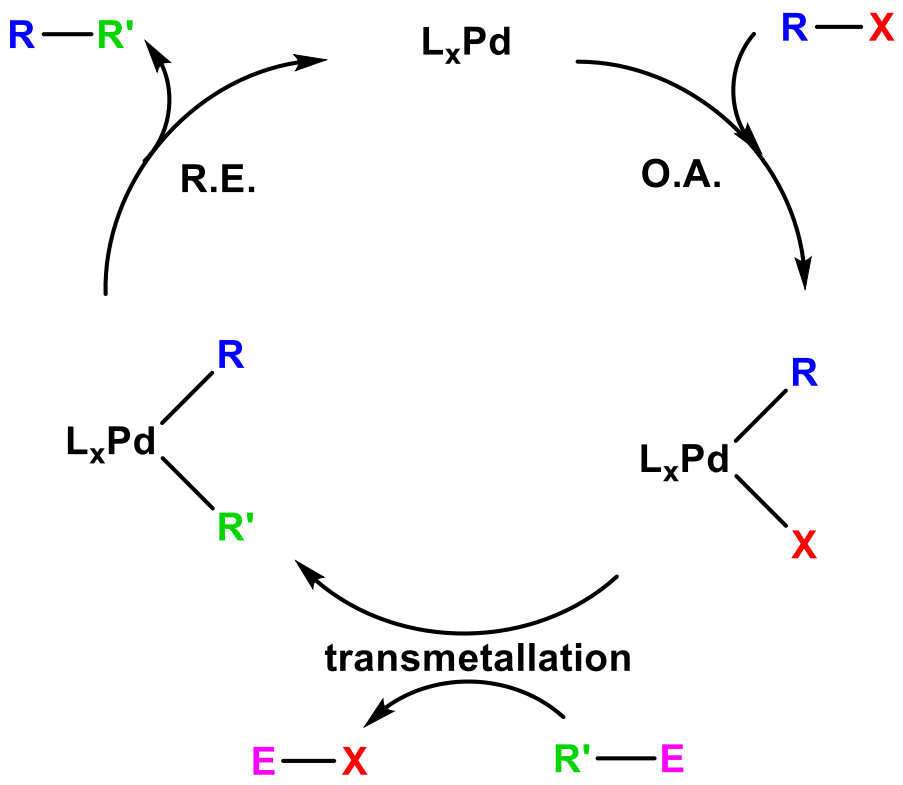
(3) Sonogashira reaction :



- Fu *JACS*, **2003**, 13642.
- Buchwald *Org. Lett.* **2000**, 1729.

Palladium Catalyzed Coupling Reactions

Mechanism:

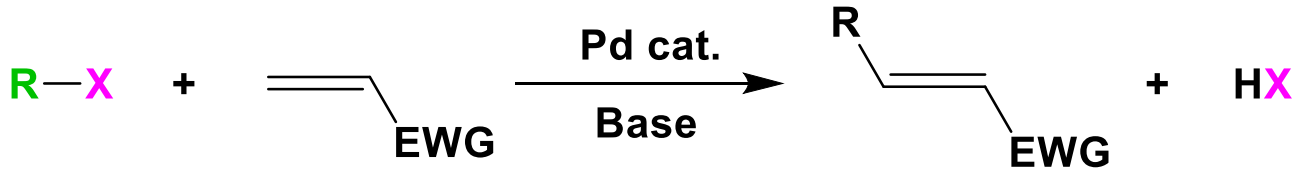


- $Pd(PPh_3)_4$ is OK for simple substrates.
- $Pd_2(dba)_3$ + 4 PR_3 → "$Pd(PR_3)_2$" often much more active and can choose PR_3. (dba = dibenzylidene acetone)
- $PdCl_2$ or $Pd(OAc)_2$ + several equiv. of PR_3 are often used → Pd^{II} is mysteriously reduced to Pd^0 before catalysis can begin.
- CsF or KF often added → F^- coordinates to $ArB(OH)_2$ or $ArSnR_3$ to make a better leaving group.
- KO^tBu often present: (1) often necessary to remove HX formed in the reaction, (2) can do same thing as F^-, (3) may help with pre-catalysis reduction of Pd^{II} to Pd^0.

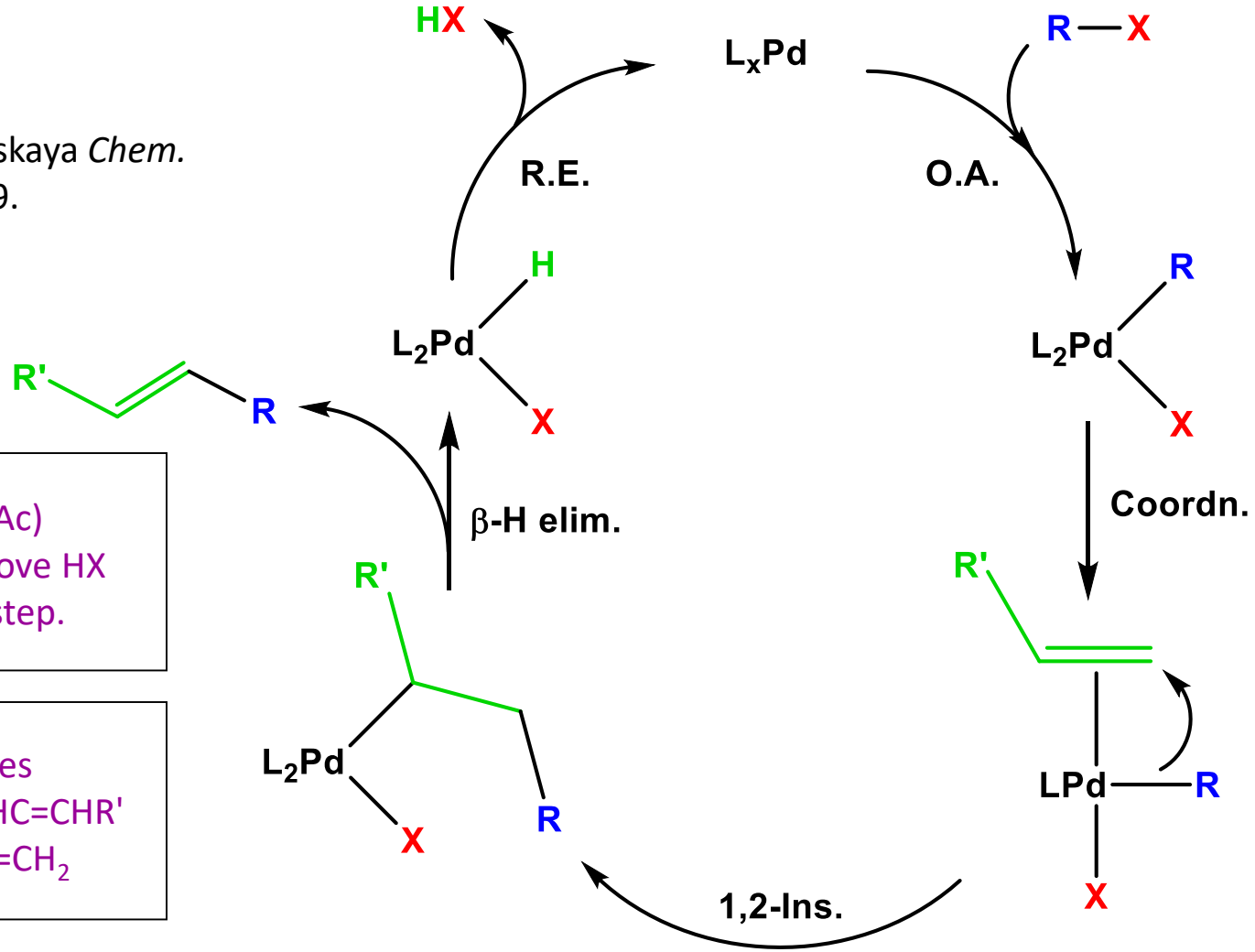
R'—B(OH)$_2$
R'—SnR$_3$
R'—MgBr
R$_2$N—H
RCC—Cu

⇦ Formed from RC_2H and CuI

Heck Reaction Mechanism



- Review = Belatskaya *Chem. Rev.* **2000**, 3009.



- Base (*e.g.* NaOAc) needed to remove HX formed in last step.

- R' = EWG ensures formation of RHC=CHR' instead of RR'C=CH$_2$