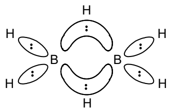
Main-group organometallics

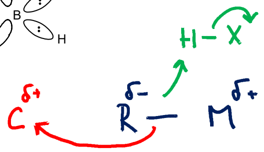
Reading: Bochmann: Organometallics and Catalysis

Chapter 1 (1.2: pages 1 – 27,
further reading: 28 -80)

Main group organometallics at a glance

- Structures
  - oligomeric structures
  - 3c-2e (or even 4c-2e) bonds
- Reactivity
  - nucleophilic and basic
  - auxiliaries in organic synthesis
  - source of organic groups for transition metals

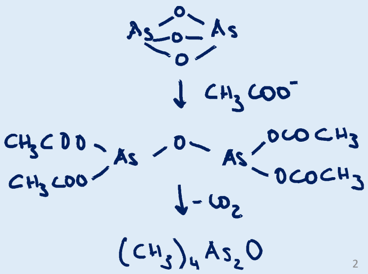




$R-Mg-Br + LPdBr \rightarrow LPdR + MgBr_2$

First organometallic compounds:

- Cadets's fuming liquid (1757): from arseneous oxide (As_2O_3) and potassium acetate.
  4 $CH_3COOK + As_2O_3 \rightarrow$ **$As_2(CH_3)_4O + 4\ K_2CO_3 + CO_2$** →→ $As_2(CH_3)_4$
  cacodyl oxide cacodyl
  (poisonous garlic-smelling red oily-liquid,
  unstable undergoing spontaneous combustion in dry air)
- First organozinc (1848): $2\ R\text{-}X + 2\ Zn \rightarrow R_2Zn + ZnX_2$
- Grignard reagents (1900): $R\text{-}X + Mg \rightarrow R\text{-}Mg\text{-}X$
- Organolithium reagents (Schlenk, 1917): $R\text{-}X + 2Li \rightarrow R\text{-}Li + LiX$



Organo-lithium compounds

- Ionic character, electron-deficient - stabilization by forming oligomeric or polymeric structures

$[EtLi]_4$

- Strongly basic and nucleophilic (applications in organic synthesis)

$\overset{\delta-}{R} - \overset{\delta+}{Li}$

- Reducing (unwanted side reactions)

$[R-Li] \longrightarrow R^{\bullet} + e^{-} + (Li^{+})_{solv.}$

↳ RADICAL REACTIONS

- Heavier analogs: organosodium and organopotassium compounds
  - "Purely" ionic
    - polymeric structures
    - pyrophoric solids
    - mostly insoluble in any solvent they don't react with
  - Very strong bases, not that good as nucleophiles
    - few applications → superbases
    - organoLi compounds are much easier to handle

Organo-Mg compounds

- Like Organolithium compounds, but milder

- Ionic character, electron-deficient
  - oligomeric or polymeric structures

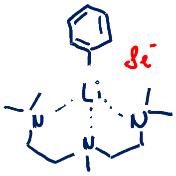
- Basic and nucleophilic
  - Mg: applications in organic synthesis (Grignard reagents !)

- Reducing
  - sometimes unwanted side reactions

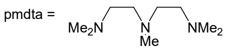
- Organo Be: extremely toxic, not used
- Organo Ca, Sr, ... compounds: ionic, insoluble, not used

Structures

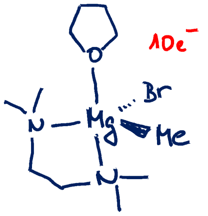
- 8 *e* "preference" rather than "rule"
- "Too many" electrons if:
  - large atomic radius
  - electropositive elements
  - small ligands
  - chelate structures
- "Too few" electrons for:
  - small atomic radius
  - less electropositive elements
  - bulky ligands



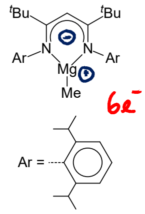
PhLi(pmdta)

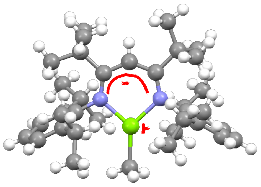


penta**m**ethyl**d**iethylene**t**ri**a**mine

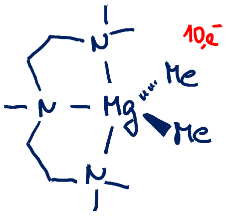


MeMgBr(THF)(tmeda)





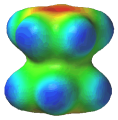
(β-diiminate)MgMe



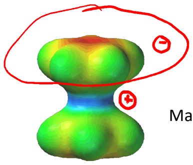
$Me_2Mg(pmdta)$

Structures

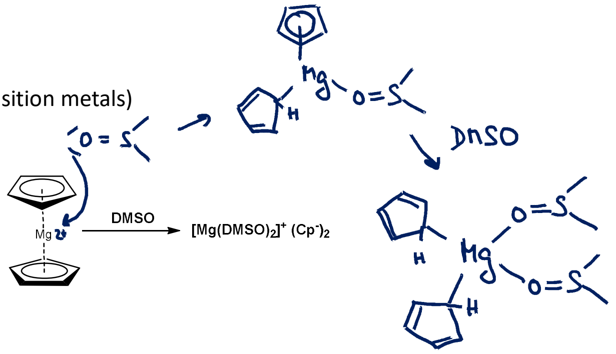
- Strong preference for σ-donor groups
  - but Cp is often π-bound (deceptively like with transition metals)



Cp_2Fe



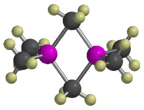
Cp_2Mg
Magnesocene

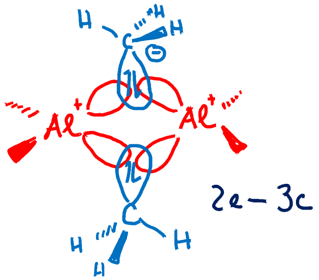


$[Mg(DMSO)_2]^+ (Cp^-)_2$

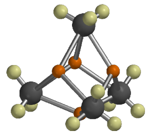
- Electropositive metals: often 3c-2e or 4c-2e hydrides/alkyls

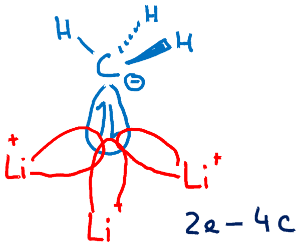
$(Me_3Al)_2$





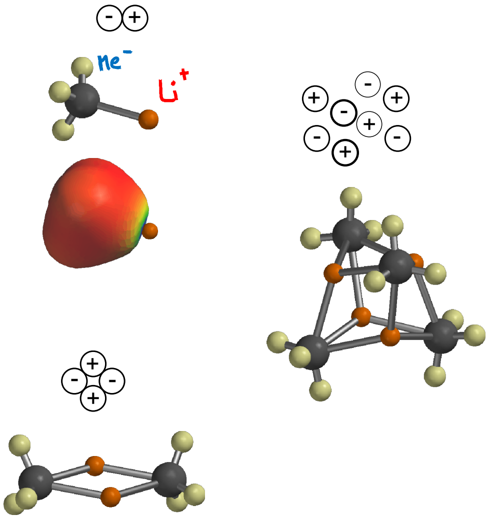
$(MeLi)_4$



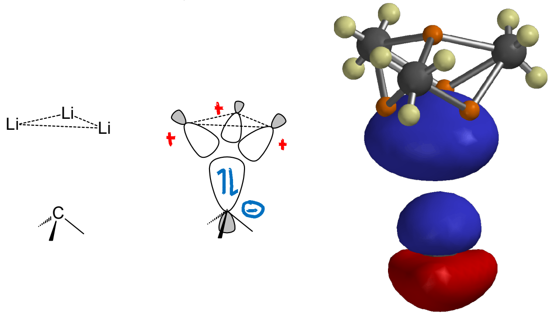


Driving force for oligomerization

- ionic interpretation:



- covalent interpretation



2e-3c and 2e-4c bonds are not just bonding between Li and C, but also bonding between the Li atoms

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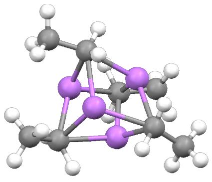
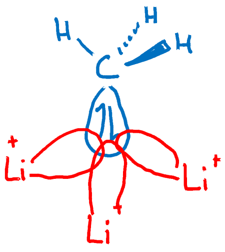
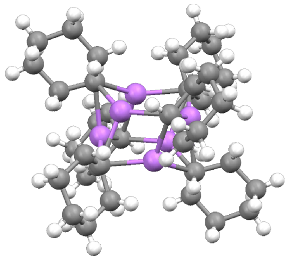
Multicenter bonding



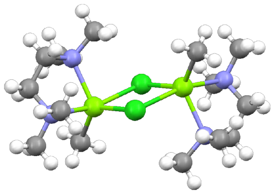
$[EtLi]_4$



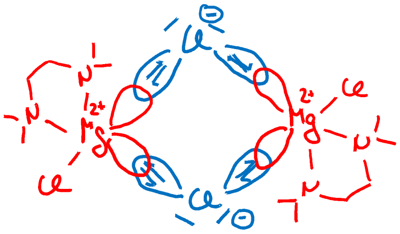
2e – 4c



$[CyLi]_6$



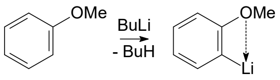
$[MeMgCl(tmeda)]_2$



2e – 2c

Synthesis

- **D**eprotonation (metallation of C-H bonds)
  - often assisted/directed by chelate effect



- **I**nsertion (direct synthesis)
  - only for electropositive metals (Li, Mg, ...)

R—X + M ⟶ R—M—X

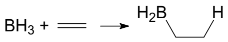
- **E**xchange (metal-halogen exchange)
  - mainly for M = Li, X = Br or I, R = alkyl, R' = aryl

RM + R'X ⟶ R'M + RX

- **T**ransmetallation
  - M more electropositive than M'
  - reason why organoLi and organoMg compounds are so popular

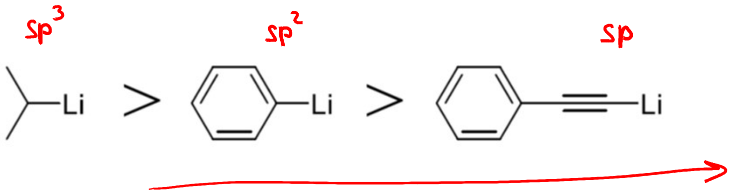
RM + M'X ⟶ RM' + MX

- **A**ddition of hydrides to olefins
  - mainly for B, Al

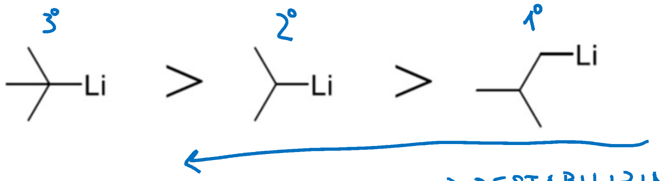


Going deeper: OrganoLi Compounds

Reactivity trends:



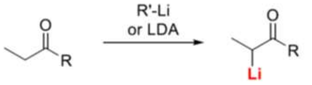
INCREASING S-CHARACTER
⇒ MORE STABLE CARBANIONS
⇒ LESS REACTIVE RLi



INCREASING INDUCTIVE EFFECT
OF THE ALKYL GROUPS
⇒ DESTABILIZING THE CARBANIONS
⇒ MORE REACTIVE RLi

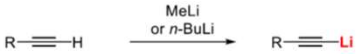
Preparation by deprotonation (of 'acidic' hydrogen atoms)

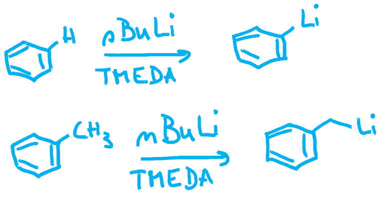
- Enolate formation



RLi - competition with the nucleophilic attack of the carbonyl

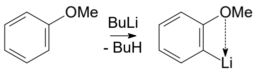
- Terminal alkyne

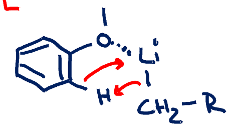




- Ortholithiation
  stabilization by coordination during formation/product

SELECTIVITY CONTROL

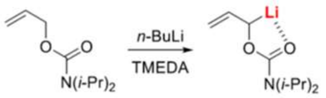




sBuLi > nBuLi

TMEDA → accelerates the rxn

- Alfa-position to EWG (atoms: O, N) + stabilization by coordination



Preparation by insertion (direct synthesis)

$$\begin{matrix}R\text{-}Cl\\ R\text{-}Br\\ R\text{-}I\end{matrix} \xrightarrow{Li_2} R\text{–}Li + \begin{matrix}LiCl\\ LiBr\\ LiI\end{matrix}$$

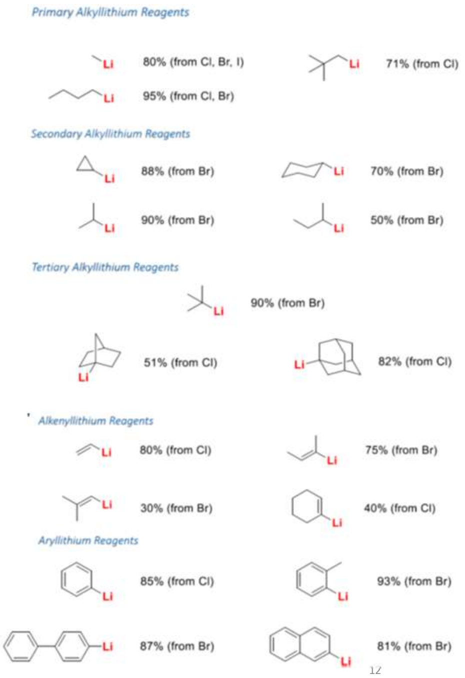
Solvent :
Et_2O, THF or PE

$$RBr \xrightarrow{Li} R^{\cdot} + Br^- \xrightarrow{Li} R\text{-}Li + Br^-$$

Li^+

Wurtz: $RLi + RX \longrightarrow R_2 + LiX$

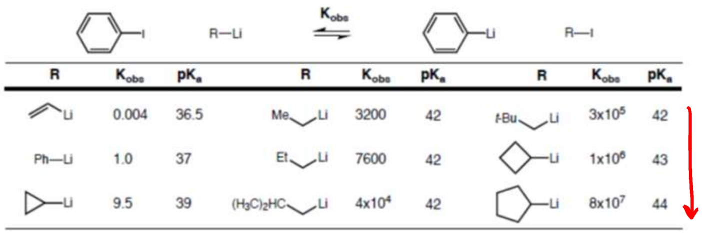
- Radical mechanism
- Reactivity: alkyl > aryl, Cl < Br < I
- Commercial synthesis: mostly from chlorides
- In laboratory: usually from *alkyl* bromides/iodides (easier to start)
- In apolar or weakly polar solvents
- Complication: Li reacts with N_2, do reaction under Ar !
- Side reaction: Wurtz coupling, especially for X = I



Preparation by metal-halogen exchange

1. Aryl fluorides do not exchange
2. Exchange rates decrease from I > Br >> Cl
3. Side reaction: Wurtz coupling

4. Exchange is a reversible process → equilibrium favoring the more stable RLi



R	K_{obs}	pK_a	R	K_{obs}	pK_a	R	K_{obs}	pK_a
⟋Li	0.004	36.5	Me⌄Li	3200	42	t-Bu⌄Li	3×10^5	42
Ph—Li	1.0	37	Et⌄Li	7600	42	◇—Li	1×10^6	43
▷—Li	9.5	39	$(H_3C)_2HC$⌄Li	4×10^4	42	⬠—Li	8×10^7	44

↓ DECREASING CARBANION STABILITY ⇒ MORE REACTIVE

MECHANISM

ATE: $\overset{\delta-}{Bu}\overset{\delta+}{Li} + \overset{\delta+}{Ar}-\overset{\delta-}{I} \rightleftharpoons [Bu-\overset{\ominus}{I}-Ar]\overset{\oplus}{Li} \rightleftharpoons BuI + ArLi$

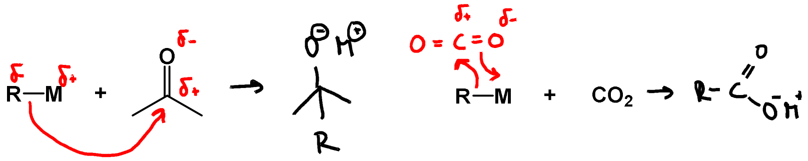
↖ IODIDE IS THE BEST BRIDGING ANION

RADICAL:

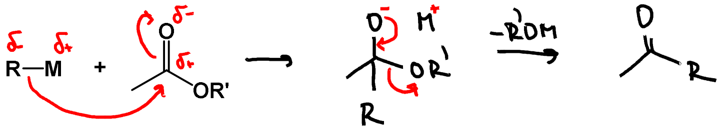
$RLi + ArBr \xrightarrow[\text{caged}]{E.T.} \left[RLi^{+\cdot} \mid Ar^{\cdot} \mid Br^{-} \right] \longrightarrow RLiAr^{+} + Br^{-} \longrightarrow ArLi + RBr$

Main-group organometallics use: Reactivity as a nucleophile

- Addition to polar C=X bonds
  - (C=O, C=N, C≡N)

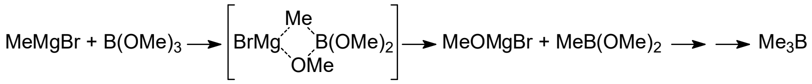


- Substitution at sp² carbon
  - (often via addition)



- Substitution at sp³ carbon does occur
  - but is far less easy and often has a multistep mechanism

- Transmetallation - substitution at other elements: often easy for polar M-X bonds (Si-Cl, B-OMe)

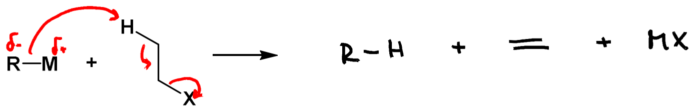


$MeMgBr + B(OMe)_3 \longrightarrow \left[BrMg\overset{Me}{\underset{OMe}{\diamond}}B(OMe)_2 \right] \longrightarrow MeOMgBr + MeB(OMe)_2 \longrightarrow \longrightarrow Me_3B$

Main-group organometallics use: Reactivity as a base

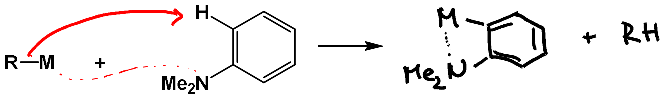
- More prominent in polar solvents (think of free R- acting as base)

→ Elimination



→ Metallation

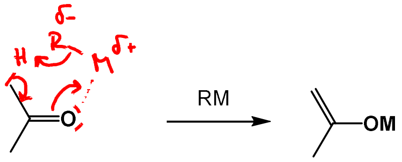
- chelate effect more important than inductive effect!



- only acidic C-H bonds (acetylenes, cyclopentadiene) react without "assistance" by coordinating groups

$R-C\equiv C-H + BuLi \rightarrow R-C\equiv C-Li + BuH$

- sometimes an unwanted side reaction of nucleophilic addition/substitution



The enolate is now "protected" from further nucleophilic attack

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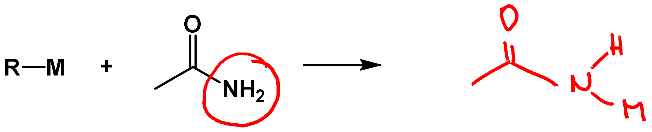
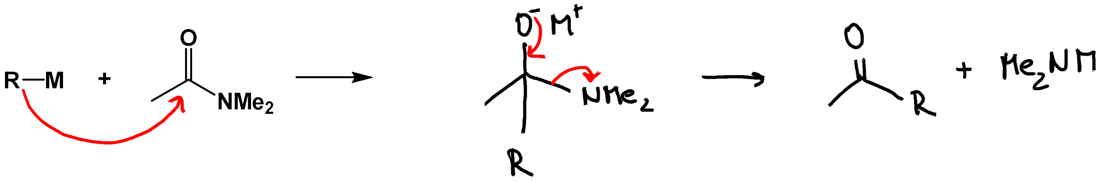
Main-group organometallics use: Reactivity as a base

- Reaction with acidic X-H bonds
  - also with amines, amides etc
  - generally very fast ("complete on mixing")
  - important issue when handling polar organometallics
  - deprotonating X-H bonds is kinetically much easier than C-H bonds

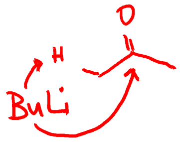
RM + R'OH → RH + R'OM

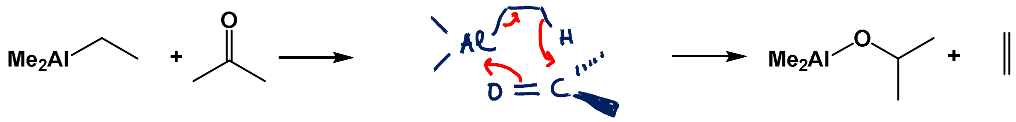




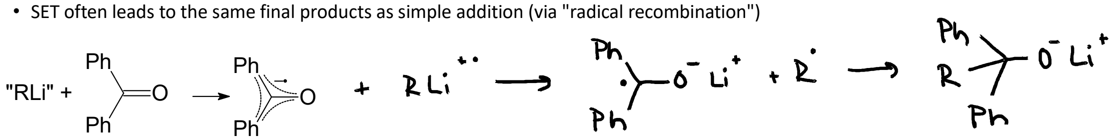
Main-group organometallics use: Reactivity as a Reductor

- β-hydrogen transfer
  - mainly for Al:
  - for more electropositive elements, deprotonation and nucleophilic attack are faster
  - for less electropositive elements, often no reaction



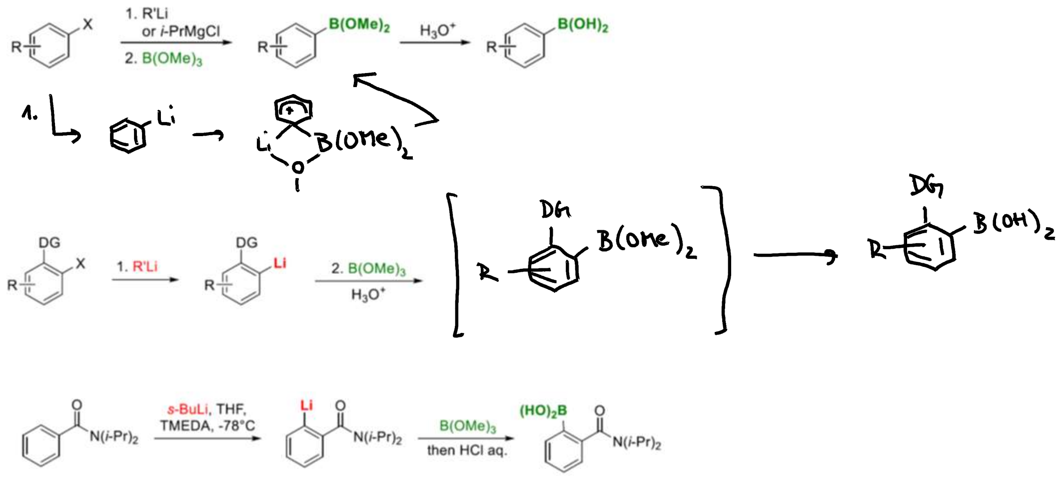


- Single-electron transfer (SET)
  - For electropositive elements:
    - Metals have low electron affinity
    - the M-C bonding orbital is high in energy
    - SET from the M-C bonding orbital to another molecule is easy
    - SET often leads to the same final products as simple addition (via "radical recombination")



Use - examples

Preparation of boronic acids:

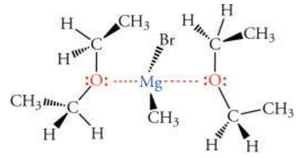


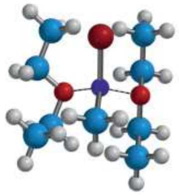
Grignard reagents RMgX

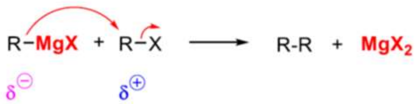
- Direct synthesis ("Grignard reaction"): Mg + RX ⟶ RMgX
- Mechanism is not simple!
  - almost certainly involves SET (Single Electron Transfer)

$$RX + Mg_s \longrightarrow RX^{\bullet -} + Mg_s^{\bullet +} \longrightarrow R^{\bullet} + XMg_s^{\bullet} \longrightarrow RMgX_{solv}$$

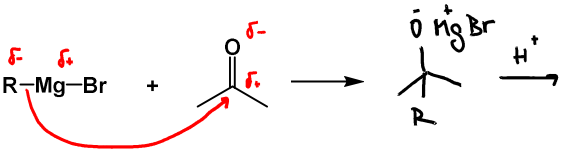
- Reactivity: I > Br > Cl >> F
- Selectivity: I gives largest amounts of side products
- In ethers:
  - Et_2O or THF
  - Also in ether/hydrocarbon mixtures
- Side reactions:
  - Radical rearrangements
  - Wurtz coupling, especially for allylic halides



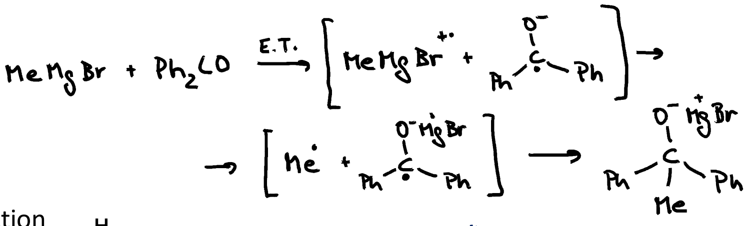




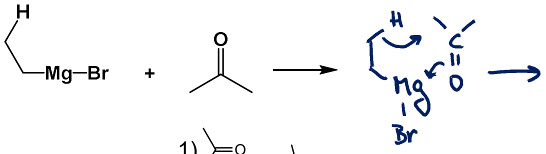
Grignard reagents RMgX



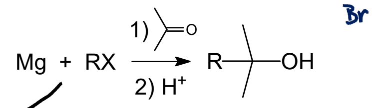
- Main application: addition to polar C=X bonds
  - C=O, C=N, C≡N
- Sometimes radical mechanism (especially for aromatic ketones):
  - same product expected, but possibly different side products

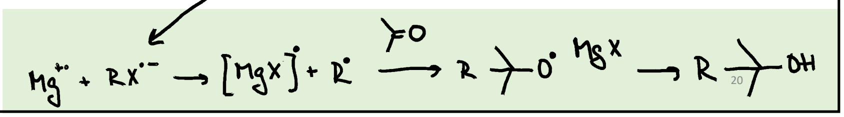


- Side reaction in C=X addition: reduction through β-H transfer
  - only for alkyls having a β-hydrogen...



- "Barbier reaction":
  - Selectivity differs from that of Grignard addition
  - Probably radical mechanism
  - Works even in water
  - Also with other metals
  - Zn, In, SmI_2





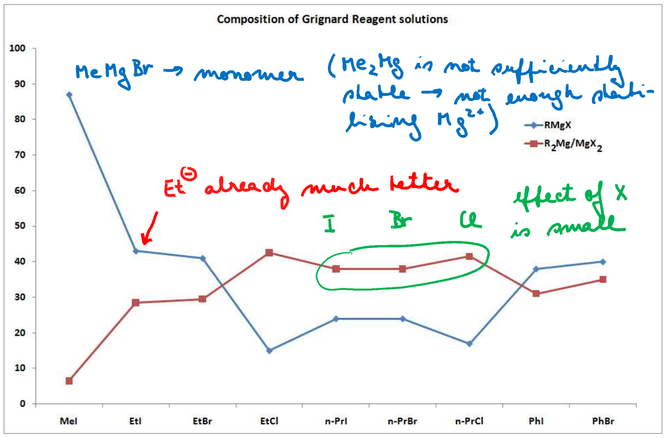
The Schlenk equilibrium

- Grignard reagents are usually mixtures of many compounds in dynamic equilibrium
- This is often written as the Schlenk equilibrium
- Crystal structures often do not represent species in solution (often oligomers, polymers)
- The equilibrium can be shifted through addition of ligands (dioxane):


$2\ R{-}MgX \rightleftharpoons R_2Mg + MgX_2$ via

$2\ RMgX + \text{dioxane} \longrightarrow R_2Mg + MgX_2(\text{dioxane})\downarrow$

Insoluble
coordination
polymer



MeMgBr → monomer (Me$_2$Mg is not sufficiently stable → not enough stabilising Mg^{2+})

Et$^{\ominus}$ already much better

I Br Cl

effect of X is small

What did you learn today about main-group organometallic compounds?

- **Structure**
  - need for stabilization of charge → electrons delocalized among 3 or 4 atoms → oligomeric structures
- Preparation
  - Deprotonation
  - Insertion (direct synthesis)
  - Exchange
  - Transmetallation
  - Addition
- Reactivity
  - as nucleophiles
  - as bases
  - as reducers
- Details exercised for organo Li and Mg compounds