

Chapter 6 Carbanions & Other Carbon Nu:

- Very useful in synthesis for C-C bond formation
 - ◆ stability/reactivity: hybridization & substituents of carbanions
- Acidity of hydrocarbons: too weak to be measured
 - ◆ weakly acidic polar solvents for equilibrium measurements: dissociation of ion pairs & clusters; DMSO, C₆H₁₁NH₂
 - ◆ basicity constant, H_- : solvent-base pairs;  580 [Table 6.1](#)
 - pH of strongly basic solutions: the larger, the greater basicity
- Thermodynamic acidity: acidity in equilibrium state
 - ◆ $pK_{RH} = H_- + \log[RH]/[R^-]$; $RH + B^- \rightleftharpoons R^- + BH$;  580 mid
 - indicators when similar UV-Vis spectra between RH & R⁻

Kinetic Acidity of Hydrocarbons with $pK_a > \sim 35$

□ Different rate of deprotonation in S-D: [📖 581 top](#)

◆ often, rate of deprotonation \propto stability of carbanions

◆ rate of isotope incorporation into the hydrocarbons

○ suitable for very weak acids: not requiring a measurable concentration of the carbanion at any time



◆ problem: internal return of the ion pairs; [📖 581 middle](#)

○ no exchange with the solvent deuterons: no satisfactory linear relationship between exchange rates & equilibrium acidity

○ factors on ion pairing: polarity of solvents (least in polar aprotic; DMSO & $C_6H_{11}NH_2$), cation (less chelating; Cs^+)

❖ Acidity of Hydrocarbons

- Relative acidities of hydrocarbons:  583 [Table 6.2](#)
 - ◆ stabilization by Ph & aromatic stabilization: No. 1-4 & 5-6
 - ◆ allyl stabilization: $pK_{\text{propene}} = 43$, $pK_{\text{cyclohexene, cycloheptene}} \cong 45$
 - ◆ Ph-H $\cong 45$, CH₂=CH-H $\cong 46$ (electrochemical methods)
 - ◆ saturated hydrocarbons: too slow deuterium exchange
 - electrochemical methods: $R^\bullet + e^- \rightarrow R^-$;  584 [Table 6.3](#)
 - ◆ phenylacetylene: 26.5 (DMSO), 23.2 (C₆H₁₁NH₂), ~20 (H₂O)
 - the more s character, the more acidic: cyclopropane
 - ◆ carbanions in gas phase: similar trends;  585 [Table 6.4](#)
 - ◆ geometry: pyramidal (4-31G); $\angle \text{HCH}_{\text{CH}_3^-} = 97\text{-}100^\circ$, more s character at the e⁻ pair (better stabilized than that with sp²)

❖ Stereochemistry of Carbanions

□ Stereochemistry in H-exchange: [📖 587 top](#)

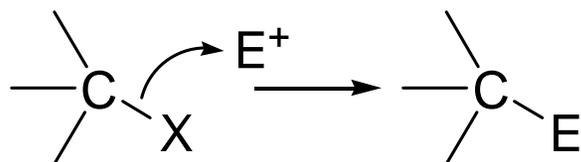
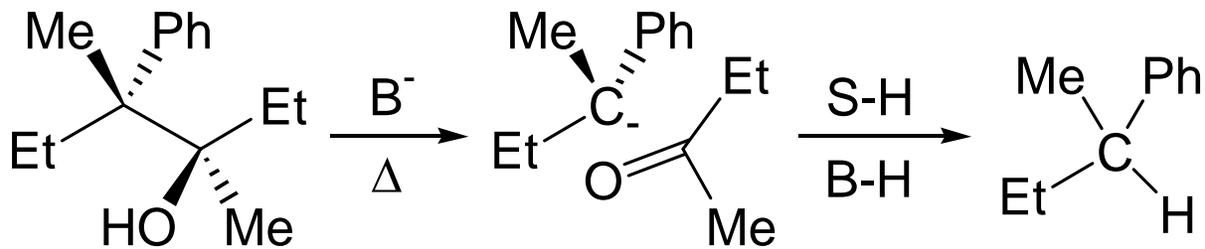
◆ the mechanisms of electrophilic substitution reactions (S_E)

- retention in nonpolar solvents: 93% with KO^tBu in PhH; a short lifetime of a tight ion pair [S_E2(front) or S_Ei]
- inversion in polar protic solvents: 48% with KOH in ethylene glycol; fast H⁺ transfer to an unsymmetrical ion pair [S_E2(back)]
- racemization in polar aprotic: KO^tBu in DMSO; enough lifetime of the carbanion for symmetric solvation; S_E1

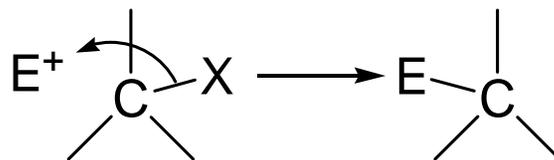
◆ H-D exchange at the chiral carbon: [📖 587 bottom](#)

- retention with KO^tBu in DO^tBu: S_Ei-like mechanism
- racemization with KO^tBu in DMSO: long lifetime of carbanions

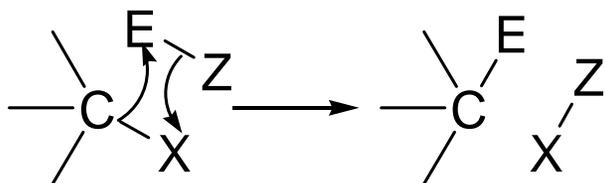
❖ Stereochemistry of Carbanions: S_E



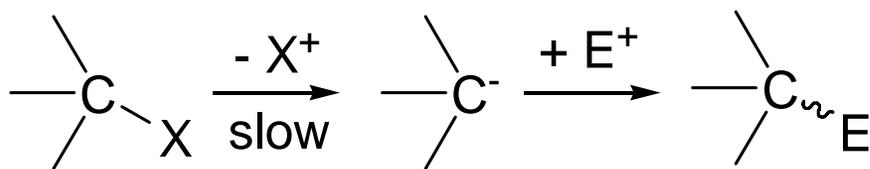
S_E2(front): retention



S_E2(back): inversion



S_Ei: retention



S_E1: racemic

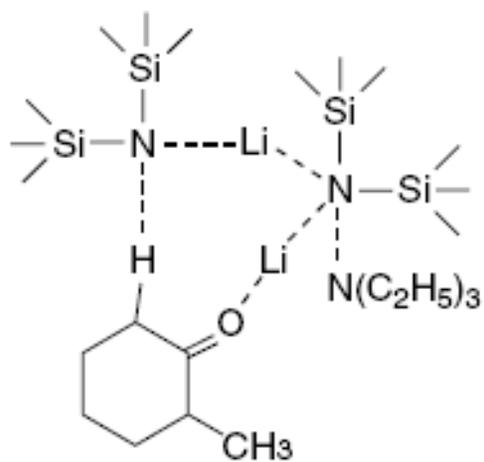
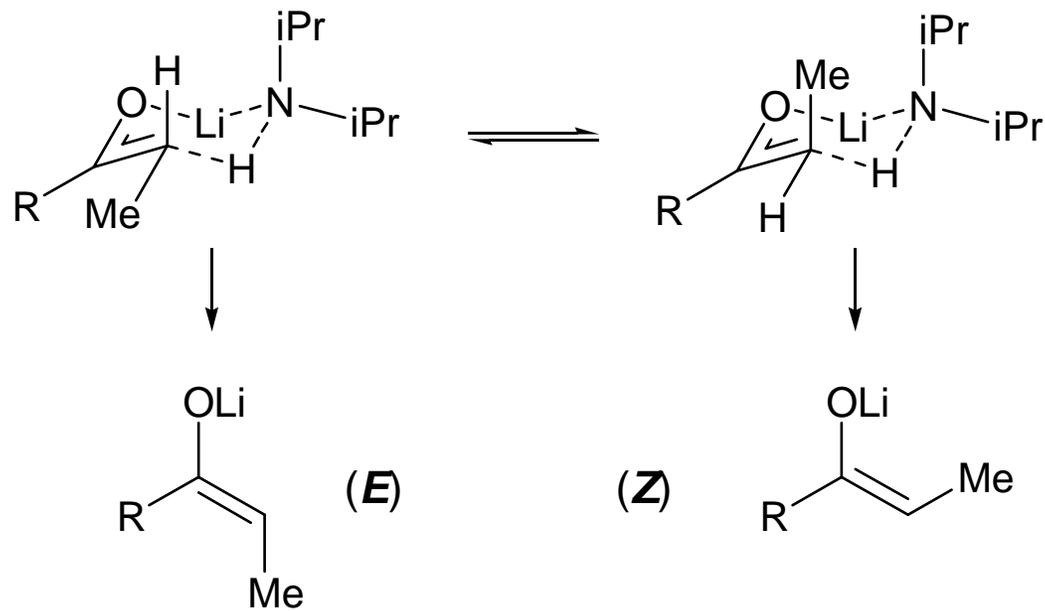


Carbanions of Organometallics

- Preparation: metal-halogen exchange; [📖 588 top](#)
 - ◆ significant covalent character of the carbon-metal bond
- Relative basicity: $\text{MeLi} < \text{BuLi} < {}^t\text{BuLi}$; $\text{p}K_{\text{a}} \cong 50\text{-}62$
- Aggregates of RLi in solution: unreactive
 - ◆ BuLi in THF: tetramer \rightleftharpoons dimer; the major being tetramer
 - X-ray structure of BuLi in solvent: [📖 590 Fig. 6.2 THF/TMEDA](#)
 - ◆ reactive with chelating agents TMEDA: dimer; [📖 589 top](#)
 - ◆ some energy required to break up the C-Li bond
 - sluggish reaction as a base & preference as a nucleophile: addition to carbonyls rather than enolate formation

❖ Stabilized Carbanions (I)

- Carbanion-stabilizing groups:  [595 Table 6.6](#)
- ◆ relative order: $\text{NO}_2 > \text{C}=\text{O} > \text{CO}_2\text{R} \sim \text{SO}_2 \sim \text{CN} > \text{CONR}_2$
 - resonance ($\text{NO}_2/\text{C}=\text{O}$) & polar effects (SO_2):  [592 middle](#)
- ◆ other pK data: [Part B](#) &  [593 Table 6.7](#) ([Meldrum's acid](#))
 - bases used: $\text{Li}(\text{Na})\text{NH}_2$, LDA, NaH, L(Na/K)HMDS, Na(K)OR
- ◆ rate of enolate formation: $\text{CH}_3 > \text{CH}_2\text{R} > \text{CHR}_2$
 - steric hindrance to base and solvation:  [594 Table 6.8](#)
 - by isotopic exchange or halogenation:  [593-4](#)
 - closed vs open TS: *E*- vs *Z*-enolate;  [596 middle & Table](#)
 - acceleration of enolate formation with Et_3N : dimer;  [595 top](#)



❖ Stabilized Carbanions (II)

□ Structural effects on the rate of enolate formation

- ◆ kinetic vs thermodynamic control:  595 [Scheme 6.1](#)
 - perpendicular H: stereoelectronic control;  597-8 [Fig. 6.3](#)
- ◆ nitroalkanes & cyano compounds:  597-8 [Tables 6.9](#)
- ◆ sulfur & phosphorus compounds:  599 [Table 6.10](#)
 - 1,3-dithiane: pK 36.5 (Cs⁺, THF), 2-Ph derivative 30.5
 - bond dipole effect (minor), delocalization with 3d (MO calculation), polarizability of S (experimental)
- ◆ R₃Si < Ar₃Si: modest stabilization due to polarizability
 - decrease of pK by 1-4 in fluorene & 3-7.5 in sulfones
- ◆ ylides X⁺-C⁻ ↔ ylene X=C: polarizability,  600-1
 - Ph₃P⁺CH₃ pK_{DMSO} = 22; Ph₃P⁺CH₂COAr pK = 4-7

❖ Enols & Enamines (I)

- Enols: more reactive Nu than alkenes; [📖 602 top](#)
 - ◆ less reactive than enolates: less e^- density due to H
 - ◆ acid-catalyzed mechanism of enol formation: [📖 601 bottom](#)
 - RDS: deprotonation step, k_H / k_D (α -position) ≈ 5
 - Brønsted catalysis law: $\alpha=0.74$ [[📖 348, Eq. 3.51](#)]
 - ◆ rates of acid-catalyzed enolization: [📖 603 Table 6.11](#)
 - relative rate differences: much less than those for base-catalyzed enolate formation; *conf.* [📖 594 Table 6.8](#)
 - more substituted enol favored: 2-butanone, H-3:H-1 = 4.2:1
 - product-like TS favored with more stable enol structure
 - bulky substituent (tBu) makes the enol unstable

❖ Enols & Enamines (II)

- Equilibrium concentration of enols:  604 [Table 6.12](#)
 - ◆ monocarbonyls: present mostly as a keto tautomer
 - ◆ 1,3-dicarbonyls: stabilized enol by intramolecular H-bonding & conjugation of the C=C with the carbonyl;  [605 bottom](#)
 - structural data: time-averaged structure;  [605-606 top](#)
 - proton transfer barrier between two oxygen atoms: 4-5 kcal
 - ◆ [solvent-dependent](#): more enols in nonpolar solvents because the decrease in molecular dipole is favored
- α -dicarbonyls: less enol form than β -dicarbonyls
 - ◆ K_{enol} (pyruvic acid) $\approx 10^{-3}$:  [606 bottom](#)

❖ Enols & Enamines (III)

□ Characteristics of enols: [📖 607 top](#)

- ◆ production I: careful hydrolysis of orthoesters with acetate
 - $t_{1/2}$ (NMR): several hrs at -20 °C, 10 min at +20 °C
 - bases promote isomerization to a keto form (acetaldehyde)
 - DMSO/DMF slows the rate by H-bonding, longer lifetime
- ◆ production II: protonation of enolates in water; [📖 607 mid](#)
 - rate of ketonization depends on pH: acid/base catalysis
- ◆ more acidic enols ($pK = 10.5$) than the α -Hs of the keto form ($pK = 18.4$): **acetophenone**; [📖 607](#) & [📖 608 top](#) (**acetone**)

□ Enamines: more reactive than enols; [📖 608 middle](#)

- ◆ less substituted isomers preferred: A^{1,3} strain; [📖 608 bot](#)
- ◆ less reactive 6-ring enamines than 5-/7-rings: favored exo double bonds for 5-/7-rings; [📖 609 top](#) [[📖 172 mid \(4th ed.\)](#)]

❖ Carbanions in S_N2 Reactions (I)

□ Unstabilized carbanions: 610 [Scheme 6.2](#)

◆ organometallics: soft good nucleophiles; mostly by S_N2

○ complications due to the aggregate structure:  [620 & 611](#)

○ allylic rearrangement with allyl halides:  [611 middle](#)

○ in practice, [transition metal-catalyzed processes](#): [Heck reaction](#)

□ Enolates: good Nu as stabilized carbanions

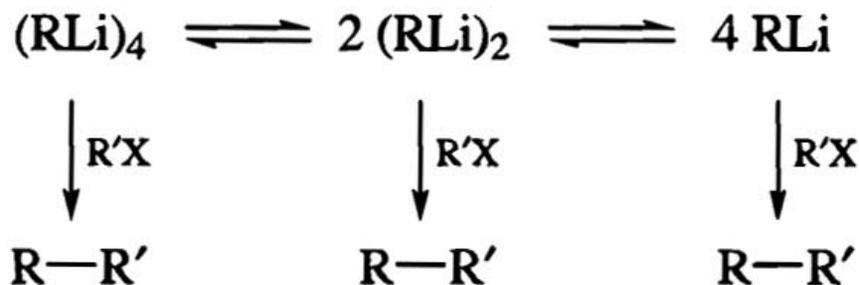
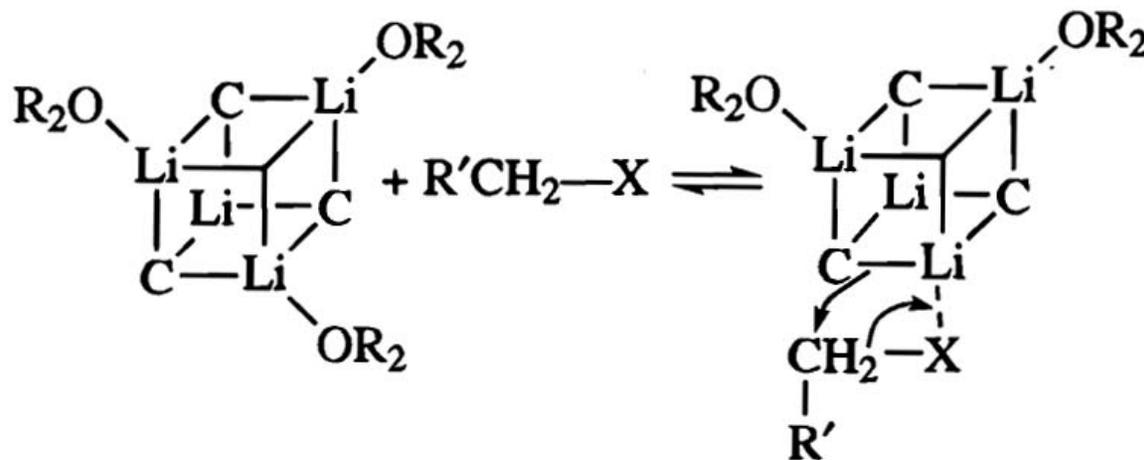
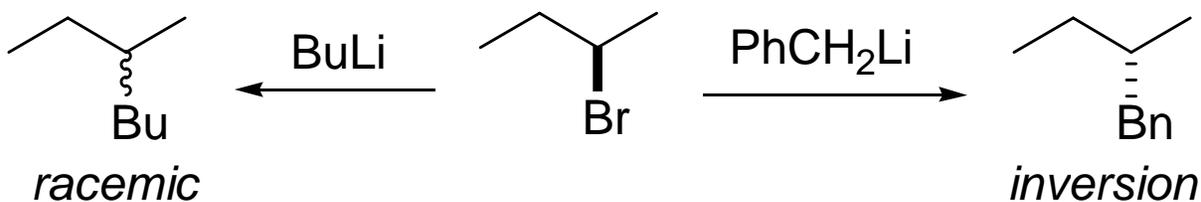
◆ aggregated structures: ester/ketone;  [612 & 613](#) [Fig. 6.4](#)

○ multiple chelation of the enolate oxygen atom to Li⁺: hindered approach of electrophiles to the oxygen or carbon atom

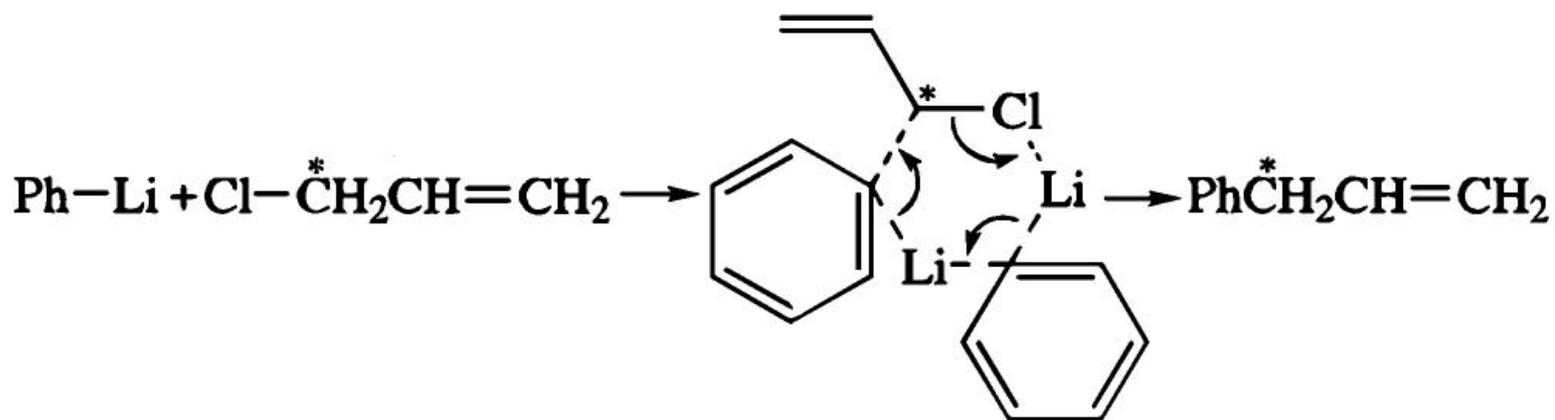
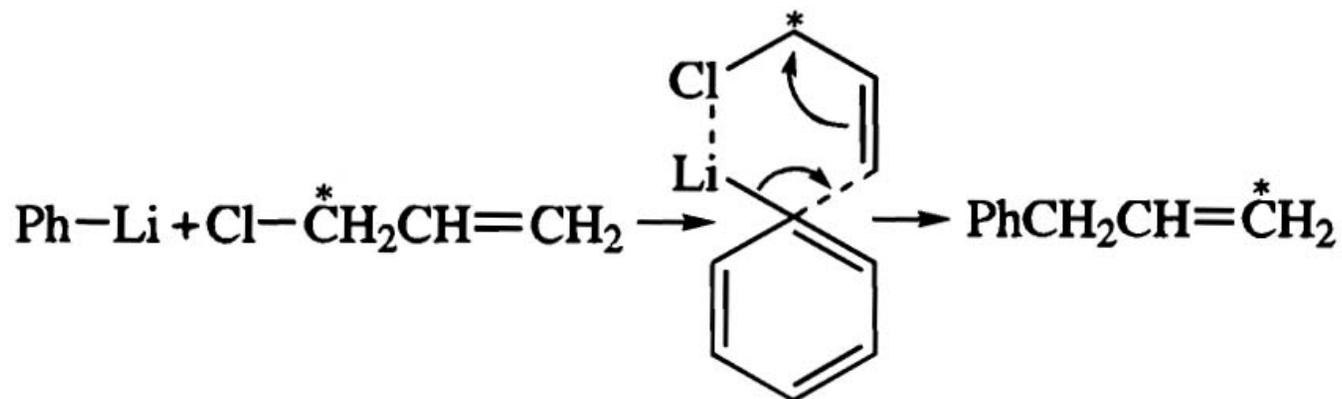
○ faster rate in HMPA, DMSO, DMF: dissociation of the aggregate

○ effect of cations on the rate: BrMg⁺ < Li⁺ < Na⁺ < K⁺

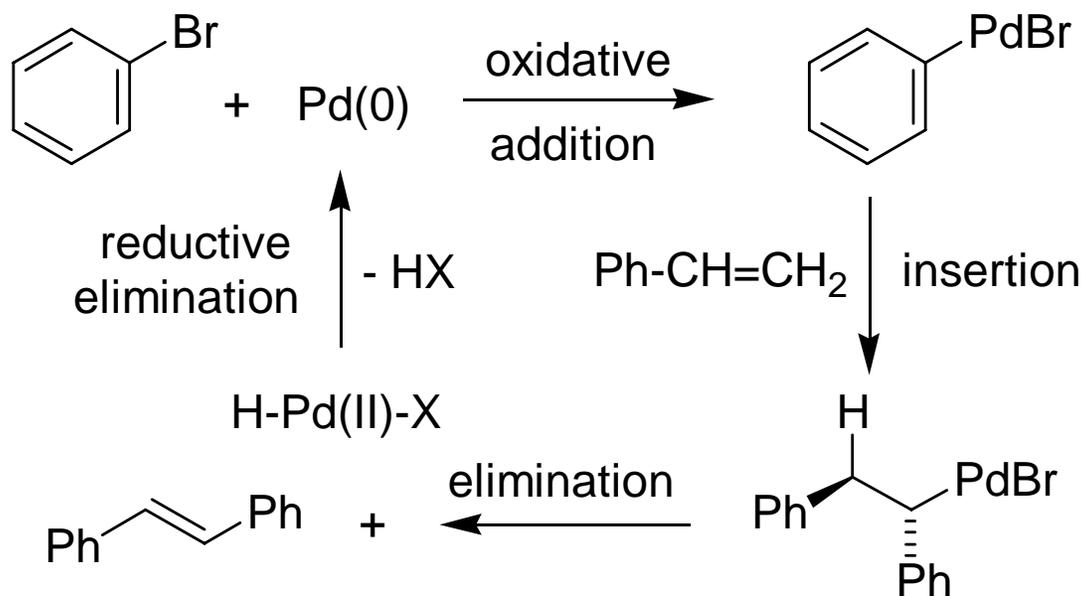
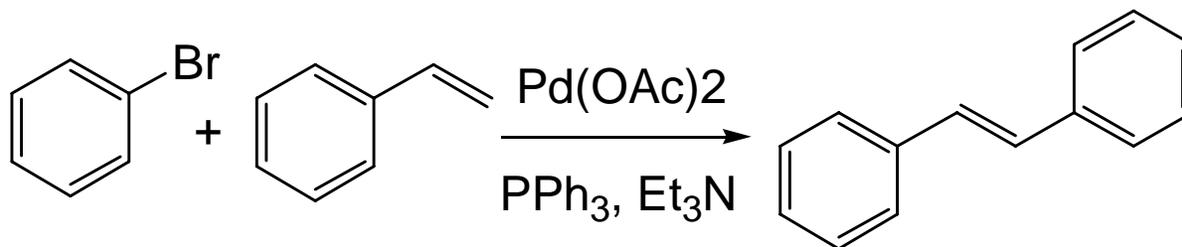
❖ Stereochemistry of S_N2 of Carbanions



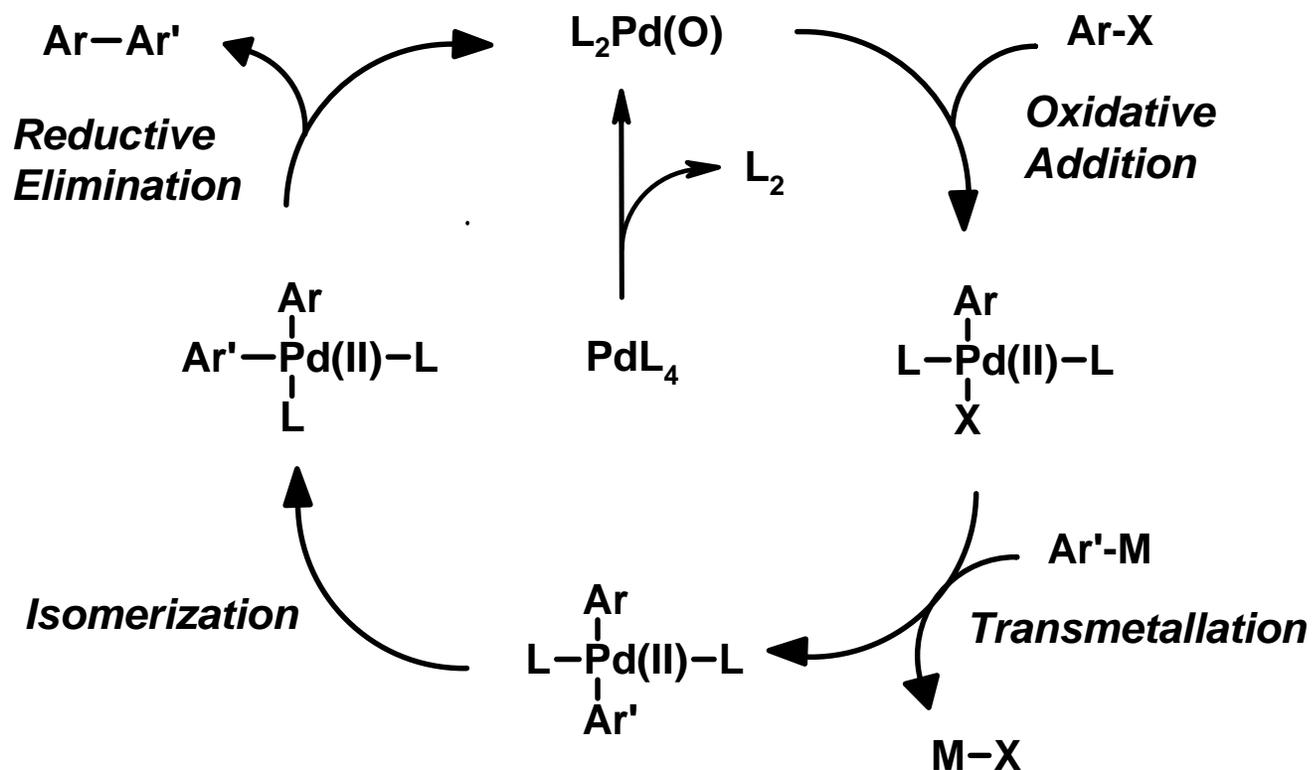
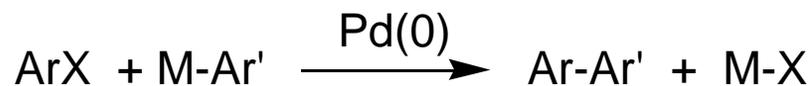
❖ S_N2 of Allyl Chloride: Allylic Transposition



❖ Transition Metal-Catalyzed Alkylations



Transition Metal-Catalyzed Coupling Reactions



❖ Carbanions in S_N2 Reactions (II)

□ Enolates: good Nu as stabilized carbanions (cont'd)

◆ C-alkylation vs O-alkylation: [615 top Table](#)

○ soft electrophile vs hard electrophile: leaving group effect

○ cyclic TS for halides (soft) vs sulfonates (hard):  [615 middle](#)

◆ stereoelectronic control: perpendicular attack; [614 top](#)

○ cyclohexanes: axial approach, chair-type TS;  [616-7](#)

○ acycles: anti to L with an H-eclipsed conformation;  [617-9](#)

◆ steric control: less hindered side of the enolates

○ equatorial approach of electrophiles favored:  [616 top](#)

○ 1-decalone: *cis*, [H vs CH₂];  [616 bottom](#), 2-decalone with Me at C-10: *trans*,  [617 top](#), cyclopentanone: *cis*, torsional effect,  [617 middle](#) & [618 Fig. 6.5](#)