Ch 10 Alkyl Halides

Nomenclature Rules
−   The parent is the longest alkyl chain or ring.
−   The #1 C for a chain is at the end that is nearest to the first substituent.
−   The #1 C for a ring possesses the first substituent.
    Choose the lowest possible set of numbers for a ring.
−   If there is a choice of #1 C's, then choose by alphabetical precedence of the substituents.
−   Assign numbers and names for substituents, and treat halides just like alkyl groups.
−   List the substituents in alphabetical order.

Periodic Table Trends
−   Atoms get bigger going down the column (7A), so the size trend is: $F < Cl < Br < I$
−   As a result, bond lengths get bigger as well, so the bond length trend is: $F < Cl < Br < I$
−   But bond strengths and dipole moments get smaller, so those trends are: $I < Br < Cl < F$

Preparation
−   Electrophilic addition reactions of alkenes (and alkynes) with X_2 or HX.
−   Radical substitution reactions of alkanes with Br_2 or Cl_2.
−   Radical substitution reactions at the allylic carbons of alkenes, using NBS to supply Br_2.
−   Nucleophilic substitution reactions of 3° alcohols with HCl, HBr, or HI.
−   Nucleophilic substitution reactions of 1° and 2° alcohols with
    PBr_3 (phosphorus tribromide) or $SOCl_2$ (thionyl chloride).

Radical Halogenation of Alkanes
−   Radical halogenation is not often used in synthesis because products are usually mixtures.
−   Halides can add to different C's to make different monohalides.
−   Multiple halides can be added to form dihalides, trihalides, etc.
−   Reactivity order is $3^o > 2^o > 1^o$
    This is because the stability of the radical and the transition state are also $3^o > 2^o > 1^o$.
    The reasons are similar to those for carbocation stability, which has the same order.
−   For Cl, selectivity of $3^o > 2^o > 1^o$ (where 3° is preferred) is 5 : 3.5 : 1.
−   Br is even more selective ratio of 3° to 1° is ~1000 : 1.
    The higher selectivity occurs because the Br reaction is more dependent
    on the stability of the alkyl radical intermediate.

Allyl Radical Halogenation (of alkenes)
- Allyl position is the C next to a double bond.
- For instance, $H_2C=CHCH_2Br$ is allyl bromide.
- The allyl radical is even more stable than a 3° radical.
  The allyl C-H has lower bond dissociation energy than normal alkyl and vinyl C-H's.
- Typical Reaction:
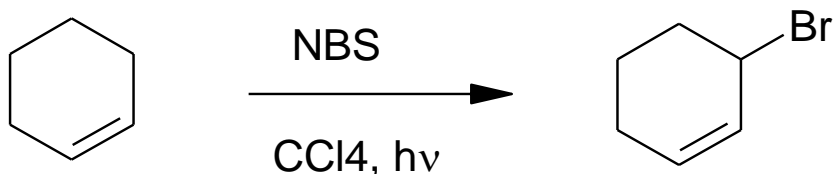
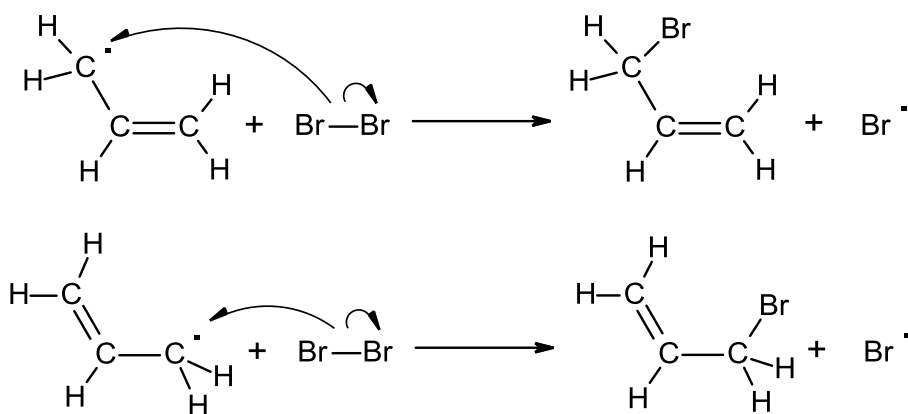- NBS is N-bromosuccinimide, which used to supply Br_2 in a slow and controlled fashion.
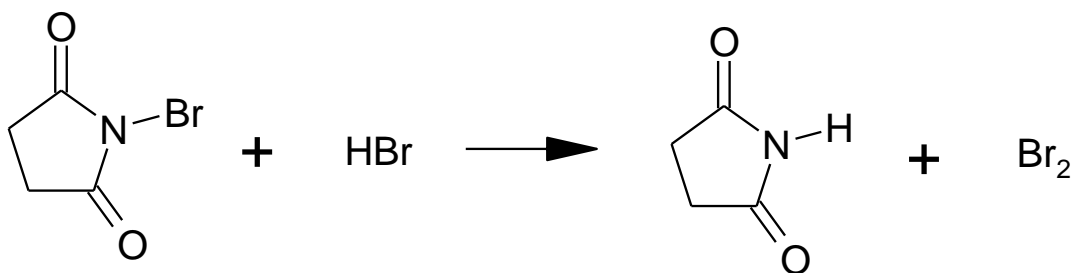
- Allyl radicals are especially stable due to resonance (• and double bond switch places).
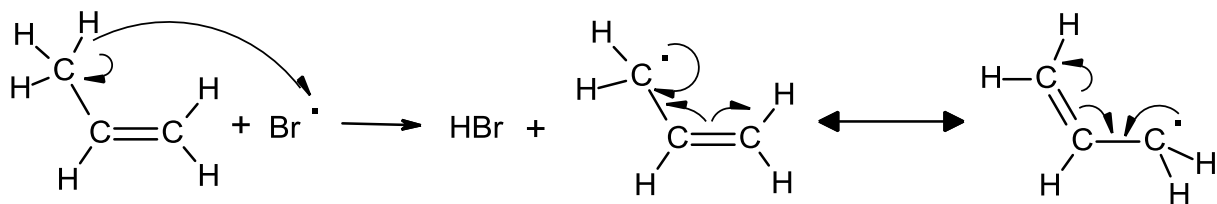
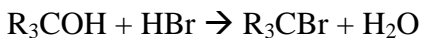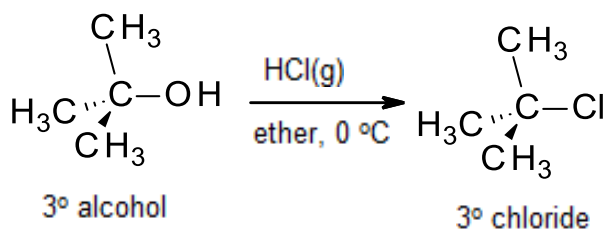All three C's are sp^2, and the unpaired e^{-1} is delocalized (spread out over Π network).
- There are two resonance forms.
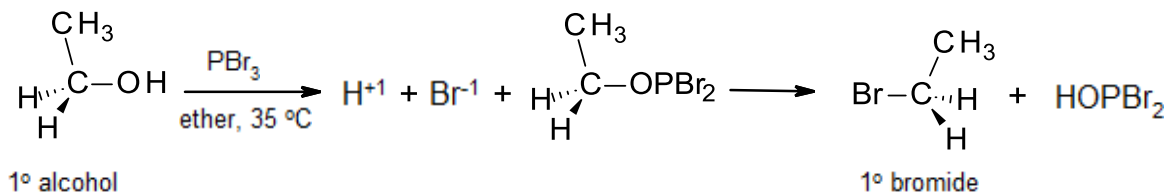 So, the Br• can add to either radical to form two different products.

Preparation of Alkyl Halides from Alcohols
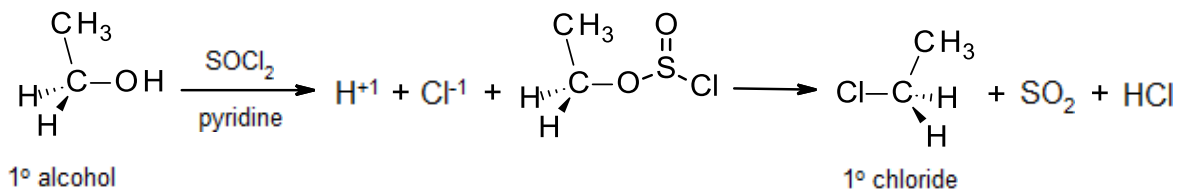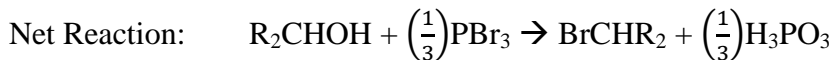-   3° alcohol and HX (acid) in ether (over ice at 0 °C) create 3° halide

3° alcohol   3° chloride
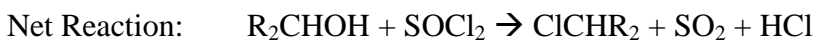
$$R_3COH + HBr \rightarrow R_3CBr + H_2O$$

-   2° and 1° alcohols need PBr_3 (in ether at 35 °C) or $SOCl_2$ (in pyridine).
    This causes fewer acid-catalyzed rearrangements and decompositions.

1° alcohol   1° bromide
                    This reaction works with both 1° and 2° alcohols.

Net Reaction: $R_2CHOH + \left(\frac{1}{3}\right)PBr_3 \rightarrow BrCHR_2 + \left(\frac{1}{3}\right)H_3PO_3$

1° alcohol   1° chloride
                    This reaction works with both 1° and 2° alcohols.

Net Reaction: $R_2CHOH + SOCl_2 \rightarrow ClCHR_2 + SO_2 + HCl$

Grignard Reagents (alkylmagnesium halides)
– Magnesium (Mg) can insert itself between C and a halogen (Cl, Br, or I) in an organic halide.
– The organic halide can be a 1°, 2°, or 3° alkyl, or alkenyl, or aromatic.
– For example, bromoethane reacts with Mg to form ethylmagnesium bromide.
– The reaction may be performed either in ether or in tetrahydrofuran (THF),
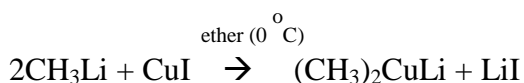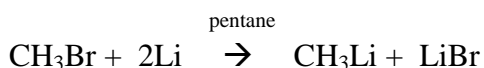   with no exposure to water or air.
– This is the general overall reaction:

$$R_2CHBr + Mg \xrightarrow{\text{ether}} R_2CHMgBr$$
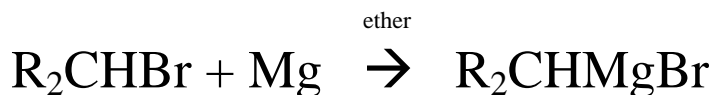
– Since Mg becomes a +2 ion and the Br gains a −1 charge,
   the C attached to the MgBr essentially has −1 charge.
   Therefore, this C^{-1} is a carbanion, with a lone pair.
   As a result, the C^{-1} is both nucleophilic and basic.
– The anionic C^{-1} will remove a proton (H^{+1}) from
   weak acids, such as water, alcohols, and amines.
   This converts the carbanion into an alkane.
   One consequence of this is that Grignard reagents must always be kept dry.
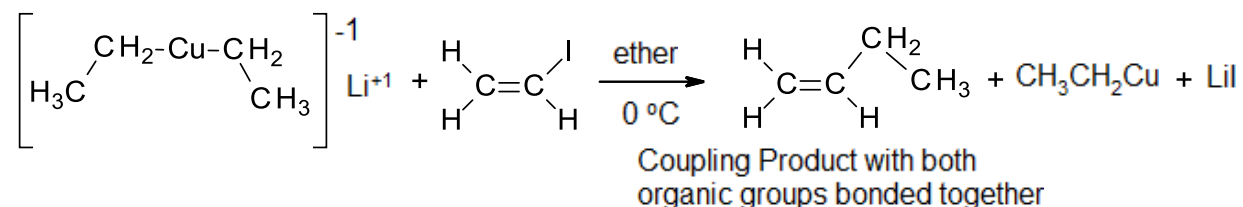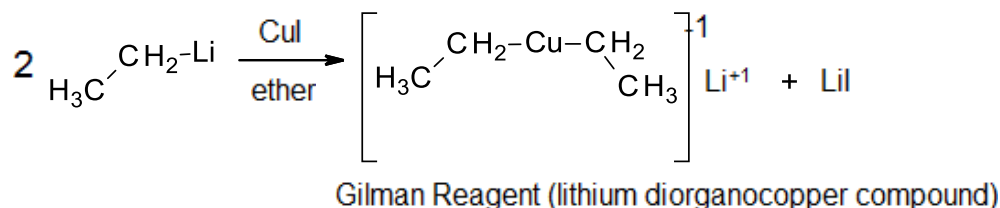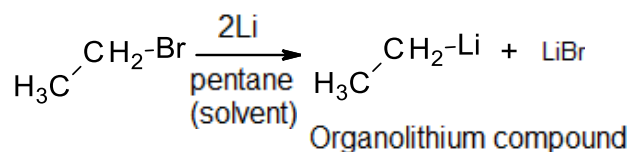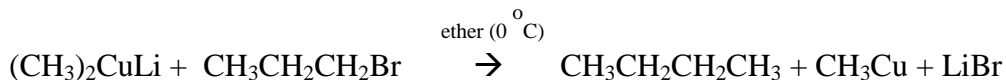
$$R_2CHMgBr + H_2O \rightarrow R_2CH_2 + MgBr(OH)$$

Gilman Reagents
- A Gilman reagent is a lithium diorganocopper compound, $(R)_2CuLi$.
- The compounds are ionic, with Li^{+1} and $(R\text{-}Cu\text{-}R)^{-1}$ ions.
- Two identical alkyl groups are each bonded to one Cu.
- Copper is +1 (that is, Cu^{+1}), so each of the two attached alkyl groups are effectively carbanions (R^{-1}).
- Gilman reagents are prepared by adding copper (I) iodide (CuI) to two equivalents of an alkyllithium (RLi) compound.
- The alkyllithium compound is generally prepared first by treating an alkyl halide (RX) with Li.

$$CH_3Br + 2Li \xrightarrow{\text{pentane}} CH_3Li + LiBr$$

$$2CH_3Li + CuI \xrightarrow{\text{ether } (0\,^\circ C)} (CH_3)_2CuLi + LiI$$

- When an alkyl halide (R′X) is added to a Gilman reagent in cold ether, an alkyl coupling reaction takes place. In this reaction, one of the two alkyl groups attached to copper will bond with the alkyl group from the alkyl halide to make one larger organic molecule (R′-R).

$$(CH_3)_2CuLi + CH_3CH_2CH_2Br \xrightarrow{\text{ether } (0\,^\circ C)} CH_3CH_2CH_2CH_3 + CH_3Cu + LiBr$$

Organolithium compound

Gilman Reagent (lithium diorganocopper compound)

Coupling Product with both organic groups bonded together

Oxidation and Reduction in Organic Chemistry

- In organic chemistry, **oxidation is loss** of e^{-1} density by C. This occurs two ways, either by **forming** a bond between **C** and an electronegative atom (**O, N, or halogen**), or by **breaking** a **C-H** bond.
- If C forms a bond with an electronegative atom, then the other atom will pull e^{-1} density towards itself and away from C. If a C-H bond is broken, the electropositive H is usually replaced with an atom that is more electronegative than H.
- Similarly, **reduction is gain** of e^{-1} density by C. This occurs two ways as well, either by **breaking** a bond between **C** and an electronegative atom (**O, N, or halogen**), or by **forming** a **C-H** bond.
- If a bond is broken between C and an electronegative atom (O, N, or halogen), then the other atom will no longer be pulling C's e^{-1} density towards itself. If a C-H bond is formed, then the electropositive H usually replaces an atom that is more electronegative than H.
- There are several levels of oxidation. A 1° alcohol (RCH_2OH) can be oxidized first to an aldehyde (RCHO). The aldehyde can then be oxidized to a carboxylic acid (RCO_2H). Finally, the carboxylic acid can be fully oxidized to create CO_2.