03.10.

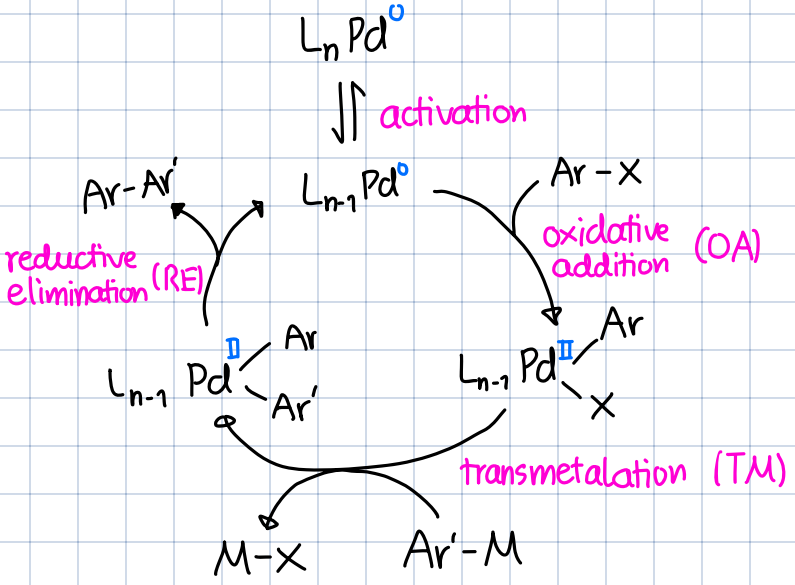
TM-cat. Cross-Coupling

$$\underset{\text{Electrophile}}{Ar-X} + \underset{\text{Nucleophile}}{Ar'-M} \xrightarrow{\text{Pd cat.}} Ar-Ar'$$

→ these rxn's are abs. every where in synth.

$X = Cl, Br, I, CN, OR, SR$, $M = B(OR)_3, Zn, Mg, SnR_3$

Mechanism:



Very popular examples: (All for Pd-cat. cross coupling)

Name	Nucleophile
Kumada	$R-MgX$
Negishi	$R-ZnX$
Stille	$R-SnR_3$
Suzuki	$R-B(OR)_3$
Hyama	$R-SiR_3$

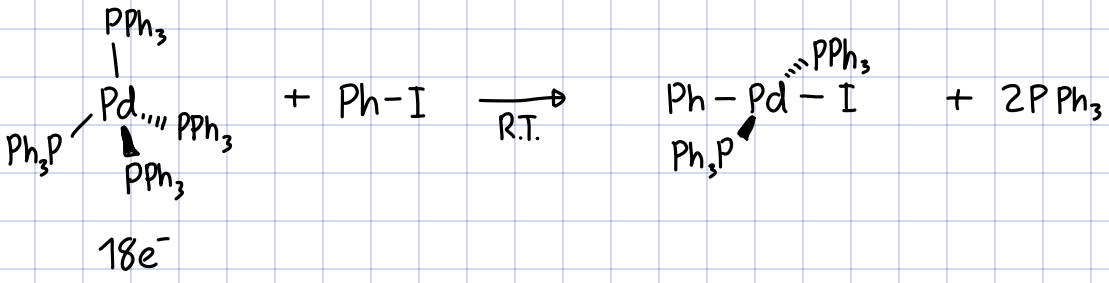
← mostly employed, because very convenient (air stable, FG tolerant, non-toxic)

Ox. Addition

$$M^{n+} + A-B \longrightarrow M^{(n+2)+}\begin{matrix} A \\ B \end{matrix}$$

- Not redox-neutral ⇒ needs d-electrons : $d^n > 0$
- Need VEC < 18, to have driving force
- Need an open coord. site

Case Study:



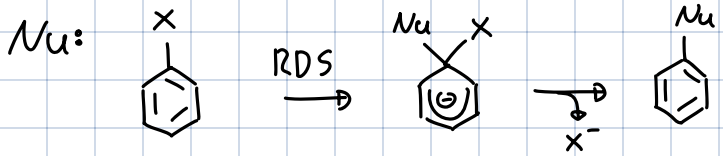
1. ^{31}P-NMR: broad signal at $\delta = 18.5$ ppm

2. rate $= k_{obs}[Pd][PhI][PPh_3]^{-1}$

3. $\Delta H^{\ddagger} = 18.4 \frac{kcal}{mol}$, $\Delta S^{\ddagger} = +3.1$ entropy units

4. Changing the halogen leads to rate → I > Br >> Cl

⇒ Analogy to S_NAr?



↳ 3,4 speak against it: $\Delta S^{\ddagger}$ is here <0 and changing halogen would be other way around due to EN

⇒ Can we explain the data either way?

~ Consider: L = PPh_3

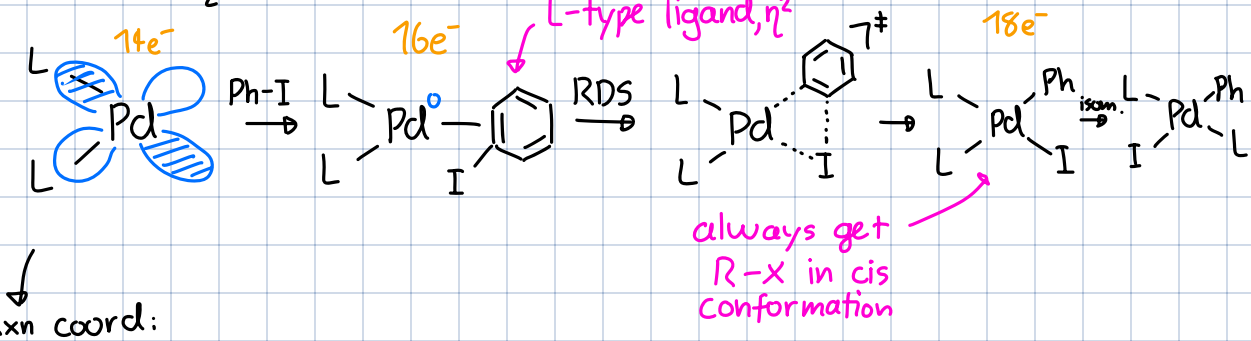
L_4Pd (18e⁻) $\overset{K_1}{\rightleftharpoons}$ L_3Pd + L $K_1 >> 1$

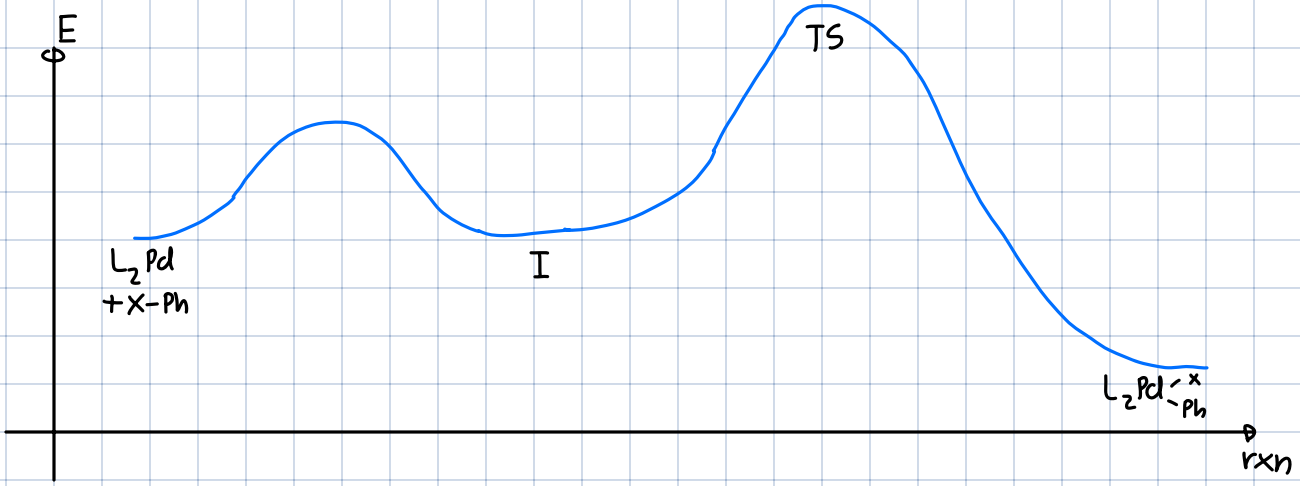
L_3Pd (16e⁻) $\overset{K_2}{\rightleftharpoons}$ L_2Pd (14e⁻) + L $K_2 \approx 10^{-5}$

⇒ Explains very broad NMR signal, as very dynamic.

⇒ Many times the cat. active form isn't the cat as added to the rxn mixture!

Consider L_2Pd then:

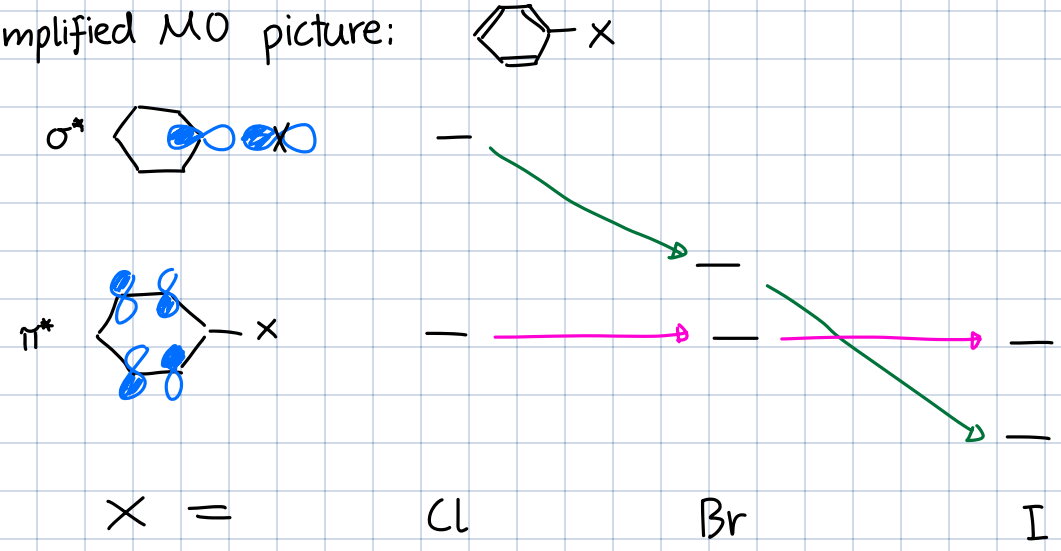




Now we still need to explain the rate trends from 4.:
↝ Consider $L_2Pd \cdots Ar-I$

- Dominated by Pd → π^*_{Ar}
- To break C-I : Pd → σ^*_{Ar-I}

Simplified MO picture:



whereas the HOMO (d_{xy}) of Pd is about on the E-level of the π^* orbs ⇒ much better overlap with σ^*_{Ar-I} than with σ^*_{Ar-Cl}