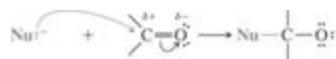


Chapter 12 –Part 2

Reaction of Carbonyl Compounds with Organometallic Compounds

Carbonyls react with nucleophiles



- ◆ The nucleophile adds to the $d+$ carbon
- ◆ The p electrons shift to the oxygen
- ◆ The carbon becomes sp^3 hybridized (tetrahedral!)
- ◆ Several chapters in Organic II
- ◆ For now, two nucleophiles that convert carbonyls to alcohols:
 - Hydride ions (H^-)
 - Carbanions (R^-) – second half of Ch. 12 (first topic Jan/08)

Organometallic Compounds = carbanions

- ◆ Carbon-metal bonds vary widely in character from mostly covalent to mostly ionic depending on the metal

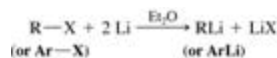


- ◆ The greater the ionic character of the bond, the more reactive the compound
 - Organopotassium compounds react explosively with water and burst into flame when exposed to air

Useful reagents - Organolithium and Organo-magnesium compounds

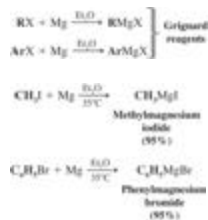
◆ Organolithium Compounds

- Organolithium compounds can be prepared by reaction of an alkyl halide with lithium metal in an ether solvent
 - ◆ The order of reactivity of halides is $R-I > R-Br > R-Cl$ ($R-F$ is seldom used)



Organo-magnesium Compounds = Grignard Reagents

- ◆ Grignard reagents are prepared by the reaction of organic halides with magnesium turnings
 - An ether solvent is used because it forms a complex with the Grignard reagent which stabilizes it



Reactions of Organolithium and Organo-magnesium Compounds

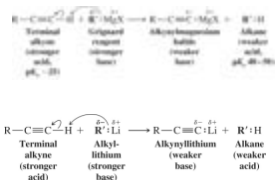
◆ With Compounds Containing Acidic Hydrogen Atoms

- Organolithium and Grignard reagents behave as if they were carbanions and they are therefore very strong bases
 - ◆ They react readily with hydrogen atoms attached to oxygen, nitrogen or sulfur, or any compound with acidic hydrogens



Reaction of RLi or RMgX to form alkyne salts

- Organolithium and Grignard reagents can be used to form alkynides by acid-base reactions
 - Alkynylmagnesium halides and alkynyllithium reagents are useful nucleophiles for C-C bond synthesis



Reactions of Grignard Reagents with Oxiranes (Epoxides)

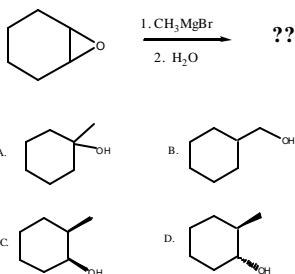
Grignard reagents are very powerful nucleophiles

React with the δ^+ carbons of oxiranes

- The reaction results in ring opening and formation of an alcohol
- Reaction occurs at the less-substituted ring carbon of the oxirane
- Net result is carbon-carbon bond forming two carbons away from the alcohol



Predict the product

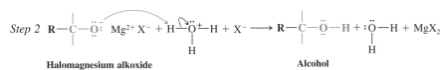
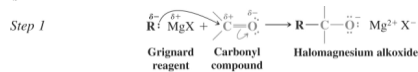


Reaction of Grignard Reagents with Carbonyl Compounds

Reaction of Grignard reagents with aldehydes and ketones yields a new carbon-carbon bond and an alcohol

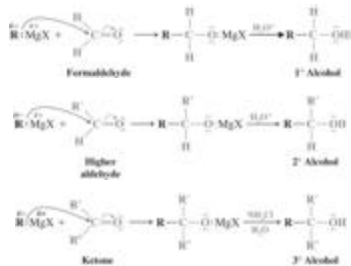


Mechanism



Alcohols from Grignard Reagents

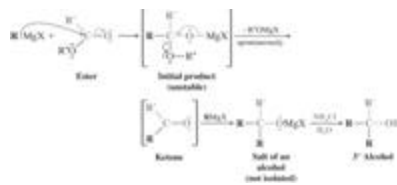
- Different classes of alcohols are formed depending on the starting carbonyl compound

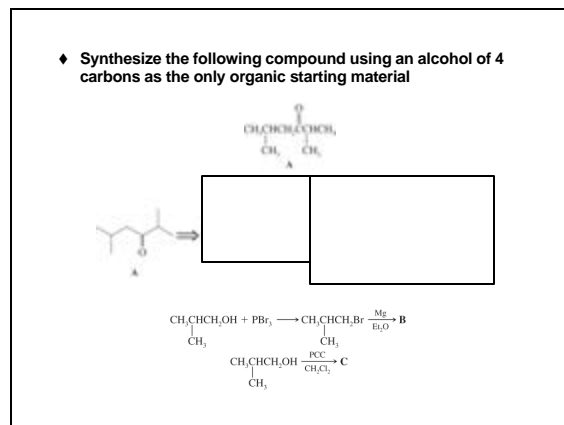
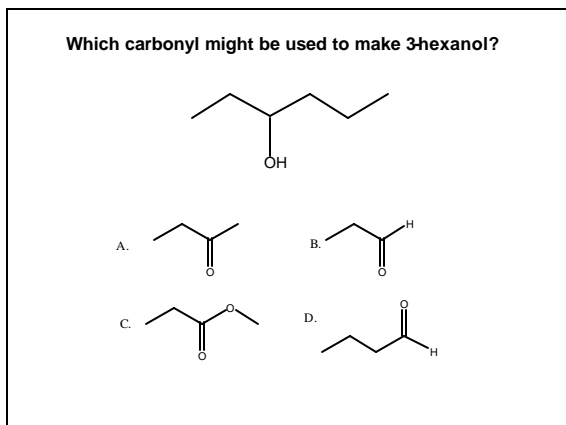
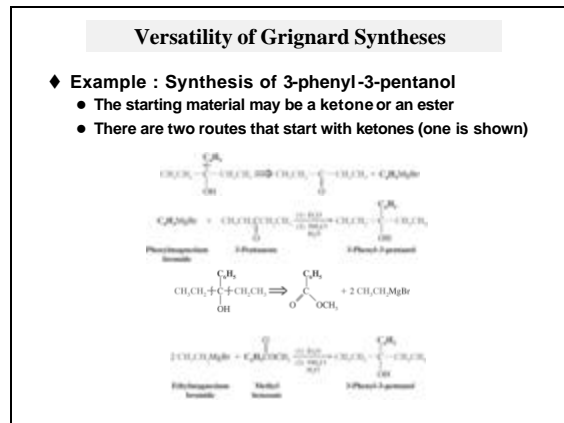
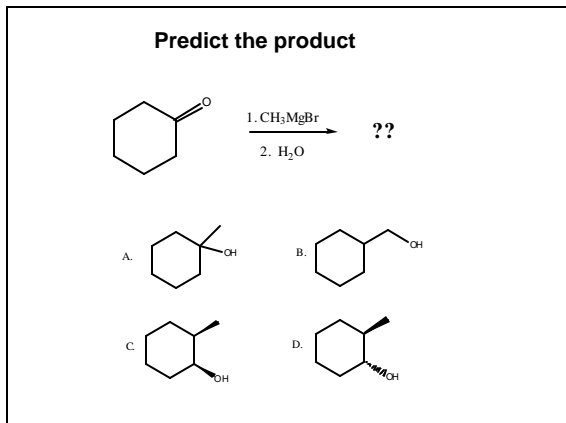
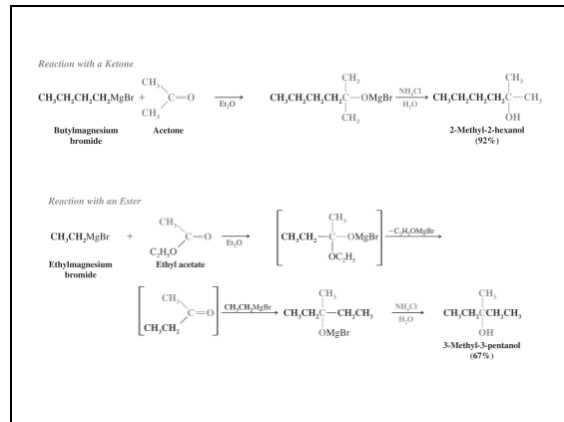
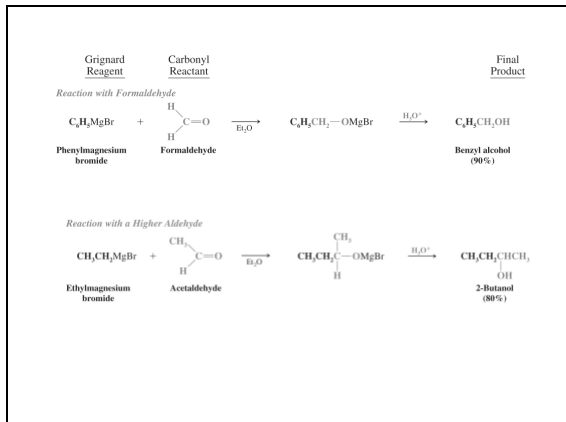


Esters react with two molar equivalents of a Grignard reagent to yield a tertiary alcohol

The ketone is formed by first equivalent of Grignard reagent reacts immediately with a second equivalent to produce the alcohol

- The final product contains two identical groups at the alcohol carbon that are both derived from the Grignard reagent



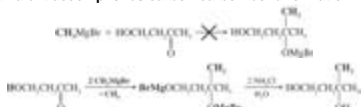


Limitations on the Use of Grignard Reagents

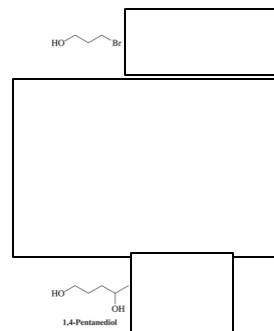
- Grignard reagents are powerful bases as well as nucleophiles
- Grignard reagents cannot be made from halides which contain acidic groups or electrophilic sites elsewhere in the molecule



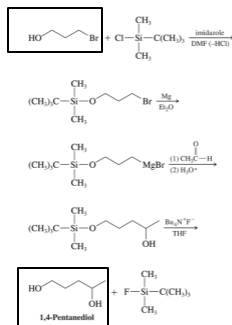
- Any acidic hydrogen atoms in the carbonyl substrate will react first, quenching the Grignard reagent
 - If Grignard is cheap, two equivalents of Grignard reagent could be used, so that after first equivalent is consumed, the second equivalent accomplishes carbon-carbon bond formation



Overcoming limitations using protecting groups



Silyl ether protecting group – from Ch. 11.11

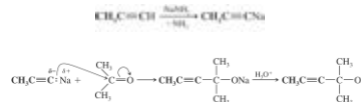


Other carbanions can also add to carbonyls

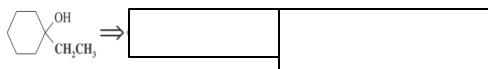
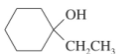
- Organolithium reagents react similarly to Grignard reagents
 - Organolithium reagents tend to be more reactive



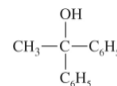
- Sodium alkynides react with carbonyl compounds such as aldehydes and ketones to form new carbon-carbon bonds



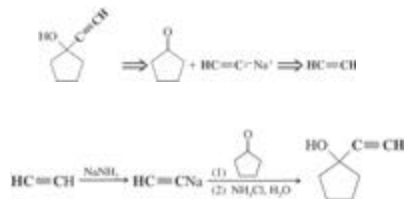
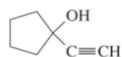
Synthesize the following compound using reagents of 6 carbons or less



Synthesize this alcohol, using reagents of 6 carbons or less

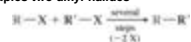


Synthesize this compound,
using reagents of 6 carbons or less



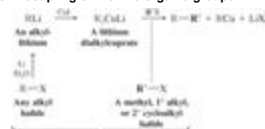
♦ Lithium Dialkylcuprates: The Corey-Posner, Whitesides-House Synthesis

→ This is an alternative formation of carbon-carbon bonds which, in effect, couples two alkyl halides



→ One of the halides is converted to a lithium dialkylcuprate by a two step sequence

→ Treatment of the lithium dialkylcuprate with the other halide results in coupling of the two organic groups



These are the organic starting materials. The R- and R'-groups need not be different.

